ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 150 mg solution for injection in pre-filled pen
Skyrizi 150 mg solution for injection in pre-filled syringe
Skyrizi 75 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Skyrizi 150 mg solution for injection in pre-filled pen

Each pre-filled pen contains 150 mg risankizumab in 1 mL solution.

Skyrizi 150 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 150 mg risankizumab in 1 mL solution.

Skyrizi 75 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 75 mg risankizumab in 0.83 mL solution.

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody produced in Chinese Hamster Ovary cells using recombinant DNA technology.

Excipients with known effect

150 mg solution for injection only

This medicinal product contains 0.2 mg of polysorbate 20 in each 150 mg dose.

75 mg solution for injection only

This medicinal product contains 68.0 mg sorbitol per 150 mg dose.

This medicinal product contains 0.34 mg of polysorbate 20 in each 150 mg dose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

Skyrizi 150 mg solution for injection in pre-filled pen and in pre-filled syringe

The solution is colourless to yellow and clear to slightly opalescent.

Skyrizi 75 mg solution for injection in pre-filled syringe

The solution is colourless to slightly yellow and clear to slightly opalescent.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Plaque psoriasis

Skyrizi is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Psoriatic arthritis

Skyrizi, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adults who have had an inadequate response or who have been intolerant to one or more disease-modifying antirheumatic drugs (DMARDs).

4.2 Posology and method of administration

This medicinal product is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Skyrizi is indicated.

Posology

The recommended dose is 150 mg administered as a subcutaneous injection at week 0, week 4, and every 12 weeks thereafter (either as two 75 mg pre-filled syringe injections or one 150 mg pre-filled pen or pre-filled syringe injection).

Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment. Some plaque psoriasis patients with initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Missed dose

If a dose is missed, the dose should be administered as soon as possible. Thereafter, dosing should be resumed at the regular scheduled time.

Special populations

Elderly

No dose adjustment is required (see section 5.2).
There is limited information in subjects aged ≥ 65 years.

Renal or hepatic impairment

No specific studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of risankizumab. These conditions are generally not expected to have any significant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary (see section 5.2).

Paediatric population

The safety and efficacy of risankizumab in children and adolescents aged 5 to less than 18 years have not been established. No data are available.

There is no relevant use of risankizumab in children aged below 6 years for the indication of moderate to severe plaque psoriasis or in children aged below 5 years for the indication of psoriatic arthritis.

Overweight patients

No dose adjustment is required (see section 5.2).

Method of administration

Skyrizi is administered by subcutaneous injection.

The injection should be administered in the thigh or abdomen. Patients should not inject into areas where the skin is tender, bruised, erythematous, indurated, or affected by psoriasis.

Patients may self-inject Skyrizi after training in subcutaneous injection technique. Patients should be instructed to read the 'Instructions for use' provided in the package leaflet before administration.

Administration of Skyrizi in the upper, outer arm may only be performed by a healthcare professional or caregiver.

Skyrizi 75 mg solution for injection in pre-filled syringe

Two pre-filled syringes should be injected for the full 150 mg dose. The two injections should be administered at different anatomic locations.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important active infections (e.g. active tuberculosis, see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Risankizumab may increase the risk of infection.

In patients with a chronic infection, a history of recurrent infection, or known risk factors for infection, risankizumab should be used with caution. Treatment with risankizumab should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Patients treated with risankizumab should be instructed to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops such an infection or is not responding to standard therapy for the infection, the patient should be closely monitored and risankizumab should not be administered until the infection resolves.

Tuberculosis

Prior to initiating treatment with risankizumab, patients should be evaluated for tuberculosis (TB) infection. Patients receiving risankizumab should be monitored for signs and symptoms of active TB. Anti-TB therapy should be considered prior to initiating risankizumab in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Immunisations

Prior to initiating therapy with risankizumab, completion of all appropriate immunisations should be considered according to current immunisation guidelines. If a patient has received live vaccination (viral or bacterial), it is recommended to wait at least 4 weeks prior to starting treatment with risankizumab. Patients treated with risankizumab should not receive live vaccines during treatment and for at least 21 weeks after treatment (see section 5.2).

Hypersensitivity

Serious hypersensitivity reactions, including anaphylaxis, have been reported with use of risankizumab (see section 4.8). If a serious hypersensitivity reaction occurs, administration of risankizumab should be discontinued immediately and appropriate therapy initiated.

Excipients with known effect

Skyrizi 150 mg solution for injection in pre-filled pen or pre-filled syringe

Polysorbate

This medicinal product contains 0.2 mg of polysorbate 20 in each 150 mg dose. Polysorbates may cause allergic reactions.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per pre-filled pen or pre-filled syringe, that is to say, essentially 'sodium free'.

Skyrizi 75 mg solution for injection in pre-filled syringe

Polysorbate

This medicinal product contains 0.34 mg of polysorbate 20 in each 150 mg dose. Polysorbates may cause allergic reactions.

Sorbitol

This medicinal product contains 68.0 mg sorbitol per 150 mg dose.
The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per 150 mg dose, that is to say, essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

Risankizumab is not expected to undergo metabolism by hepatic enzymes or renal elimination. Interactions between risankizumab and inhibitors, inducers, or substrates of medicinal product metabolising enzymes are not expected, and no dose adjustment is needed (see section 5.2).

Concomitant immunosuppressive therapy or phototherapy

The safety and efficacy of risankizumab in combination with immunosuppressants, including biologics or phototherapy, have not been evaluated.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 21 weeks after treatment.

Pregnancy

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of risankizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of risankizumab during pregnancy.

Breast-feeding

It is unknown whether risankizumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which decreases to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period. A decision should be made whether to discontinue/abstain from risankizumab therapy, taking into account the benefit of breast-feeding to the child and the benefit of risankizumab therapy to the woman.

Fertility

The effect of risankizumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Risankizumab has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions were upper respiratory infections (13.0% in psoriasis).

Tabulated list of adverse reactions

Adverse reactions for risankizumab from clinical studies (Table 1) are listed by MedDRA system organ class and are based on the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: List of adverse reactions

System Organ Class	Frequency	Adverse reactions
Infections and infestations	Very common	Upper respiratory infections[a]
	Common	Tinea infections[b]
	Uncommon	Folliculitis
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache[c]
Skin and subcutaneous tissue disorders	Common	Pruritus Rash Eczema
	Uncommon	Urticaria
General disorders and administration site conditions	Common	Fatigue[d] Injection site reactions[e]

[a] Includes: respiratory tract infection (viral, bacterial or unspecified), sinusitis (including acute), rhinitis, nasopharyngitis, pharyngitis (including viral), tonsillitis, laryngitis, tracheitis
[b] Includes: tinea pedis, tinea cruris, body tinea, tinea versicolor, tinea manuum, onychomycosis, fungal skin infection
[c] Includes: headache, tension headache, sinus headache
[d] Includes: fatigue, asthenia
[e] Includes: injection site bruising, erythema, haematoma, haemorrhage, irritation, pain, pruritus, reaction, swelling, induration, rash

Description of selected adverse reactions

Infections

The rate of infections was 75.5 events per 100 subject-years from the psoriasis clinical studies and 43.0 events per 100 subject-years from the psoriatic arthritis clinical studies, including long-term exposure to risankizumab. The majority of cases were non-serious and mild to moderate in severity and did not lead to discontinuation of risankizumab. The rate of serious infections was 1.7 events per 100 subject-years from the psoriasis studies and 2.6 events per 100 subject-years from the psoriatic arthritis studies (see section 4.4).

Immunogenicity

For subjects treated with risankizumab at the recommended clinical dose for up to 52 weeks in psoriasis clinical trials, treatment-emergent anti-drug antibodies and neutralising antibodies were detected in 24% (263/1 079) and 14% (150/1 079) of evaluated subjects, respectively. For subjects exposed to long term treatment of risankizumab in the extension study, the immunogenicity profile observed up to 204 weeks of treatment was consistent compared to the first 52 weeks of treatment.

For most subjects with psoriasis, antibodies to risankizumab including neutralising antibodies were not associated with changes in clinical response or safety. Among the few subjects (approximately 1%; 7/1 000 at week 16 and 6/598 at week 52) with high antibody titres (>128), clinical response appeared to be reduced. The incidence of injection site reactions is numerically higher in the anti-drug antibody-positive groups compared with anti-drug antibody-negative groups over short-term (16 weeks: 2.7% vs 1.3%) and longer-term treatment (52 weeks: 5.0% vs 3.3%). The injection site reactions were all mild to moderate in severity, none were serious, and none led to discontinuation of risankizumab.

For subjects treated with risankizumab at the recommended clinical dose for up to 28 weeks in psoriatic arthritis clinical trials, treatment-emergent anti-drug antibodies and neutralizing antibodies

were detected in 12.1% (79/652) and 0% (0/652) of evaluated subjects, respectively. Antibodies to risankizumab were not associated with changes in clinical response or safety for psoriatic arthritis.

Psoriatic arthritis

Overall, the safety profile observed in patients with psoriatic arthritis treated with risankizumab was consistent with the safety profile observed in patients with plaque psoriasis.

Elderly

There is limited safety information in subjects aged ≥65 years.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC18

Mechanism of action

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds with high affinity to the p19 subunit of human interleukin 23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor complex. IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, risankizumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokines.

Pharmacodynamic effects

In a study of subjects with psoriasis, expression of genes associated with the IL-23/IL-17 axis was decreased in the skin after single doses of risankizumab. Reductions in epidermal thickness, infiltration of inflammatory cells, and expression of psoriatic disease markers were also observed in psoriatic lesions.

In a study of subjects with psoriatic arthritis, statistically significant and clinically meaningful reduction from baseline was observed at week 24 in IL-23 and IL-17-associated biomarkers, including serum IL-17A, IL-17F, and IL-22 following treatment with risankizumab 150 mg subcutaneously at week 0, week 4, and every 12 weeks thereafter.

Clinical efficacy and safety

Plaque Psoriasis

The efficacy and safety of risankizumab was assessed in 2 109 subjects with moderate to severe plaque psoriasis in four multicentre, randomised, double-blind studies (ULTIMMA-1, ULTIMMA-2,

IMMHANCE, and IMMVENT). Enrolled subjects were 18 years of age and older with plaque psoriasis who had a body surface area (BSA) involvement of ≥10%, a static Physician Global Assessment (sPGA) score of ≥3 in the overall assessment (plaque thickness/induration, erythema, and scaling) of psoriasis on a severity scale of 0 to 4, a Psoriasis Area and Severity Index (PASI) score ≥12, and who were candidates for systemic therapy or phototherapy.

Overall, subjects had a median baseline PASI score of 17.8, a median BSA of 20.0%, and a median baseline DLQI score of 13.0. Baseline sPGA score was severe in 19.3% of subjects and moderate in 80.7% of subjects. A total of 9.8% of study subjects had a history of diagnosed psoriatic arthritis.

Across all studies, 30.9% of subjects were naïve to any systemic therapy (including non-biologic and biologic), 38.1% had received prior phototherapy or photochemotherapy, 48.3% had received prior non-biologic systemic therapy, 42.1% had received prior biologic therapy, and 23.7% had received at least one anti-TNF alpha agent for the treatment of psoriasis. Patients who completed these studies and other Phase 2/3 studies had the opportunity to enrol in an open-label extension study, LIMMITLESS.

ULTIMMA-1 and ULTIMMA-2

ULTIMMA-1 and ULTIMMA-2 enrolled 997 subjects (598 randomised to risankizumab 150 mg, 199 to ustekinumab 45 mg or 90 mg [according to baseline weight], and 200 to placebo). Subjects received treatment at week 0, week 4, and every 12 weeks thereafter. The two co-primary endpoints in ULTIMMA-1 and ULTIMMA-2 were the proportion of subjects who achieved 1) PASI 90 response and 2) sPGA score of clear or almost clear (sPGA 0 or 1) at week 16 versus placebo. The results for the co-primary and other endpoints are presented in Table 2 and Figure 1.

Table 2: Efficacy and quality of life results in adults with plaque psoriasis in ULTIMMA-1 and ULTIMMA-2

	ULTIMMA-1			ULTIMMA-2		
	Risankizumab (N=304) n (%)	**Ustekinumab (N=100) n (%)**	**Placebo (N=102) n (%)**	**Risankizumab (N=294) n (%)**	**Ustekinumab (N=99) n (%)**	**Placebo (N=98) n (%)**
sPGA of clear or almost clear (0 or 1)						
Week 16[a]	267 (87.8)	63 (63.0)	8 (7.8)	246 (83.7)	61 (61.6)	5 (5.1)
Week 52	262 (86.2)	54 (54.0)	--	245 (83.3)	54 (54.5)	--
sPGA of clear (0)						
Week 16	112 (36.8)	14 (14.0)	2 (2.0)	150 (51.0)	25 (25.3)	3 (3.1)
Week 52	175 (57.6)	21 (21.0)	--	175 (59.5)	30 (30.3)	--
PASI 75						
Week 12	264 (86.8)	70 (70.0)	10 (9.8)	261 (88.8)	69 (69.7)	8 (8.2)
Week 52	279 (91.8)	70 (70.0)	--	269 (91.5)	76 (76.8)	--
PASI 90						
Week 16[a]	229 (75.3)	42 (42.0)	5 (4.9)	220 (74.8)	47 (47.5)	2 (2.0)
Week 52	249 (81.9)	44 (44.0)	--	237 (80.6)	50 (50.5)	--
PASI 100						
Week 16	109 (35.9)	12 (12.0)	0 (0.0)	149 (50.7)	24 (24.2)	2 (2.0)
Week 52	171 (56.3)	21 (21.0)	--	175 (59.5)	30 (30.3)	--
DLQI 0 or 1[b]						
Week 16	200 (65.8)	43 (43.0)	8 (7.8)	196 (66.7)	46 (46.5)	4 (4.1)
Week 52	229 (75.3)	47 (47.0)	--	208 (70.7)	44 (44.4)	--
PSS 0 (symptom-free)[c]						
Week 16	89 (29.3)	15 (15.0)	2 (2.0)	92 (31.3)	15 (15.2)	0 (0.0)
Week 52	173 (56.9)	30 (30.0)	--	160 (54.4)	30 (30.3)	--

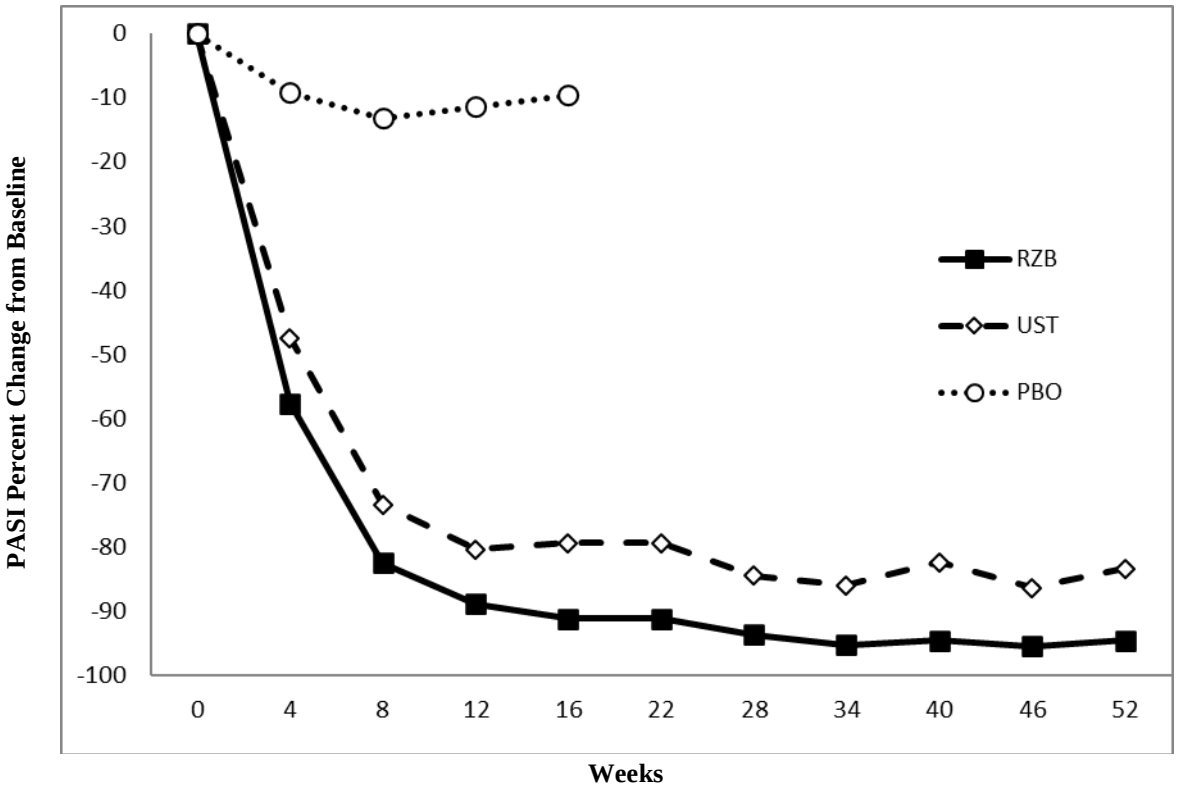
All comparisons of risankizumab versus ustekinumab and placebo achieved $p<0.001$ except for PASI 75 at week 52 in ULTIMMA-2 where $p=0.001$

[a] Co-primary endpoints versus placebo

[b] No impact on health-related quality of life

[c] Psoriasis Symptom Scale (PSS) of 0 means no symptoms of pain, itching, redness, and burning during the last 24 hours

Figure 1: Time course of mean percent change from baseline of PASI in ULTIMMA-1 and ULTIMMA-2



RZB = risankizumab
UST = ustekinumab
PBO = placebo
$p<0.001$ at each time point

Examination of age, gender, race, body weight ≤130 kg, baseline PASI score, concurrent psoriatic arthritis, previous non-biologic systemic treatment, previous biologic treatment, and previous failure of a biologic did not identify differences in response to risankizumab among these subgroups.

Improvements were observed in psoriasis involving the scalp, the nails, and the palms and soles at week 16 and week 52 in subjects treated with risankizumab.

Table 3: Mean changes from baseline in NAPSI, PPASI, and PSSI

	ULTIMMA-1		ULTIMMA-2		IMMHANCE	
	Risankizumab	**Placebo**	**Risankizumab**	**Placebo**	**Risankizumab**	**Placebo**
NAPSI: Change at Week 16 (SE)	N=178; -9.0 (1.17)	N=56; 2.1 (1.86) ***	N=177; -7.5 (1.03)	N=49; 3.0 (1.76) ***	N=235; -7.5 (0.89)	N=58; 2.5 (1.70) ***
PPASI: Change at Week 16 (SE)	N=95; -5.93 (0.324)	N=34; -3.17 (0.445) ***	N=86; -7.24 (0.558)	N=23; -3.74 (1.025) **	N=113; -7.39 (0.654)	N=26; -0.27 (1.339) ***
PSSI: Change at Week 16 (SE)	N=267; -17.6 (0.47)	N=92; -2.9 (0.69) ***	N=252; -18.4 (0.52)	N=83; -4.6 (0.82) ***	N=357; -20.1 (0.40)	N=88; -5.5 (0.77) ***
NAPSI: Change at Week 52 (SE)	N=178; -15.7 (0.94)	-	N=183; -16.7 (0.85)	-	-	-
PPASI: Change at Week 52 (SE)	N=95; -6.16 (0.296)	-	N=89; -8.35 (0.274)	-	-	-
PSSI: Change at Week 52 (SE)	N=269; -17.9 (0.34)	-	N=259; -18.8 (0.24)	-	-	-

Nail Psoriasis Severity Index (NAPSI), Palmoplantar Psoriasis Severity Index (PPASI), Psoriasis Scalp Severity Index (PSSI), and Standard Error (SE)
** P < 0.01 comparing to risankizumab
*** P < 0.001 comparing to risankizumab

Anxiety and depression, as measured by the Hospital Anxiety and Depression Scale (HADS), improved in the risankizumab group at week 16 compared with the placebo group.

Maintenance of response

In an integrated analysis of subjects receiving risankizumab in ULTIMMA-1 and ULTIMMA-2 for PASI 100 responders at week 16, 79.8% (206/258) of the subjects who continued on risankizumab maintained the response at week 52. For PASI 90 responders at week 16, 88.4% (398/450) of subjects maintained the response at week 52.

Of the patients who received risankizumab in ULTIMMA-1 and ULTIMMA-2, 525 continued to receive risankizumab every 12 weeks in LIMMITLESS. Of these, 376 (71.6%) completed an additional 252 weeks of open-label treatment. Among subjects remaining in the study, improvements achieved with risankizumab in rates of PASI 90 and sPGA of clear or almost clear at week 52 were maintained through week 304.

Of the patients who received ustekinumab in ULTIMMA-1 and ULTIMMA-2, 172 received risankizumab every 12 weeks in LIMMITLESS. Of these, 116 (67.4%) completed the study, including 252 weeks of open-label risankizumab treatment and end of study follow-up. Among subjects remaining in the study, rates of PASI 90 and sPGA response of clear or almost clear increased from week 52 through week 76 and were then maintained through week 304.

Figures 2 and 3 show the response rates for PASI 90 and sPGA of clear or almost clear, respectively, in subjects who completed 252 weeks of open-label treatment in LIMMITLESS.

Figure 2: Percent of subjects who achieved a PASI 90 response (OC) in LIMMITLESS

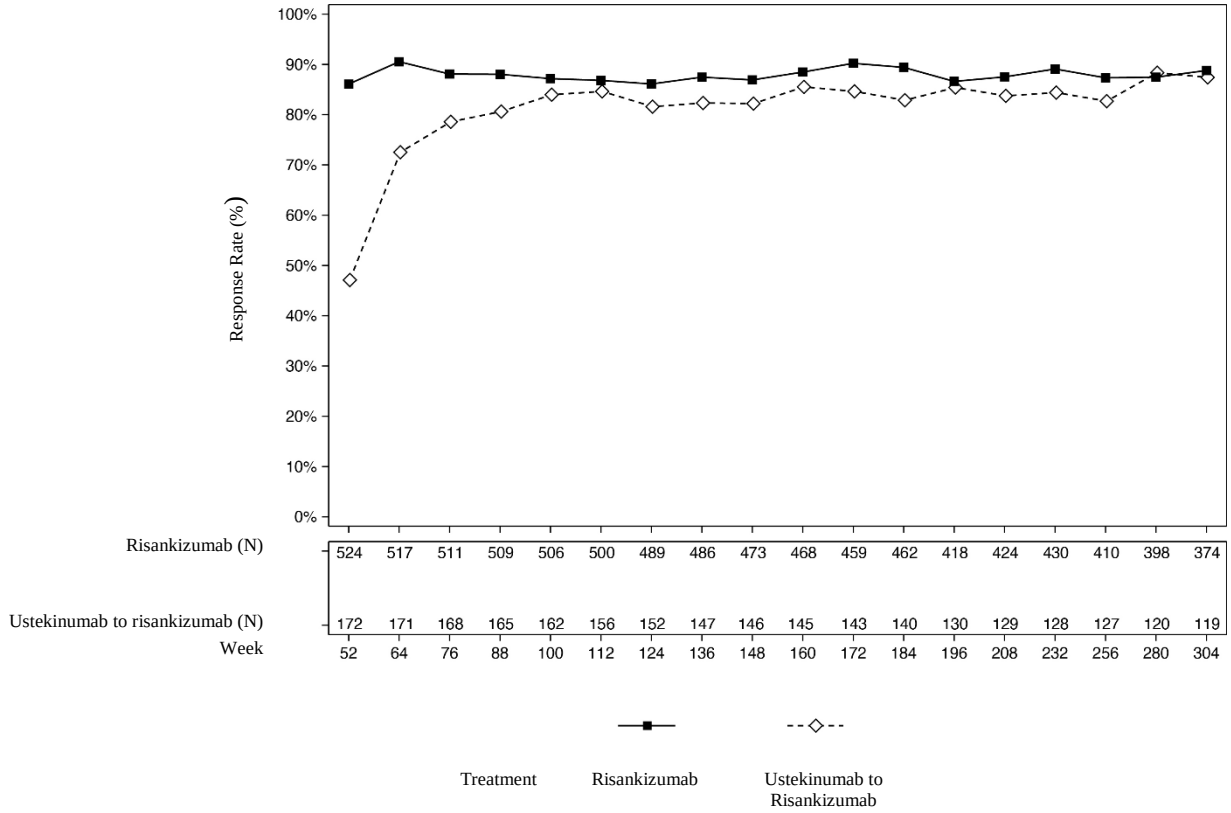
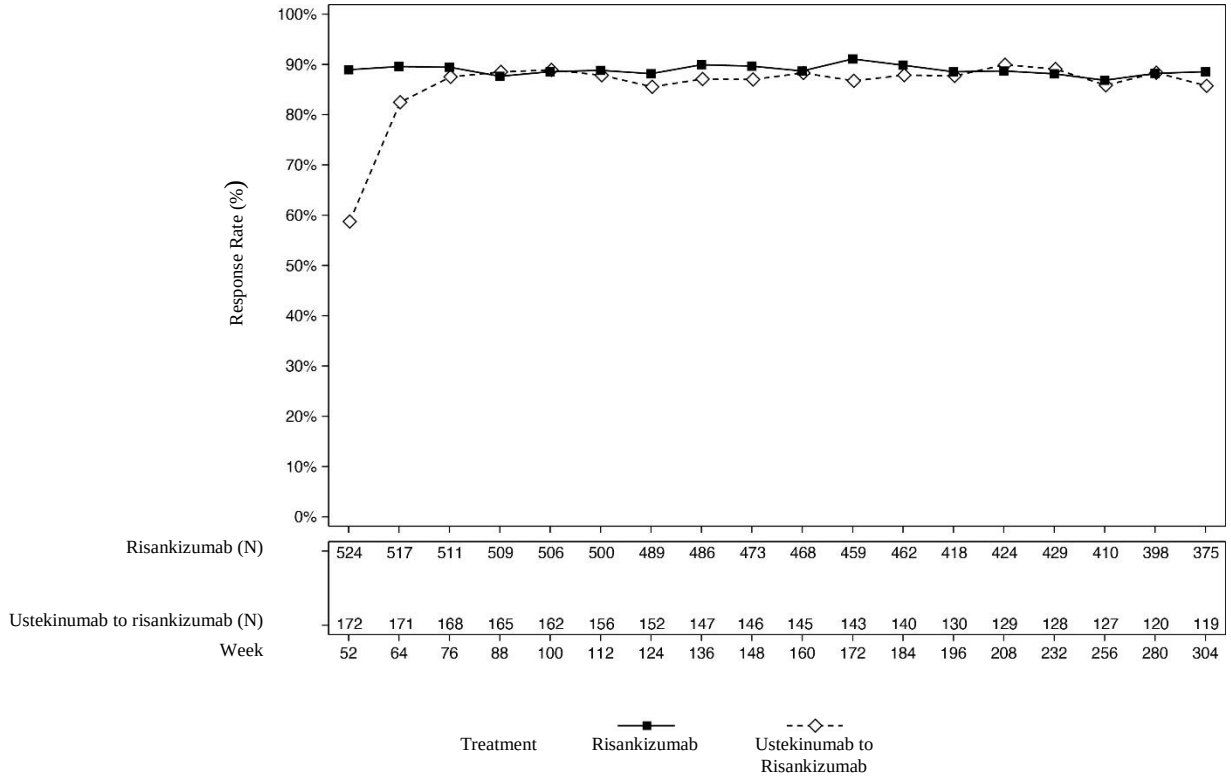


Figure 3: Percent of subjects who achieved an sPGA clear or almost clear response by visit (OC) in LIMMITLESS



Improvements in Dermatology Life Quality Index (DLQI 0 or 1) were maintained in patients receiving continuous risankizumab treatment through week 304 in the open label extension study LIMMITLESS.

The safety profile of risankizumab with more than 5 years of exposure was consistent with the profile observed up to 16 weeks.

IMMHANCE

IMMHANCE enrolled 507 subjects (407 randomised to risankizumab 150 mg and 100 to placebo). Subjects received treatment at week 0, week 4, and every 12 weeks thereafter. Subjects who were originally on risankizumab and had a sPGA of clear or almost clear at week 28 were re-randomised to continue risankizumab every 12 weeks through week 88 (with follow-up 16 weeks after last risankizumab dose) or have treatment withdrawn.

At week 16, risankizumab was superior to placebo on the co-primary endpoints of sPGA of clear or almost clear (83.5% risankizumab vs 7.0% placebo) and PASI 90 (73.2% risankizumab vs 2.0% placebo).

Of the 31 subjects from the IMMHANCE study with latent tuberculosis (TB) who did not receive prophylaxis during the study, none developed active TB during the mean follow-up of 55 weeks on risankizumab.

Among subjects with sPGA of clear or almost clear at week 28 in IMMHANCE, 81.1% (90/111) of subjects re-randomised to continued treatment with risankizumab maintained this response at week 104 compared with 7.1% (16/225) who were re-randomised to withdrawal from risankizumab. Of these subjects, 63.1% (70/111) of subjects re-randomised to continued treatment with risankizumab achieved a sPGA clear response at week 104 compared with 2.2% (5/225) who were re-randomised to withdrawal from risankizumab.

Among subjects who achieved sPGA of clear or almost clear at week 28 and relapsed to sPGA of moderate or severe following withdrawal from risankizumab, 83.7% (128/153) regained sPGA of clear or almost clear after 16 weeks of retreatment. Loss of sPGA of clear or almost clear was observed as early as 12 weeks after a missed dose. Of those subjects who were re-randomised to withdraw from treatment, 80.9% (182/225) relapsed, and the median time to relapse was 295 days. No characteristics were identified to predict the time to loss of response or likelihood of regaining response at the individual patient level.

IMMVENT

IMMVENT enrolled 605 subjects (301 randomised to risankizumab and 304 to adalimumab). Subjects randomised to risankizumab received 150 mg of treatment at week 0, week 4, and every 12 weeks thereafter. Subjects randomised to adalimumab received 80 mg at week 0, 40 mg at week 1, and 40 mg every other week through week 15. Starting at week 16, subjects who were receiving adalimumab continued or switched treatment based on response:

- <PASI 50 were switched to risankizumab
- PASI 50 to <PASI 90 were re-randomised to either continue adalimumab or switch to risankizumab
- PASI 90 continued to receive adalimumab

Results are presented in Table 4.

Table 4: Efficacy and quality of life results at week 16 in adults with plaque psoriasis in IMMVENT

	Risankizumab (N=301) n (%)	Adalimumab (N=304) n (%)
sPGA of clear or almost clear[a]	252 (83.7)	183 (60.2)
PASI 75	273 (90.7)	218 (71.7)
PASI 90[a]	218 (72.4)	144 (47.4)
PASI 100	120 (39.9)	70 (23.0)
DLQI 0 or 1[b]	198 (65.8)	148 (48.7)
All comparisons achieved p<0.001 [a] Co-primary endpoints [b] No impact on health-related quality of life		

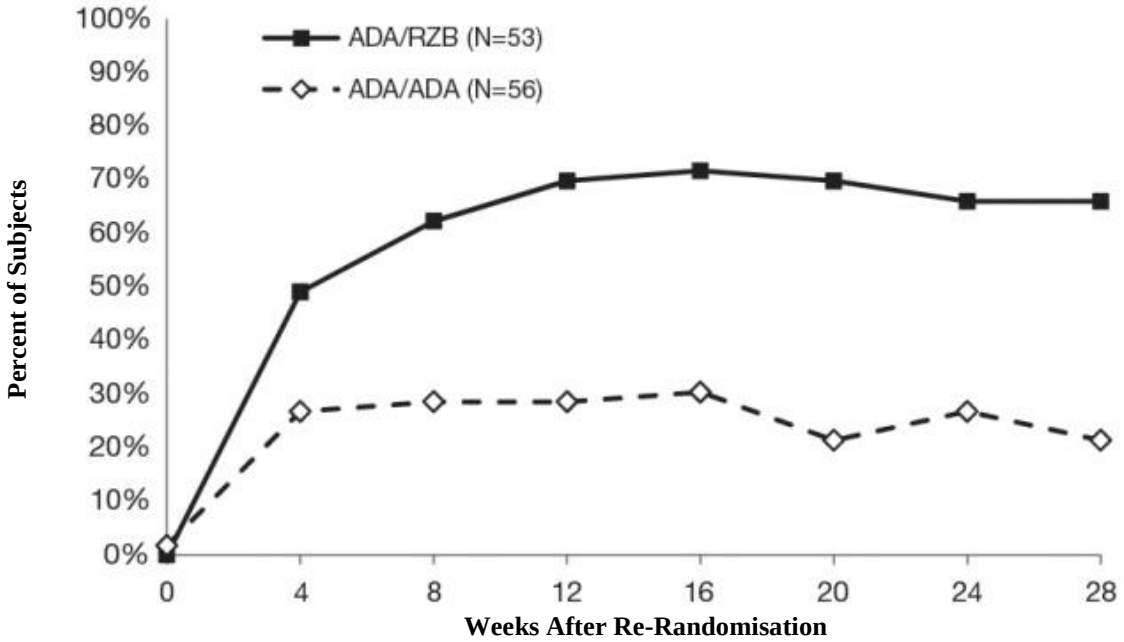
For subjects who had PASI 50 to <PASI 90 with adalimumab at week 16 and were re-randomised, differences in PASI 90 response rates between switching to risankizumab and continuing adalimumab were noted 4 weeks after re-randomisation (49.1% vs 26.8%, respectively).

Results 28 weeks after re-randomisation are presented in Table 5 and Figure 4.

Table 5: Efficacy results 28 weeks after re-randomisation in IMMVENT

	Switched to Risankizumab (N=53) n (%)	Continued on Adalimumab (N=56) n (%)
PASI 90	35 (66.0)	12 (21.4)
PASI 100	21 (39.6)	4 (7.1)
All comparisons achieved p<0.001		

Figure 4: Time course of PASI 90 after re-randomisation in IMMVENT



ADA/ADA: Subjects randomised to adalimumab and continued on adalimumab
ADA/RZB: Subjects randomised to adalimumab and switched to risankizumab
p<0.05 at week 4 and p<0.001 at each time point beginning at week 8

In 270 subjects who switched from adalimumab to risankizumab without a washout period, the safety profile of risankizumab was similar to that in subjects who initiated risankizumab after washout of any prior systemic therapies.

Plaque psoriasis involving the scalp or genital area

The efficacy and safety of risankizumab was assessed in a multicenter, randomised, double-blind, placebo-controlled study (UNLIMMITED) that enrolled subjects 18 years of age and older with moderate to severe scalp psoriasis (UNLIMMITED-S), defined as Psoriasis Scalp Severity Index (PSSI) ≥12, scalp Investigator Global Assessment (scalp IGA) ≥3, and ≥30% of the scalp affected, or moderate to severe genital psoriasis (UNLIMMITED-G), defined as static Physician's Global Assessment of Genitalia (sPGA-G) ≥3 at baseline. All subjects had BSA ≥1% and sPGA ≥3 at baseline.

In UNLIMMITED, subjects were randomised to receive either risankizumab 150 mg or placebo subcutaneously at weeks 0 and 4. Starting at week 16, all subjects received risankizumab 150 mg every 12 weeks until the last dose at week 40.

Scalp area (UNLIMMITED-S)

UNLIMMITED-S enrolled 105 subjects. Baseline BSA involvement was ≥10% for 61.9% of the subjects and <10% for 38.1% of the subjects. Mean baseline BSA involvement was 16.8%. At baseline, 76.2% of subjects had sPGA = 3 and 23.8% had sPGA = 4.

At baseline, 54.3% of subjects were naïve to any systemic therapy (including non-biologic and biologic), 0% of subjects had received prior phototherapy, 15.2% had received prior non-biologic systemic therapy, and 37.1% had received prior biologic therapy.

The results for the primary and key secondary endpoints are presented in Table 6.

Table 6. Efficacy results in adults with scalp psoriasis in UNLIMMITED-S at week 16

Endpoint	**Risankizumab (N=51) n (%)**	**Placebo (N=54) n (%)**	**Treatment difference (95% CI)**
scalp IGA of clear or almost clear (0 or 1)[a]	31 (60.8)	7 (13.0)	47.0 [31.2, 62,8]
PSSI 75[b]	38 (74.5)	12 (22.2)	52.9 [37.5, 68.3]
PSSI 90[c]	27 (52.9)	7 (13.0)	39.8 [24.4, 55.2]
PSSI 100[d]	23 (45.1)	7 (13.0)	31.2 [15.4, 46.9]
Mean change from baseline in PSS	N=44 -6.0	N=49 -1.0	-5.0 [-6.6, -3.3]
All comparisons achieved p<0.001, adjusted treatment difference (95% CI) [a] Primary endpoint [b] Achievement of ≥75% improvement from baseline in PSSI [c] Achievement of ≥90% improvement from baseline in PSSI [d] Achievement of 100% improvement from baseline in PSSI			

A greater proportion of subjects treated with risankizumab achieved a scalp IGA score of 0 at week 16 compared with placebo (41.2% vs 11.1%, respectively).

Scalp Itch Numeric rating scale (NRS) response, defined as achievement of ≥4-point improvement (reduction) from baseline on the Scalp Itch NRS among subjects with baseline scores ≥4, was

achieved in a greater proportion of subjects treated with risankizumab at week 16 compared to placebo (50.0% vs 11.1%, respectively).

A greater proportion of subjects treated with risankizumab achieved a DLQI score of 0 or 1 (no impact on health-related quality of life) at week 16 compared with placebo (47.1% vs 11.1%, respectively).

Genital area (UNLIMMITED-G)

UNLIMMITED-G enrolled 109 subjects. Baseline BSA involvement was ≥10% for 63.3% of the subjects and <10% for 36.7% of the subjects. Mean baseline BSA involvement was 17.2%. At baseline, 80.7% of subjects had sPGA = 3 and 19.3% had sPGA = 4.

At baseline, 61.5% of subjects were naïve to any systemic therapy (including non-biologic and biologic), 2.8% of subjects had received prior phototherapy, 16.5% had received prior non-biologic systemic therapy, and 25.7% had received prior biologic therapy.

The results for the primary and all secondary endpoints are presented in Table 7.

Table 7. Efficacy results in adults with genital psoriasis in UNLIMMITED-G at week 16

Endpoint	**Risankizumab (N=55) n (%)**	**Placebo (N=54) n (%)**	**Treatment difference (95% CI)**
sPGA-G of clear or minimal (0 or 1)[a]	38 (69.1)	7 (13.0)	57.0 [42.3, 71.7]
sPGA-G of clear (0)	28 (50.9)	3 (5.6)	46.7 [32.6, 60.8]
DLQI of 0 or 1[b]	33 (60.0)	2 (3.7)	56.5 [43.0, 70.0]
GPI-NRS reduction of ≥4-point from baseline[c]	N=41 20 (48.8)	N=45 3 (6.7)	43.0 [26.6, 59.3]
GenPs-SFQ item 2 score of 0 (never) or 1 (rarely)[d,e]	N=31 22 (71.0)	N=32 7 (21.9)	46.1 [26.7, 65.6]

All comparisons achieved p<0.001, adjusted treatment difference (95% CI)
[a] Primary endpoint
[b] Total DLQI score of 0 or 1 indicates skin condition has no impact on patient's health-related quality of life
[c] Improvement of genital itch severity as measured by a reduction of at least 4 points in the 11-point Genital Psoriasis Itch (GPI) Numeric Rating Scale (NRS) from the Genital Psoriasis Symptom Scale (GPSS) among subjects with baseline score ≥4
[d] Genital Psoriasis Sexual Frequency Questionnaire (GenPs-SFQ) Item 2 measures patient-perceived impact on sexual health due to genital area psoriasis on sexual activity frequency (intercourse or other activities) in the past week (uses a scale from 0 to 4 with higher scores indicating greater limitations)
[e] Among subjects with baseline score ≥2

Subjects treated with risankizumab achieved greater reduction in psoriasis symptoms severity in the genital area (itch, pain, discomfort, stinging, burning, redness, scaling, and cracking) from baseline as measured by GPSS at week 16 compared to placebo. The change from baseline in GPSS total score at week 16 was -26.5 for risankizumab and -1.0 for placebo.

A greater proportion of subjects treated with risankizumab compared to placebo achieved at least 2-point reduction on Patient's Global Assessment of Genital Psoriasis (PatGA-Genital), among subjects with baseline score ≥2 (71.7% vs 22.9%, respectively).

The safety profile of risankizumab in studies UNLIMMITED-S and UNLIMMITED-G was consistent with the safety profile observed in previous studies of patients with plaque psoriasis.

Psoriatic arthritis

Risankizumab has been shown to improve signs and symptoms, physical function, health-related quality of life, and the proportion of subjects with no radiographic progression in adults with active psoriatic arthritis (PsA).

The safety and efficacy of risankizumab were assessed in 1 407 subjects with active PsA in 2 randomised, double-blind, placebo-controlled studies (964 in KEEPSAKE1 and 443 in KEEPSAKE2).

Subjects in these studies had a diagnosis of PsA for at least 6 months based on the Classification Criteria for Psoriatic Arthritis (CASPAR), a median duration of PsA of 4.9 years at baseline, ≥ 5 tender joints and ≥ 5 swollen joints, and active plaque psoriasis or nail psoriasis at baseline. 55.9% of subjects had ≥ 3% BSA with active plaque psoriasis. 63.4% and 27.9% of subjects had enthesitis and dactylitis, respectively. In KEEPSAKE1, where nail psoriasis was further assessed, 67.3% had nail psoriasis.

In both studies, subjects were randomised to receive risankizumab 150 mg or placebo at weeks 0, 4, and 16. Starting from week 28, all subjects received risankizumab every 12 weeks.

In KEEPSAKE1, all subjects had a previous inadequate response or intolerance to non-biologic DMARD therapy and were biologic naïve. In KEEPSAKE2, 53.5% of subjects had a previous inadequate response or intolerance to non-biologic DMARD therapy and 46.5% of subjects had a previous inadequate response or intolerance to biologic therapy.

In both studies, 59.6% of subjects were receiving concomitant methotrexate (MTX), 11.6% were receiving concomitant non-biologic DMARDs other than MTX, and 28.9% were receiving risankizumab monotherapy.

Clinical response

Treatment with risankizumab resulted in significant improvement in measures of disease activity compared with placebo at week 24. For both studies, the primary endpoint was the proportion of subjects who achieved an American College of Rheumatology (ACR) 20 response at week 24. The key efficacy results are shown in Table 8.

Table 8. Efficacy results in studies KEEPSAKE1 and KEEPSAKE2

	KEEPSAKE1		**KEEPSAKE2**	
Endpoint	**Placebo N=481** n (%)	**Risankizumab N=483** n (%)	**Placebo N=219** n (%)	**Risankizumab N=224** n (%)
ACR20 Response				
Week 16	161 (33.4)	272 (56.3) [a]	55 (25.3)	108 (48.3) [a]
Week 24	161 (33.5)	277 (57.3) [a]	58 (26.5)	115 (51.3) [a]
Week 52*	-	338/433 (78.1)	-	131/191 (68.6)
ACR50 Response				
Week 24	54 (11.3)	162 (33.4) [b]	20 (9.3)	59 (26.3) [b]
Week 52*	-	209/435 (48.0)	-	72/192 (37.5)
ACR70 Response				
Week 24	23 (4.7)	74 (15.3) [b]	13 (5.9)	27 (12.0) [c]
Week 52*	-	125/437 (28.6)	-	37/192 (19.3)
Resolution of Enthesitis (LEI=0)				
Week 24*	156/448 (34.8) [d]	215/444 (48.4) [a, d]	-	-

Week 52*	-	244/393 (62.1) [d]	-	-
Resolution of Dactylitis (LDI=0)				
Week 24*	104/204 (51.0) [e]	128/188 (68.1) [a, e]	-	-
Week 52*	-	143/171 (83.6) [e]	-	-
Minimal Disease Activity (MDA) Response				
Week 24	49 (10.2)	121 (25.0) [a]	25 (11.4)	57 (25.6) [a]
Week 52*	-	183/444 (41.2)	-	61/197 (31.0)

*data are shown for available subjects in the format of n/N observed (%)

a) multiplicity-controlled p≤0.001 risankizumab vs placebo comparison.

b) nominal p≤0.001 risankizumab vs placebo comparison.

c) nominal p≤0.05 risankizumab vs placebo comparison.

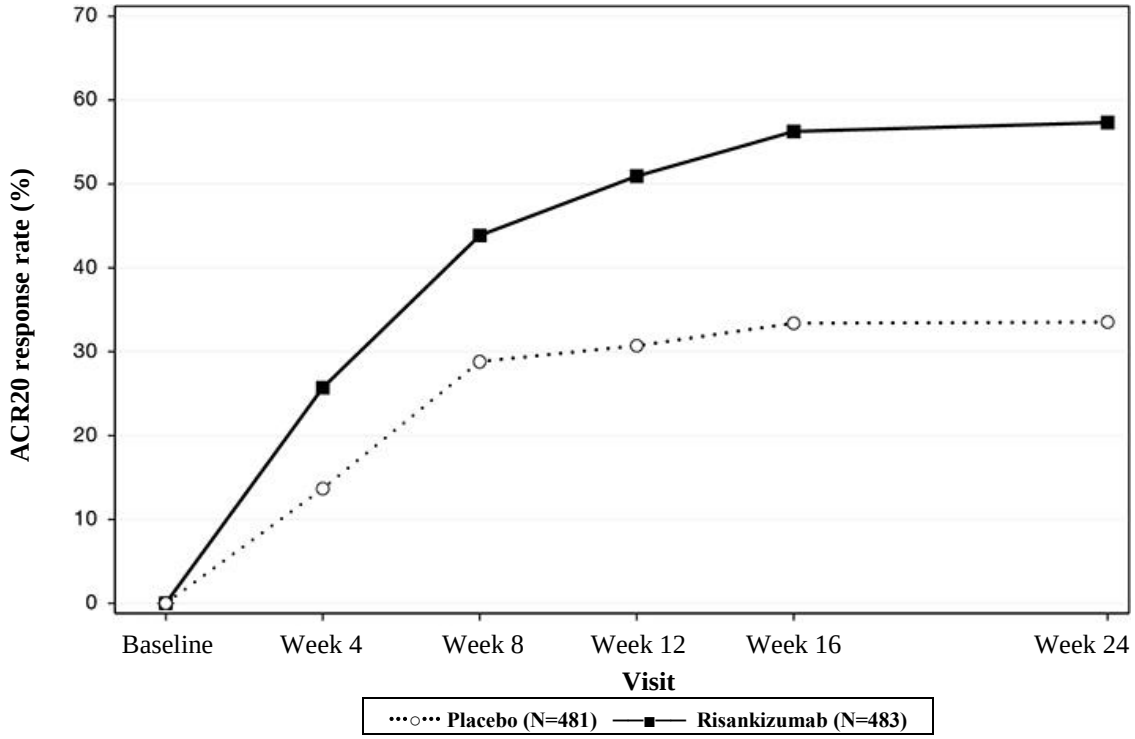
d) Summarized from pooled data from KEEPSAKE1 and KEEPSAKE2 for subjects with baseline LEI >0.

e) Summarized from pooled data from KEEPSAKE1 and KEEPSAKE2 for subjects with baseline LDI >0.

Response over time

In KEEPSAKE1, a greater ACR20 response was observed in the risankizumab group compared to placebo as early as week 4 (25.7%) and the treatment difference continued over time to week 24 (Figure 5).

Figure 5. Percent of subjects achieving ACR20 responses in study KEEPSAKE1 through week 24



A greater ACR20 response for risankizumab versus placebo was seen as early as week 4 in 19.6% of subjects in KEEPSAKE2.

Responses observed in risankizumab groups were similar regardless of concomitant non-biologic DMARD use, number of prior non-biologic DMARDs, age, gender, race, and BMI. In KEEPSAKE2, responses were seen regardless of prior biologic therapy.

The safety profile of risankizumab with up to 52 weeks of exposure was consistent with the profile observed up to 24 weeks.

In both studies, the proportion of subjects achieving modified PsA Response Criteria (PsARC) at week 24 was higher in subjects receiving risankizumab compared with placebo. In addition, subjects receiving risankizumab achieved greater improvement in Disease Activity Score (28 joints) using CRP (DAS28-CRP) compared with placebo at week 24. Improvements were maintained through week 52 for PsARC and DAS28-CRP.

Treatment with risankizumab resulted in improvements in individual ACR components, Health Assessment Questionnaire-Disability Index (HAQ-DI), pain assessment, and high-sensitivity C-reactive protein (hsCRP) compared with placebo.

Treatment with risankizumab resulted in statistically significant improvement in the skin manifestations of psoriasis in subjects with PsA.

Treatment with risankizumab resulted in statistically significant improvement in the modified Nail Psoriasis Severity Index (mNAPSI) and the 5-point Physician's Global Assessment of Fingernail Psoriasis (PGA-F) scores in subjects with nail psoriasis at baseline (67.3%) in KEEPSAKE1. This improvement was maintained through week 52 (see Table 9).

Table 9. Nail psoriasis efficacy results in KEEPSAKE1

	Placebo N=338	**Risankizumab N=309**
mNAPSI change from baseline [a]		
Week 24	-5.57	-9.76 [b]
Week 52	-	-13.64
PGA-F change from baseline [a]		
Week 24	-0.4	-0.8 [b]
Week 52	-	-1.2
PGA-F clear/minimal and ≥2-grade improvement [c]		
Week 24 n (%)	30 (15.9)	71 (37.8) [d]
Week 52 n (%)	-	105 (58.0)

a) Summarized for subjects with baseline nail psoriasis (Placebo N=338; risankizumab N=309; at week 52, for mNAPSI, observed risankizumab N=290, for PGA-F, observed risankizumab N=291).
b) Multiplicity-controlled p≤0.001 risankizumab vs placebo comparison.
c) Summarized for subjects with nail psoriasis and a PGA-F overall global assessment score of 'Mild', 'Moderate' or 'Severe' at Baseline (Placebo N=190; risankizumab N=188, at week 52 observed risankizumab N=181).
d) Nominal p≤0.001 risankizumab vs placebo comparison.

Radiographic response

In KEEPSAKE1, inhibition of progression of structural damage was assessed radiographically and expressed as the change in modified Total Sharp Score (mTSS) at week 24, compared with baseline. The mTSS score was modified for PsA by addition of hand distal interphalangeal (DIP) joints. At week 24, the mean progression of structural damage with risankizumab (mean mTSS 0.23) compared with placebo (mean mTSS 0.32) was not statistically significant. At week 24, the proportion of subjects with no radiographic progression (defined as a change from baseline in mTSS ≤ 0) was higher

with risankizumab (92.4%) compared with placebo (87.7%). This response was maintained through week 52.

Physical function and health related quality of life

In both studies, subjects treated with risankizumab showed statistically significant improvement from baseline in physical function as assessed by HAQ-DI at week 24 (KEEPSAKE1 (-0.31) compared with placebo (-0.11) ($p \leq 0.001$)), (KEEPSAKE2 (-0.22) compared with placebo (-0.05) ($p \leq 0.001$)). At week 24, a greater proportion of subjects achieved a clinically meaningful reduction of at least 0.35 in HAQ-DI score from baseline in the risankizumab group compared with placebo. Improvements in physical function were maintained through week 52.

In both studies, subjects treated with risankizumab demonstrated significant improvements in the SF-36 V2 physical component summary scores and in FACIT-Fatigue scores at week 24, compared with placebo, with improvements maintained through week 52.

At baseline, psoriatic spondylitis was reported in 19.6% (7.9% diagnosed by radiograph or MRI) of subjects in KEEPSAKE1 and 19.6% (5% diagnosed by radiograph or MRI) of subjects in KEEPSAKE2. Subjects with clinically assessed psoriatic spondylitis who were treated with risankizumab showed improvements from baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores compared with placebo at week 24. Improvements were maintained through week 52. There is insufficient evidence of the efficacy of risankizumab in subjects with radiograph- or MRI-confirmed ankylosing spondylitis-like psoriatic arthropathy due to the small number of subjects studied.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Skyrizi in one or more subsets of the paediatric population in the treatment of plaque psoriasis and psoriatic arthritis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetics of risankizumab was similar between subjects with plaque psoriasis and subjects with psoriatic arthritis.

Absorption

Risankizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure across dose ranges of 18 to 300 mg and 0.25 to 1 mg/kg administered subcutaneously, and 200 to 1 200 mg and 0.01 to 5 mg/kg administered intravenously.

Following subcutaneous dosing of risankizumab, peak plasma concentrations were achieved between 3-14 days after dosing with an estimated absolute bioavailability of 89%. With dosing of 150 mg at week 0, week 4, and every 12 weeks thereafter, estimated steady-state peak and trough plasma concentrations are 12 and 2 µg/mL, respectively.

Bioequivalence was demonstrated between a single risankizumab 150 mg injection and two risankizumab 75 mg injections in pre-filled syringe. Bioequivalence was also demonstrated between risankizumab 150 mg pre-filled syringe and pre-filled pen.

Distribution

The mean (±standard deviation) steady-state volume of distribution (V_{ss}) of risankizumab was 11.4 (±2.7) L in Phase 3 studies in subjects with psoriasis, indicating that the distribution of risankizumab is primarily confined to the vascular and interstitial spaces.

Biotransformation

Therapeutic IgG monoclonal antibodies are typically degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgGs. Risankizumab is not expected to be metabolised by cytochrome P450 enzymes.

Elimination

The mean (±standard deviation) systemic clearance (CL) of risankizumab was 0.3 (±0.1) L/day in Phase 3 studies in subjects with psoriasis. The mean terminal elimination half-life of risankizumab ranged from 28 to 29 days in Phase 3 studies in subjects with psoriasis.

As an IgG1 monoclonal antibody, risankizumab is not expected to be filtered by glomerular filtration in the kidneys or to be excreted as an intact molecule in the urine.

Linearity/non-linearity

Risankizumab exhibited linear pharmacokinetics with approximately dose-proportional increases in systemic exposure (C_{max} and AUC) in the evaluated dose ranges of 18 to 300 mg or 0.25 to 1 mg/kg subcutaneous administration in healthy subjects or subjects with psoriasis.

Interactions

An interaction study was conducted in subjects with plaque psoriasis to assess the effect of repeated administration of risankizumab on the pharmacokinetics of cytochrome P450 (CYP) sensitive probe substrates. The exposure of caffeine (CYP1A2 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate) and midazolam (CYP3A substrate) following risankizumab treatment were comparable to their exposures prior to risankizumab treatment, indicating no clinically meaningful interactions through these enzymes.

Population pharmacokinetic analyses indicated that risankizumab exposure was not impacted by concomitant treatment used by some subjects with plaque psoriasis or psoriatic arthritis during the clinical studies.

Special populations

Paediatric population

The pharmacokinetics of risankizumab in paediatric subjects has not been established.

Elderly

Of the 2 234 subjects with plaque psoriasis exposed to risankizumab, 243 were 65 years or older and 24 subjects were 75 years or older. Of the 1 542 subjects with psoriatic arthritis exposed to risankizumab, 246 were 65 years or older and 34 subjects were 75 years or older. No overall differences in risankizumab exposure were observed between older and younger subjects who received risankizumab.

Patients with renal or hepatic impairment

No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of risankizumab. Based on population pharmacokinetic analyses, serum creatinine levels, creatinine clearance, or hepatic function markers (ALT/AST/bilirubin) did not have a meaningful impact on risankizumab clearance in subjects with plaque psoriasis or psoriatic arthritis.

As an IgG1 monoclonal antibody, risankizumab is mainly eliminated via intracellular catabolism and is not expected to undergo metabolism via hepatic cytochrome P450 enzymes or renal elimination.

Body weight

Risankizumab clearance and volume of distribution increase as body weight increases which may result in reduced efficacy in subjects with high body weight (>130 kg). However, this observation is based on a limited number of subjects. No dose adjustment based on body weight is currently recommended.

Gender or race

The clearance of risankizumab was not significantly influenced by gender or race in adult subjects with plaque psoriasis or psoriatic arthritis. No clinically meaningful differences in risankizumab exposure were observed in Chinese or Japanese subjects compared to Caucasian subjects in a clinical pharmacokinetic study in healthy volunteers.

5.3 Preclinical safety data

Nonclinical data revealed no special hazard for humans based on repeat-dose toxicity studies including safety pharmacology evaluations, and an enhanced pre- and post-natal developmental toxicity study in cynomolgus monkeys at doses of up to 50 mg/kg/week (producing exposures of about 70 times the clinical exposure at maximum recommended human dose [MRHD]).

Mutagenicity and carcinogenicity studies have not been conducted with risankizumab. In a 26-week chronic toxicology study in cynomolgus monkeys at doses of up to 50 mg/kg/week (about 70 times the clinical exposure at the MRHD), there were no pre-neoplastic or neoplastic lesions observed and no adverse immunotoxicity or cardiovascular effects were noted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Skyrizi 150 mg solution for injection in pre-filled pen and pre-filled syringe

Sodium acetate trihydrate
Acetic acid
Trehalose dihydrate
Polysorbate 20
Water for injections

Skyrizi 75 mg solution for injection in pre-filled syringe

Disodium succinate hexahydrate
Succinic acid
Sorbitol
Polysorbate 20
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the pre-filled pen or the pre-filled syringe(s) in the outer carton in order to protect from light.

Skyrizi 150 mg pre-filled pen or pre-filled syringe may be stored out of the refrigerator (up to a maximum of 25°C) for up to 24 hours in the original carton to protect from light.

6.5 Nature and contents of container

Skyrizi 150 mg solution for injection in pre-filled pen

Pre-filled glass syringe assembled in a pre-filled pen with an automatic needle sleeve.

Skyrizi 150 mg solution for injection in pre-filled syringe

Pre-filled glass syringe with a fixed needle and needle cover, assembled in an automatic needle guard.

Skyrizi 150 mg is available in packs containing 1 pre-filled pen or 1 pre-filled syringe.

Skyrizi 75 mg solution for injection in pre-filled syringe

Pre-filled glass syringe with a fixed needle and needle cover, assembled in an automatic needle guard.

Skyrizi 75 mg is available in packs containing 2 pre-filled syringes and 2 alcohol pads.

Not all presentations may be marketed.

6.6 Special precautions for disposal and other handling

Skyrizi 150 mg solution for injection in pre-filled pen

Before injecting, patients should remove the carton from the refrigerator and allow to reach room temperature out of direct sunlight (30 to 90 minutes) without removing the pre-filled pen from the carton.

The solution should be colourless to yellow and clear to slightly opalescent.

Skyrizi 150 mg solution for injection in pre-filled syringe

Before injecting, patients may remove the carton from the refrigerator and allow to reach room temperature out of direct sunlight (15 to 30 minutes) without removing the pre-filled syringe from the carton.

The solution should be colourless to yellow and clear to slightly opalescent.

Skyrizi 75 mg solution for injection in pre-filled syringe

Before injecting, patients may remove the carton from the refrigerator and allow to reach room temperature out of direct sunlight (15 to 30 minutes) without removing the pre-filled syringes from the carton.

The solution should be colourless to slightly yellow and clear to slightly opalescent.

Two pre-filled syringes should be injected for the full 150 mg dose.

General special precautions

Prior to use, a visual inspection of each pre-filled pen or pre-filled syringe is recommended. The solution may contain a few translucent to white product-related particles. Skyrizi should not be used if the solution is cloudy or discoloured, or contains large particles. Do not shake the pre-filled pen or pre-filled syringe.

Comprehensive instructions for use are provided in the package leaflet.

Each pre-filled pen or pre-filled syringe is for single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER(S)

Skyrizi 150 mg solution for injection in pre-filled pen

EU/1/19/1361/002

Skyrizi 150 mg solution for injection in pre-filled syringe

EU/1/19/1361/003

Skyrizi 75 mg solution for injection in pre-filled syringe

EU/1/19/1361/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 April 2019
Date of latest renewal: 5 January 2024

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 600 mg concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 600 mg of risankizumab in 10.0 mL of solution.

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody produced in Chinese Hamster Ovary cells using recombinant DNA technology.

Excipients with known effect

This medicinal product contains 2 mg of polysorbate 20 in each 600 mg dose and 4 mg of polysorbate 20 in each 1 200 mg dose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate)

The solution is colourless to slightly yellow and clear to slightly opalescent.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Crohn’s disease

Skyrizi is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy.

Ulcerative colitis

Skyrizi is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy.

4.2 Posology and method of administration

This medicinal product is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Skyrizi is indicated.

Posology

Crohn’s disease

The recommended dose is 600 mg administered by intravenous infusion at week 0, week 4, and week 8, followed by 360 mg administered by subcutaneous injection at week 12, and every 8 weeks thereafter. Consideration should be given to discontinuing treatment in patients who have shown no evidence of therapeutic benefit by week 24.

For the posology of the subsequent subcutaneous dosing regimen, see section 4.2 of the Skyrizi 360 mg solution for injection in cartridge, Skyrizi 180 mg pre-filled syringe and Skyrizi 90 mg pre-filled syringe Summary of Product Characteristics.

Ulcerative colitis

The recommended induction dose is 1 200 mg administered by intravenous infusion at week 0, week 4, and week 8. Starting at week 12 and every 8 weeks thereafter, the recommended maintenance dose is based on individual patient presentation:

- A dose of 180 mg administered by subcutaneous injection is recommended for patients with adequate improvement in disease activity after induction
- A dose of 360 mg administered by subcutaneous injection is recommended for patients with inadequate improvement in disease activity after induction

Consideration should be given to discontinuing treatment in patients who have shown no evidence of therapeutic benefit by week 24.

For the posology of the subsequent subcutaneous dosing regimen, see section 4.2 of the Skyrizi 180 mg and 360 mg solution for injection in cartridge and Skyrizi 180 mg pre-filled syringe Summary of Product Characteristics.

Missed dose

If a dose is missed, the dose should be administered as soon as possible. Thereafter, dosing should be resumed at the regular scheduled time.

Special populations

Elderly

No dose adjustment is required (see section 5.2).
There is limited information in subjects aged ≥65 years.

Renal or hepatic impairment

No specific studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of Skyrizi. These conditions are generally not expected to have any significant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary (see section 5.2).

Paediatric population

The safety and efficacy of Skyrizi in children aged 0-17 years for the treatment of Crohn's disease and ulcerative colitis have not yet been established. Currently available data are described in section 5.1 and 5.2 but no recommendation on posology can be made.

Overweight patients

No dose adjustment is required (see section 5.2).

Method of administration

For intravenous infusion.

Skyrizi concentrate for solution for infusion is for intravenous use only. The 600 mg dose should be administered over at least one hour, and the 1 200 mg dose should be administered over at least two hours. For instructions on dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important active infections (e.g. active tuberculosis, see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Risankizumab may increase the risk of infection.

In patients with a chronic infection, a history of recurrent infection, or known risk factors for infection, risankizumab should be used with caution. Treatment with risankizumab should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Patients treated with risankizumab should be instructed to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops such an infection or is not responding to standard therapy for the infection, the patient should be closely monitored and risankizumab should not be administered until the infection resolves.

Tuberculosis

Prior to initiating treatment with risankizumab, patients should be evaluated for tuberculosis (TB) infection. Patients receiving risankizumab should be monitored for signs and symptoms of active TB. Anti-TB therapy should be considered prior to initiating risankizumab in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Immunisations

Prior to initiating therapy with risankizumab, completion of all appropriate immunisations should be considered according to current immunisation guidelines. If a patient has received live vaccination (viral or bacterial), it is recommended to wait at least 4 weeks prior to starting treatment with risankizumab. Patients treated with risankizumab should not receive live vaccines during treatment and for at least 21 weeks after treatment (see section 5.2).

Hypersensitivity

Serious hypersensitivity reactions, including anaphylaxis, have been reported with use of risankizumab (see section 4.8). If a serious hypersensitivity reaction occurs, administration of risankizumab should be discontinued immediately and appropriate therapy initiated.

Excipients with known effect

Polysorbate

This medicinal product contains 2 mg of polysorbate 20 in each 600 mg dose and 4 mg of polysorbate 20 in each 1 200 mg dose. Polysorbates may cause allergic reactions.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Risankizumab is not expected to undergo metabolism by hepatic enzymes or renal elimination. Interactions between risankizumab and inhibitors, inducers, or substrates of medicinal product metabolising enzymes are not expected and no dose adjustment is needed (see section 5.2).

Concomitant immunosuppressive therapy

The safety and efficacy of risankizumab in combination with immunosuppressants, including biologics, have not been evaluated.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 21 weeks after treatment.

Pregnancy

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of risankizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of risankizumab during pregnancy.

Breast-feeding

It is unknown whether risankizumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which decreases to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period. A decision should be made whether to discontinue/abstain from risankizumab therapy, taking into account the benefit of breast-feeding to the child and the benefit of risankizumab therapy to the woman.

Fertility

The effect of risankizumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Risankizumab has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions were upper respiratory infections (15.6% in Crohn's disease and 26.2% in ulcerative colitis).

Tabulated list of adverse reactions

Adverse reactions for risankizumab from clinical studies (Table 1) are listed by MedDRA system organ class and are based on the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: List of adverse reactions

System Organ Class	Frequency	Adverse reactions
Infections and infestations	Very common	Upper respiratory infections[a]
	Common	Tinea infections[b]
	Uncommon	Folliculitis
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache[c]
Skin and subcutaneous tissue disorders	Common	Pruritus Rash Eczema
	Uncommon	Urticaria
General disorders and administration site conditions	Common	Fatigue[d] Injection site reactions[e]

[a] Includes: respiratory tract infection (viral, bacterial or unspecified), sinusitis (including acute), rhinitis, nasopharyngitis, pharyngitis (including viral), tonsillitis, laryngitis, tracheitis

[b] Includes: tinea pedis, tinea cruris, body tinea, tinea versicolor, tinea manuum, onychomycosis, tinea infection

[c] Includes: headache, tension headache, sinus headache

[d] Includes: fatigue, asthenia, malaise

[e] Includes: injection site bruising, erythema, haematoma, haemorrhage, irritation, pain, pruritus, reaction, swelling, induration, hypersensitivity, nodule, rash, urticaria, vesicles, warmth; infusion site erythema, extravasation, reaction, swelling

Description of selected adverse reactions

Psoriasis

Infections

Over the entire psoriasis programme including long-term exposure to risankizumab, the rate of infections was 75.5 events per 100 subject-years. The majority of cases were non-serious and mild to moderate in severity and did not lead to discontinuation of risankizumab. The rate of serious infections was 1.7 events per 100 subject-years (see section 4.4).

Crohn's disease

Overall, the safety profile observed in patients with Crohn's disease treated with risankizumab was consistent with the safety profile observed in patients across indications.

Infections

The rate of infections in the pooled data from the 12-week induction studies was 83.3 events per 100 subject-years in subjects treated with risankizumab 600 mg intravenously compared to 117.7 events per 100 subject-years in placebo. The rate of serious infections was 3.4 events per 100 subject-years in subjects treated with risankizumab 600 mg intravenously compared to 16.7 events per 100 subject-years in placebo (see section 4.4).

The rate of infections in the 52-week maintenance study was 57.7 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 76.0 events per 100 subject-years in subjects who received placebo after risankizumab induction. The rate of serious infections was 6.0 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 5.0 events per 100 subject-years in subjects who received placebo after risankizumab induction (see section 4.4).

Ulcerative colitis

Overall, the safety profile observed in patients with ulcerative colitis treated with risankizumab was consistent with the safety profile observed in patients across indications.

Infections

The rate of infections in the pooled data from the 12-week induction study was 78.3 events per 100 subject-years in subjects treated with risankizumab 1 200 mg intravenously compared to 74.2 events per 100 subject-years in placebo. The rate of serious infections was 3.0 events per 100 subject-years in subjects treated with risankizumab 1 200 mg intravenously compared to 5.4 events per 100 subject-years in placebo (see section 4.4).

The rate of infections in the 52-week maintenance study was 67.4 events per 100 subject-years in subjects treated with risankizumab 180 mg subcutaneously and 56.5 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 64.6 events per 100 subject-years in subjects who received placebo after risankizumab induction. The rate of serious infections was 1.1 events per 100 subject-years in subjects treated with risankizumab 180 mg subcutaneously and 0.6 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 2.3 events per 100 subject-years in subjects who received placebo after risankizumab induction (see section 4.4).

Immunogenicity

For subjects with Crohn's disease treated with risankizumab at the recommended intravenous induction and subcutaneous maintenance doses for up to 64 weeks in CD clinical trials, treatment-emergent anti-drug antibodies and neutralizing antibodies were detected in 3.4% (2/58) and 0% (0/58) of evaluated subjects, respectively.

For subjects with ulcerative colitis treated with risankizumab at the recommended intravenous induction and subcutaneous maintenance doses (180 mg or 360 mg) for up to 64 weeks in ulcerative colitis clinical trials, treatment-emergent anti-drug antibodies and neutralising antibodies were detected in 8.9% (8/90) and 6.7% (6/90) for the 180 mg subcutaneous dose, or 4.4% (4/91) and 2.2% (2/91) for the 360 mg subcutaneous dose, of evaluated subjects, respectively.

Antibodies to risankizumab including neutralizing antibodies were not associated with changes in clinical response or safety.

Elderly

There is limited safety information in subjects aged ≥65 years.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC18

Mechanism of action

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds with high affinity to the p19 subunit of human interleukin 23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor complex. IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, risankizumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokines.

Pharmacodynamic effects

In a study of subjects with psoriasis, expression of genes associated with the IL-23/IL-17 axis was decreased in the skin after single doses of risankizumab. Reductions in epidermal thickness, infiltration of inflammatory cells, and expression of psoriatic disease markers were also observed in psoriatic lesions.

In a Phase 2 study of subjects with Crohn's disease, expression of genes associated with the IL-23/Th17 axis were decreased in gut tissue after multiple doses of risankizumab. Reductions in faecal calprotectin (FCP), serum C reactive protein (CRP) and IL-22 were also observed after multiple doses in Phase 3 induction studies in Crohn's patients. Decreases in FCP, CRP and serum IL-22 were maintained out to week 52 of the maintenance study.

In a Phase 2b/3 study of subjects with ulcerative colitis, statistically significant and clinically meaningful reduction from baseline was observed in the inflammatory biomarkers, FCP and CRP, and in the IL-23 pathway-associated biomarker, serum IL-22, at week 12 of the induction study. Decreases in FCP, CRP and serum IL-22 were maintained out to week 52 of the maintenance study.

Clinical efficacy and safety

Crohn's disease

The efficacy and safety of risankizumab were assessed in 1 419 subjects with moderately to severely active Crohn's disease in three multicentre, randomised, double-blind, placebo-controlled clinical studies. Enrolled subjects were 16 years of age or older with a Crohn's Disease Activity Index (CDAI)

of 220 to 450, an average daily stool frequency (SF) ≥4 and/or average daily abdominal pain score (APS) ≥2, and a Simple Endoscopic Score for CD (SES-CD) of ≥6, or ≥4 for isolated ileal disease, excluding the narrowing component and confirmed by a central reviewer.

There were two 12-week intravenous induction studies (ADVANCE and MOTIVATE), which included a 12-week extension period for subjects who did not achieve SF/APS clinical response (≥ 30% decrease in SF and/or ≥ 30% decrease in APS and both not worse than baseline) at week 12. ADVANCE and MOTIVATE were followed by a 52-week randomised withdrawal study of subcutaneous maintenance treatment (FORTIFY) that enrolled subjects with SF/APS clinical response to intravenous induction treatment, representing at least 64 weeks of therapy.

ADVANCE and MOTIVATE

In studies ADVANCE and MOTIVATE, subjects were randomised to receive risankizumab at either 600 mg (recommended dose), 1 200 mg, or placebo, at week 0, week 4, and week 8.

In ADVANCE, 58% (491/850) subjects had failed or were intolerant to treatment with one or more biologic therapies (prior biologic failure), and 42% (359/850) had failed or were intolerant to therapy with conventional therapies but not biologic therapies (without prior biologic failure). In ADVANCE, among the subjects without prior biologic failure, (87%) 314/359 were naïve to biologic therapy and the remaining 13% had received a biologic but never failed or demonstrated intolerance. All patients in MOTIVATE had prior biologic failure.

In both studies, a greater proportion of subjects treated with risankizumab achieved the co-primary endpoints of clinical remission at week 12 and endoscopic response at week 12 compared to placebo. Enhanced SF/APS clinical response and clinical remission were significant as early as week 4 in subjects treated with risankizumab and continued to improve through week 12 (Table 2).

Table 2. Efficacy results in ADVANCE and MOTIVATE

	ADVANCE			**MOTIVATE**		
	Placebo intravenously (N=175) %	**Risankizumab 600 mg intravenously (N=336) %**	**Treatment difference[d] (95% CI)**	**Placebo intravenously (N=187) %**	**Risankizumab 600 mg intravenously (N=191) %**	**Treatment difference[d] (95% CI)**
Co-primary endpoints						
Clinical remission at week 12[e]	22%	43%	22% [14%, 30%][a]	19%	35%	15% [6%, 24%][b]
Endoscopic response at week 12[f]	12%	40%	28% [21%, 35%][a]	11%	29%	18% [10%, 25%][a]
Additional endpoints						
Enhanced SF/APS clinical response at week 4[g]	31%	46%	15% [6%, 23%][b]	32%	45%	14% [4%, 23%][c]
Enhanced SF/APS clinical response at week 12[g]	42%	63%	21% [12%, 30%][a]	39%	62%	23% [13%, 33%][a]
CDAI <150 at week 4	10%	18%	8% [1%, 14%][c]	11%	21%	10% [2%, 17%][c]

CDAI <150 at week 12	25%	45%	21% [12%, 29%][a]	20%	42%	22% [13%, 31%][a]
Mucosal healing at week 12[h]	(N=173) 8%	(N=336) 21%	14% [8%, 19%][a]	(N=186) 4%	(N=190) 14%	9% [4%, 15%][b]
Endoscopic remission at week 12[i]	9%	24%	15% [9%, 21%][a]	4%	19%	15% [9%, 21%][a]

[a] Statistically significant under multiplicity-control for risankizumab vs placebo comparison (p<0.001).
[b] Statistically significant under multiplicity-control for risankizumab vs placebo comparison (p≤0.01).
[c] Nominal p ≤ 0.05 risankizumab vs placebo comparison.
[d] Adjusted treatment difference.
[e] Clinical remission based on SF/APS: average daily SF ≤2.8 and not worse than baseline and average daily AP score ≤1 and not worse than baseline.
[f] Endoscopic response: greater than 50% decrease in SES-CD from baseline, or a decrease of at least 2 points for subjects with a baseline score of 4 and isolated ileal disease.
[g] Enhanced SF/APS clinical response: ≥60% decrease in average daily SF and/or ≥35% decrease in average daily AP score and both not worse than Baseline, and/or clinical remission.
[h] Mucosal healing: SES-CD ulcerated surface subscore of 0 in subjects with a subscore of ≥1 at Baseline.
[i] Endoscopic remission: SES-CD ≤4 and at least a 2 point reduction versus Baseline and no subscore greater than 1 in any individual variable.

At week 12, a higher proportion of subjects treated with risankizumab achieved a decrease of at least 100 points in baseline CDAI compared to placebo (ADVANCE, risankizumab =60%, placebo=37%, p<0.001; MOTIVATE, risankizumab =60%, placebo=30%, p<0.001).

At week 12, a higher proportion of subjects treated with risankizumab achieved both enhanced SF/APS clinical response and endoscopic response at week 12 compared to placebo (ADVANCE, risankizumab =31%, placebo=8%, p<0.001; MOTIVATE, risankizumab =21%, placebo=7%, p<0.001).

The results for the co-primary endpoints for the subgroups (without allowing for multiplicity) of subjects with and without prior biologic failure are presented in Table 3.

Table 3. Efficacy results at week 12 in subgroups of subjects with prior biologic treatment failure and subjects without prior biologic failure in ADVANCE

	ADVANCE		
	Placebo intravenously	**Risankizumab 600 mg**	**Treatment difference (95% CI)**
Clinical remission per SF/AP Score			
Prior biologic failure	23% (N=97)	41% (N=195)	18% [7%, 29%]
Without prior biologic failure	21% (N=78)	48% (N=141)	27% [15%, 39%]
Endoscopic response			
Prior biologic failure	11% (N=97)	33% (N=195)	21% [12%, 31%]
Without prior biologic failure	13% (N=78)	50% (N=141)	38% [27%, 49%]

In ADVANCE, a higher proportion of subjects treated with risankizumab with and without prior biologic failure achieved CDAI<150 compared to placebo (With prior biologic failure, risankizumab =42%, placebo=26%; Without prior biologic failure, risankizumab =49%, placebo=23%).

CD-related hospitalisations

Rates of CD-related hospitalisations through week 12 were lower in subjects treated with risankizumab compared to placebo (ADVANCE, risankizumab =3%, placebo=12%, p<0.001; MOTIVATE, risankizumab =3%, placebo=11%, p≤0.01).

FORTIFY

The maintenance study FORTIFY evaluated 462 subjects with SF/APS clinical response to 12 weeks of risankizumab intravenous induction treatment in studies ADVANCE and MOTIVATE. Subjects were randomised to continue to receive a maintenance regimen of risankizumab 360 mg subcutaneously (recommended dose), or risankizumab 180 mg subcutaneously every 8 weeks, or to withdraw from risankizumab induction and receive placebo subcutaneously every 8 weeks for up to 52 weeks.

The co-primary endpoints were clinical remission at week 52 and, endoscopic response at week 52. Co-primary endpoints were also measured in subjects with and without prior biologic failure (see Table 4).

Table 4. Efficacy results in FORTIFY at week 52 (64 weeks from initiation of induction dose)

	FORTIFY		
	Risankizumab intravenous induction/ Placebo subcutaneously [f] (N=164) %	**Risankizumab intravenous induction/ Risankizumab 360 mg subcutaneously (N=141) %**	**Treatment difference (95% CI)**
Co-primary endpoints			
Clinical remission	40%	52%	15% [5%, 25%][a,g]
Prior biologic failure	34% (N=123)	48% (N=102)	14% [1%, 27%]
Without prior biologic failure	56% (N=41)	62% (N=39)	5% [-16%, 27%]
Endoscopic response	22%	47%	28% [19%, 37%][b,g]
Prior biologic failure	20% (N=123)	44% (N=102)	23% [11%, 35%]
Without prior biologic failure	27% (N=41)	54% (N=39)	27% [6%, 48%]
Additional endpoints			
Enhanced SF/APS clinical response	49%	59%	13% [2%, 23%][e,g]
Maintenance of clinical remission[h]	(N = 91) 51%	(N = 72) 69%	21% [6%, 35%][d,g]
Endoscopic remission	13%	39%	28% [20%, 37%][c,g]
Mucosal healing	(N = 162) 10%	(N = 141) 31%	22% [14%, 30%][c,g]

[a] Statistically significant under multiplicity-control for risankizumab vs placebo comparison (p≤0.01).
[b] Statistically significant under multiplicity-control for risankizumab vs placebo comparison (p<0.001).
[c] Nominal p<0.001 risankizumab vs placebo comparison without overall type I error control.
[d] Nominal p≤0.01 risankizumab vs placebo comparison without overall type I error control.
[e] Nominal p≤0.05 risankizumab vs placebo comparison without overall type I error control.
[f] The induction-only group consisted of subjects who achieved clinical response to risankizumab induction therapy and were randomised to receive placebo in the maintenance study (FORTIFY).
[g] Adjusted treatment difference.
[h] Maintenance of clinical remission: clinical remission at week 52 in subjects with clinical remission at week 0.

Deep remission (clinical remission and endoscopic remission) at week 52 was observed at higher rates in subjects treated with risankizumab intravenously / risankizumab subcutaneously compared to subjects who received risankizumab intravenously/placebo subcutaneously (28% vs. 10%, respectively, nominal $p<0.001$).

At week 52, a higher proportion of subjects treated with risankizumab intravenously / risankizumab subcutaneously achieved CDAI < 150 compared to risankizumab intravenously /placebo subcutaneously (52% vs. 41%, respectively, nominal $p\leq0.01$). A higher proportion of subjects treated with risankizumab intravenously / risankizumab subcutaneously achieved a decrease of at least 100 points in baseline CDAI score compared to subjects treated with risankizumab intravenously /placebo subcutaneously (62% vs. 48%, respectively, nominal $p\leq 0.01$).

91 subjects who did not demonstrate SF/APS clinical response 12 weeks after risankizumab induction in studies ADVANCE and MOTIVATE received subcutaneous 360 mg dose of risankizumab at week 12 and week 20. Of these subjects, 64% (58/91) achieved SF/APS clinical response at week 24; 33 of the subjects achieving SF/APS clinical response enrolled in FORTIFY and continued receiving risankizumab 360 mg subcutaneously every 8 weeks for up to 52 weeks. Among these subjects, 55% (18/33) achieved clinical remission and 45% (15/33) achieved endoscopic response at week 52.

During FORTIFY, 30 subjects had loss of response to risankizumab 360 mg subcutaneously treatment and received rescue treatment with risankizumab (1 200 mg intravenous single dose, followed by 360 mg subcutaneously every 8 weeks). Of these subjects, 57% (17/30) achieved SF/APS clinical response at week 52. In addition, 20% (6/30) and 34% (10/29) of subjects achieved clinical remission and endoscopic response at week 52, respectively.

Health-related and quality of life outcomes

Health-related quality of life was assessed by the Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-Item Short Form Health Survey (SF-36). Improvement in fatigue was evaluated by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale. Work productivity was assessed by the Work Productivity and Activity Impairment CD (WPAI-CD) Questionnaire.

At week 12 of ADVANCE and MOTIVATE, subjects treated with risankizumab achieved clinically meaningful improvements from baseline in IBDQ total score, all IBDQ domain scores (bowel symptoms, systemic function, emotional function, and social function), SF-36 Physical and Mental Component Summary Score, FACIT-Fatigue and WPAI-CD compared to placebo. For WPAI-CD greater reductions in impairment while working, overall work impairment, and activity impairment were demonstrated in ADVANCE; and greater reduction in activity impairment was demonstrated in MOTIVATE. These improvements were maintained in subjects treated with risankizumab intravenously/ risankizumab subcutaneously in FORTIFY through week 52.

Ulcerative colitis

The efficacy and safety of risankizumab was assessed in subjects with moderately to severely active ulcerative colitis in two multicentre, randomised, double-blind, placebo-controlled clinical studies. Enrolled subjects were ≥ 18 and ≤ 80 years of age with adapted Mayo Score (aMS) of 5 to 9 (using the Mayo scoring system, excluding Physician's Global Assessment) with an endoscopic subscore (ES) of 2 or 3 on screening endoscopy, confirmed by central review.

The 12-week intravenous induction study (INSPIRE) included a 12-week extension period for subjects who did not achieve clinical response [defined as a decrease from baseline in the aMS ≥ 2 points and ≥ 30% from baseline, and a decrease in rectal bleeding subscore (RBS) ≥ 1 or an absolute RBS ≤ 1] at Week 12. INSPIRE was followed by a 52-week randomised withdrawal study of subcutaneous maintenance treatment (COMMAND) that enrolled subjects with clinical response to 12 weeks of risankizumab intravenous induction treatment, representing at least 64 weeks of therapy.

INSPIRE

In study INSPIRE, 975 subjects were randomised and received either risankizumab 1 200 mg or placebo, at week 0, week 4, and week 8.

In INSPIRE, 52% (503/975) of subjects had failed (inadequate response or intolerance) one or more biologics therapies, JAK inhibitors, and/or S1P receptor modulators. Of these 503 subjects, 488 (97%) failed biologics and 90 (18%) failed JAK inhibitors.

Enrolled subjects were permitted to use a stable dose of oral corticosteroids (up to 20 mg/day prednisone or equivalent), immunomodulators, and aminosalicylates. At baseline in INSPIRE, 36% of subjects received corticosteroids, 17% of subjects received immunomodulators and 73% of subjects received aminosalicylates. Patient disease activity was moderate (aMS ≤7) in 58% of subjects and severe (aMS >7) in 42% of subjects.

In INSPIRE, a significantly greater proportion of subjects treated with risankizumab achieved the primary endpoint of clinical remission per aMS [defined as stool frequency subscore (SFS) ≤ 1, and not greater than baseline, RBS = 0, and ES ≤ 1 without evidence of friability] at week 12 compared to placebo (Table 5). Results of the primary endpoint and key secondary endpoints are listed in Table 5.

Table 5. Efficacy results in INSPIRE at week 12

Endpoint	**Placebo intravenously (N=325) %**	**Risankizumab 1 200 mg intravenously (N=650) %**	**Treatment difference (95% CI)**
Disease activity and UC symptoms			
Clinical remission[ab]	6%	20%	14%[f] [10%, 18%]
With biologic and/or JAK inhibitor failure	4% (N=170)	11% (N=333)	7% [3%, 12%]
Without biologic and/or JAK inhibitor failure	8% (N=155)	30% (N=317)	21% [15%, 28%]
Clinical response[c]	36%	64%	29%[f] [22%, 35%]
With biologic and/or JAK inhibitor failure	31% (N=170)	55% (N=333)	24% [15%, 33%]
Without biologic and/or JAK inhibitor failure	41% (N=155)	74% (N=317)	33% [24%, 42%]
Endoscopic and histologic assessment			
Mucosal healing[d]	12%	37%	24%[f] [19%, 29%]
With biologic and/or JAK inhibitor failure	10% (N=170)	26% (N=333)	16% [9%, 22%]
Without biologic and/or JAK inhibitor failure	14% (N=155)	48% (N=317)	33% [26%, 41%]
Histologic-endoscopic mucosal healing[e]	8%	24%	17%[f] [12%, 21%]
With biologic and/or JAK inhibitor failure	7% (N=170)	16% (N=333)	9% [3%, 14%]
Without biologic and/or JAK inhibitor failure	8% (N=155)	33% (N=317)	25%

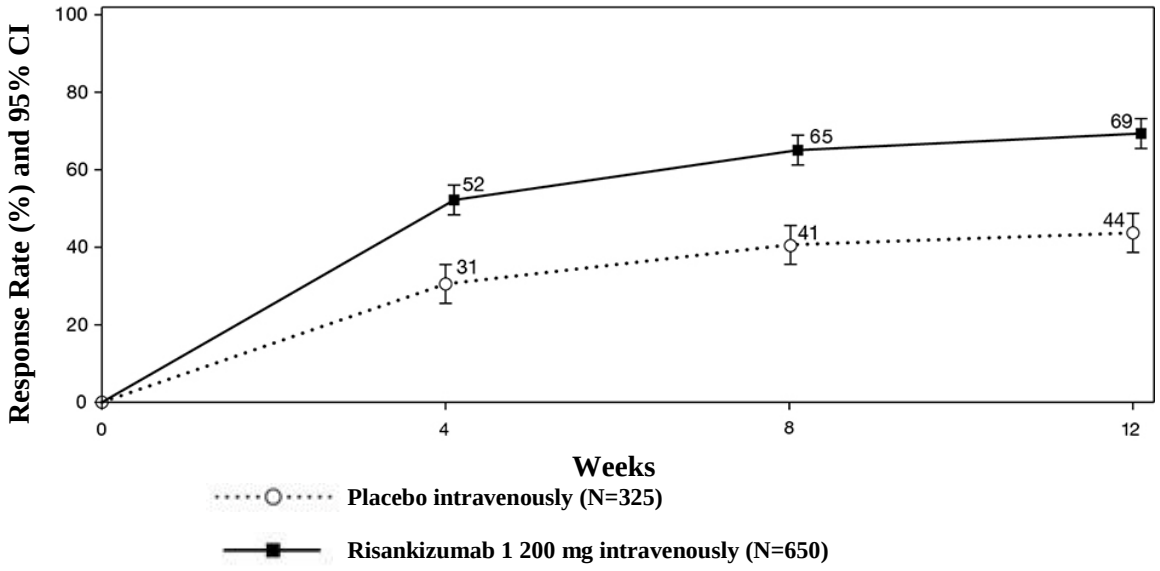
			[18%, 32%]

[a] Primary endpoint
[b] Clinical remission per aMS: SFS ≤ 1, and not greater than baseline, RBS = 0, and ES ≤ 1 without evidence of friability
[c] Clinical response per aMS: decrease from Baseline ≥ 2 points and ≥ 30%, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1
[d] ES ≤ 1 without the evidence of friability
[e] ES ≤ 1 without the evidence of friability and Geboes score ≤ 3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations or granulation tissue)
[f] p < 0.00001, adjusted treatment difference (95% CI)

Clinical disease activity and symptoms

The partial adapted Mayo score (paMS) is composed of SFS and RBS. Clinical response per paMS is defined as a decrease of ≥1 point and ≥30% from Baseline and a decrease in RBS ≥1 or an absolute RBS ≤1. The results of clinical response per paMS over time in INSPIRE are shown in Figure 1. Onset of efficacy was rapid with a greater proportion of subjects treated with risankizumab achieving clinical response as early as week 4 compared to placebo (52% vs 31%, respectively, p < 0.00001).

Figure 1. Proportion of subjects achieving clinical response per paMS over time in induction study INSPIRE



A significantly greater proportion of subjects treated with risankizumab compared to placebo had no abdominal pain (36% vs 26%, respectively, p < 0.01) and no bowel urgency (44% vs 28%, respectively, p < 0.00001) at week 12.

Other UC Symptoms

Number of faecal incontinence episodes per week was reduced in a significantly greater amount in subjects treated with risankizumab compared to placebo at week 12 (change from baseline in risankizumab = -3.8, placebo = -2.2, p = 0.00003).

The proportion of subjects who had no nocturnal bowel movements was significantly greater in subjects treated with risankizumab compared to placebo at week 12 (67% vs 43%, respectively, p < 0.00001).

The proportion of subjects who had no tenesmus was significantly greater in subjects treated with risankizumab compared to placebo at week 12 (49% vs 30%, respectively, p < 0.00001).

Number of days with sleep interruption due to UC symptoms per week were reduced in a significantly greater amount in subjects treated with risankizumab compared to placebo at week 12 (change from baseline in risankizumab = -2.5, placebo = -1.5, $p < 0.00001$).

UC-related hospitalisations

Rates of UC-related hospitalisations through week 12 were significantly lower in subjects treated with risankizumab compared to placebo (1% vs 6%, respectively, $p < 0.00001$).

Extended treatment in week 12 non-responders

A total of 141 subjects who did not demonstrate clinical response at week 12 of risankizumab induction in INSPIRE received either subcutaneous 180 mg or 360 mg dose of risankizumab at week 12 and week 20. Of the 71 subjects who received risankizumab 180 mg subcutaneously and 70 subjects who received risankizumab 360 mg subcutaneously, 56% and 57% achieved clinical response at week 24, respectively.

COMMAND

The maintenance study COMMAND evaluated 548 subjects with clinical response after 12 weeks of risankizumab intravenous induction treatment in study INSPIRE. Subjects were randomised to receive a maintenance regimen of risankizumab 180 mg subcutaneously or 360 mg subcutaneously every 8 weeks, or to withdraw from risankizumab induction and receive placebo subcutaneously every 8 weeks for up to 52 weeks.

In COMMAND, 75% (411/548) of subjects had failed (inadequate response or intolerance) one or more biologics therapies, JAK inhibitors, and/or S1P receptor modulators prior to induction baseline. Of these 411 subjects, 407 (99%) failed biologics and 78 (19%) failed JAK inhibitors.

In COMMAND, a significantly greater proportion of the above 548 subjects treated with risankizumab 180 mg subcutaneously or risankizumab 360 mg subcutaneously achieved the primary endpoint of clinical remission per aMS at week 52 compared to placebo (see Table 6). Results of the primary endpoint and key secondary endpoints are listed in Table 6.

Table 6. Efficacy results in COMMAND at week 52 (64 weeks from initiation of induction dose)

Endpoint	**Risankizumab intravenous induction/ Placebo subcutaneously[+] (N=183) %**	**Risankizumab intravenous induction/ Risankizumab 180 mg subcutaneously (N=179) %**	**Risankizumab intravenous induction/ Risankizumab 360 mg subcutaneously (N=186) %**	**Treatment difference (97.5% CI)[++]**	
				Risankizumab intravenous induction/ Risankizumab 180 mg subcutaneously	**Risankizumab intravenous induction/ Risankizumab 360 mg subcutaneously**
Disease activity and UC symptoms					
Clinical remission[ab]	25%	40%	38%	16%[h] [6%, 27%]	14%[h] [4%, 24%]
With biologic and/or JAK inhibitor failure	23% (N=138)	37% (N=134)	29% (N=139)	13% [1%, 26%]	6% [-6%, 18%]
Without biologic and/or JAK inhibitor failure	31% (N=45)	51% (N=45)	62% (N=47)	20% [-3%, 43%]	31% [8%, 53%]
Maintenance of clinical remission[c]	40% (N=53)	70% (N=44)	50% (N=40)	29%[h] [7%, 51%]	13%[k] [-11%, 36%]

With biologic and/or JAK inhibitor failure	37% (N=35)	65% (N=26)	44% (N=25)	28% [0%, 56%]	7% [-22%, 36%]
Without biologic and/or JAK inhibitor failure	44% (N=18)	77% (N=18)	60% (N=15)	33% [-2%, 67%]	16% [-23%, 54%]
Corticosteroid-free clinical remission[d]	25%	40%	37%	16% [h] [6%, 26%]	14% [h] [3%, 24%]
With biologic and/or JAK inhibitor failure	23% (N=138)	36% (N=134)	29% (N=139)	13% [0%, 25%]	6% [-6%, 18%]
Without biologic and/or JAK inhibitor failure	31% (N=45)	51% (N=45)	60% (N=47)	20% [-3%, 43%]	28% [6%, 51%]
Clinical response[e]	52%	68%	62%	17%[i] [6%, 28%]	11%[j] [0%, 23%]
With biologic and/or JAK inhibitor failure	46% (N=138)	63% (N=134)	57% (N=139)	18% [4%, 31%]	11% [-2%, 25%]
Without biologic and/or JAK inhibitor failure	71% (N=45)	82% (N=45)	79% (N=47)	11% [-9%, 31%]	8% [-13%, 28%]
Endoscopic and histologic assessment					
Mucosal healing[f]	32%	51%	48%	20% [h] [9%, 31%]	17% [h] [7%, 28%]
With biologic and/or JAK inhibitor failure	30% (N=138)	48% (N=134)	39% (N=139)	17% [4%, 30%]	8% [-4%, 21%]
Without biologic and/or JAK inhibitor failure	36% (N=45)	60% (N=45)	76% (N=47)	24% [1%, 47%]	41% [19%, 62]
Histologic-endoscopic mucosal healing[g]	23%	43%	42%	20%[h] [10%, 31%]	20% [h] [10%, 30%]
With biologic and/or JAK inhibitor failure	22% (N=138)	39% (N=134)	33% (N=139)	17% [5%, 29%]	11% [-1%, 23%]
Without biologic and/or JAK inhibitor failure	29% (N=45)	55% (N=45)	69% (N=47)	26% [3%, 49%]	40% [19%, 62%]

[+] The induction-only group consisted of subjects who achieved clinical response to risankizumab induction therapy and were randomised to receive placebo in the maintenance study (COMMAND).
[++] Adjusted difference for the overall treatment difference.
[a] Primary endpoint
[b] Clinical remission per aMS: SFS ≤ 1, and not greater than baseline, RBS = 0, and ES ≤ 1 without evidence of friability
[c] Clinical remission per aMS at week 52 among subjects who achieved clinical remission at the end of induction treatment
[d] Clinical remission per aMS at week 52 and corticosteroid-free for ≥90 days
[e] Clinical response per aMS: decrease from Baseline ≥ 2 points and ≥ 30%, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1
[f] ES of ≤ 1 without the evidence of friability
[g] ES ≤ 1 without the evidence of friability and Geboes score ≤ 3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations or granulation tissue)
[h] Statistically significant under multiplicity-control for risankizumab vs placebo comparison ($p \leq 0.01$).
[i] Nominal $p \leq 0.01$ risankizumab vs placebo comparison
[j] Nominal $p \leq 0.05$ risankizumab vs placebo comparison
[k] $p = 0.2234$

Clinical disease activity and symptoms

A significantly greater proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously compared to risankizumab intravenously/placebo had no abdominal pain (47% vs 30%, respectively, $p < 0.001$) and no bowel urgency (54% vs 31%, respectively, $p < 0.00001$) at

week 52. A greater proportion of subjects treated with risankizumab intravenously /risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo had no bowel urgency (49% vs 31%, respectively, $p < 0.001$) at week 52, and a numerically higher proportion of subjects had no abdominal pain compared to risankizumab intravenously/placebo (38% vs 30%, respectively, $p = 0.0895$) at week 52.

Other UC symptoms

The proportion of subjects who had no nocturnal bowel movements was greater in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo at week 52 (42% and 43% vs 30%, $p < 0.01$ and $p < 0.001$, respectively).

The proportion of subjects who had no tenesmus was greater in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo at week 52 (37% and 37% vs 23%, respectively, $p < 0.01$).

UC-related hospitalisations

Occurrence of UC-related hospitalisations through week 52 were numerically lower in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo (0.6 per 100 subject-years and 1.2 per 100 subject-years vs 3.1 per 100 subject-years, $p = 0.0949$ and $p = 0.2531$, respectively).

Endoscopic and histologic assessment

Endoscopic remission (normalisation of the endoscopic appearance of the mucosa) was defined as ES of 0. At week 12 of INSPIRE, a significantly greater proportion of subjects treated with risankizumab compared to placebo achieved endoscopic remission (11% vs 3%, respectively, $p < 0.00001$). At week 52 of COMMAND, a significantly greater proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo achieved endoscopic remission (23% and 24% vs 15%, respectively, $p < 0.05$).

Deep mucosal healing was defined as ES of 0 and Geboes score < 2.0 (indicating no neutrophil in crypts or lamina propria and no increase in eosinophil, no crypt destruction, and no erosions, ulcerations or granulation tissue). At week 12 of INSPIRE, a significantly greater proportion of subjects treated with risankizumab compared to placebo achieved deep mucosal healing (6% vs 1%, respectively, $p < 0.00001$). At week 52 of COMMAND, a numerically higher proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo achieved deep mucosal healing (13% and 16% vs 10%, $p = 0.2062$ and $p = 0.0618$, respectively).

In COMMAND, maintenance of mucosal healing at week 52 (ES $\leq$1 without friability) was seen in a greater proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo among subjects who achieved mucosal healing at the end of induction (74% and 54% vs 47%, $p < 0.01$ and $p = 0.5629$, respectively).

Rescue treatment

During COMMAND, subjects who had loss of response to risankizumab subcutaneously treatment received rescue treatment with risankizumab (a single intravenous induction dose, followed by 360 mg subcutaneously every 8 weeks). Among these subjects, in the risankizumab 180 mg subcutaneous and risankizumab 360 mg subcutaneous treatment group, 85% (17/20) and 74% (26/35) achieved clinical

response at week 52, respectively. In addition, 24% (6/25) and 35% (13/37) of subjects achieved clinical remission per aMS, and 38% (10/26) and 45% (17/38) of subjects achieved endoscopic improvement at week 52 in the risankizumab 180 mg subcutaneous and risankizumab 360 mg subcutaneous treatment group, respectively.

Week 24 responders

A total of 100 subjects did not demonstrate clinical response after 12 weeks of induction treatment, received either subcutaneous 180 mg (N=56) or 360 mg (N=44) dose of risankizumab at week 12 and week 20, demonstrated clinical response at week 24, and continued receiving risankizumab 180 mg or 360 mg subcutaneously every 8 weeks for up to 52 weeks in COMMAND. Among these subjects, 46% and 45% achieved clinical response per aMS at week 52, and 18% and 23% achieved clinical remission per aMS at week 52, for risankizumab 180 mg and 360 mg subcutaneously respectively.

Health-related and quality of life outcomes

Subjects treated with risankizumab achieved clinically meaningful improvements from baseline in the Inflammatory Bowel Disease Questionnaire (IBDQ) (bowel symptoms, systemic function, emotional function, and social function) compared to placebo. Changes from baseline in IBDQ total score at week 12 with risankizumab compared to placebo were 42.6 and 24.3, respectively. Changes from baseline in IBDQ total score at week 52 were 52.6, 50.3 and 35.0 in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously, risankizumab intravenously/risankizumab 360 mg subcutaneously and risankizumab intravenously/placebo, respectively.

Subjects receiving risankizumab experienced significantly greater improvement from baseline in fatigue, as measured by FACIT-F score at week 12 compared to placebo. Changes from baseline in FACIT-F score at Week 12 with risankizumab compared to placebo were 7.9 and 3.3, respectively. Changes from baseline in FACIT-F score at week 52 were 10.9, 10.3 and 7.0 in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously, risankizumab intravenously/risankizumab 360 mg subcutaneously and risankizumab intravenously/placebo, respectively.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Skyrizi in one or more subsets of the paediatric population in the treatment of Crohn's disease and ulcerative colitis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetics of risankizumab was similar between plaque psoriasis and psoriatic arthritis, and between Crohn's disease and ulcerative colitis.

Absorption

Risankizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure across dose ranges of 18 to 360 mg and 0.25 to 1 mg/kg administered subcutaneously, and 200 to 1 800 mg and 0.01 to 5 mg/kg administered intravenously.

Following subcutaneous dosing of risankizumab, peak plasma concentrations were achieved between 3-14 days after dosing with an estimated absolute bioavailability of 74-89%. With dosing of 150 mg at week 0, week 4 and every 12 weeks thereafter, estimated steady-state peak and trough plasma concentrations are 12 and 2 µg/mL, respectively.

In subjects with Crohn's disease treated with 600 mg intravenous induction dose at weeks 0, 4, and 8 followed by 360 mg subcutaneous maintenance dose at week 12 and every 8 weeks thereafter, maximum median peak and trough concentrations are estimated to be 156 and 38.8 µg/mL respectively during the induction period (weeks 8-12) and steady-state median peak and trough concentrations are estimated to be 28.0 and 8.13 µg/mL respectively during the maintenance period (weeks 40-48).

In subjects with ulcerative colitis treated with 1 200 mg intravenous induction dose at weeks 0, 4, and 8 followed by 180 mg or 360 mg subcutaneous maintenance dose at week 12 and every 8 weeks thereafter, maximum median peak and trough concentrations are estimated to be 350 and 87.7 µg/mL respectively during the induction period (weeks 8-12) and steady-state median peak and trough concentrations are estimated to be 19.6 and 4.64 µg/mL for the 180 mg subcutaneous dose and 39.2 and 9.29 µg/mL for the 360 mg subcutaneous dose, respectively, during the maintenance period (weeks 40-48).

Distribution

The mean (±standard deviation) steady-state volume of distribution (V_{ss}) of risankizumab was 11.4 (±2.7) L in Phase 3 studies in subjects with psoriasis, indicating that the distribution of risankizumab is primarily confined to the vascular and interstitial spaces. In a typical 70 kg subject with Crohn's disease, V_{ss} was 7.68 L.

Biotransformation

Therapeutic IgG monoclonal antibodies are typically degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgGs. Risankizumab is not expected to be metabolised by cytochrome P450 enzymes.

Elimination

The mean (±standard deviation) systemic clearance (CL) of risankizumab was 0.3 (±0.1) L/day in Phase 3 studies in subjects with psoriasis. The mean terminal elimination half-life of risankizumab ranged from 28 to 29 days in Phase 3 studies in subjects with psoriasis. For a typical 70 kg subject with Crohn's disease, CL was 0.30 L/day and terminal elimination half-life was 21 days.

As an IgG1 monoclonal antibody, risankizumab is not expected to be filtered by glomerular filtration in the kidneys or to be excreted as an intact molecule in the urine.

Linearity/non-linearity

Risankizumab exhibited linear pharmacokinetics with approximately dose-proportional increases in systemic exposure (C_{max} and AUC) in the evaluated dose ranges of 18 to 360 mg or 0.25 to 1 mg/kg subcutaneous administration and 200 to 1 800 mg and 0.01 to 5 mg/kg administered intravenously in healthy subjects or subjects with psoriasis, Crohn's disease or ulcerative colitis.

Interactions

Interaction studies were conducted in subjects with plaque psoriasis, Crohn's disease, or ulcerative colitis to assess the effect of repeated administration of risankizumab on the pharmacokinetics of cytochrome P450 (CYP) sensitive probe substrates. The exposure of caffeine (CYP1A2 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate) and midazolam (CYP3A substrate) following risankizumab treatment were comparable to their exposures prior to risankizumab treatment, indicating no clinically meaningful interactions through these enzymes.

Population pharmacokinetic analyses indicated that risankizumab exposure was not impacted by concomitant medicinal products used by some subjects with plaque psoriasis during the clinical

studies. Similar lack of impact by concomitant medicinal products was observed based on population pharmacokinetic analyses in Crohn's disease or ulcerative colitis.

Special populations

Paediatric population

The pharmacokinetics of risankizumab in paediatric subjects under 16 years of age has not been established. Of the 1 574 subjects with Crohn's disease exposed to risankizumab, 12 were 16 to 17 years old. Risankizumab exposures in 16 to 17 year-old subjects with Crohn's disease were similar to those in adults. Age was not found to have any significant impact on risankizumab exposures based on the population pharmacokinetic analyses.

Elderly

Of the 2 234 subjects with plaque psoriasis exposed to risankizumab, 243 were 65 years or older and 24 subjects were 75 years or older. Of the 1 574 subjects with Crohn's disease exposed to risankizumab, 72 were 65 years or older and 5 subjects were 75 years or older. Of the 1 512 subjects with ulcerative colitis exposed to risankizumab, 103 were 65 years or older and 8 subjects were 75 years or older. No overall differences in risankizumab exposure were observed between older and younger subjects who received risankizumab.

Patients with renal or hepatic impairment

No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of risankizumab. Based on population pharmacokinetic analyses, serum creatinine levels, creatinine clearance, or hepatic function markers (ALT/AST/bilirubin) did not have a meaningful impact on risankizumab clearance in subjects with psoriasis, Crohn's disease, or ulcerative colitis.

As an IgG1 monoclonal antibody, risankizumab is mainly eliminated via intracellular catabolism and is not expected to undergo metabolism via hepatic cytochrome P450 enzymes or renal elimination.

Body weight

Risankizumab clearance and volume of distribution increase as body weight increases which may result in reduced efficacy in subjects with high body weight (>130 kg). However, this observation is based on a limited number of subjects with plaque psoriasis. Body weight had no clinically meaningful impact on risankizumab exposure or efficacy in psoriatic arthritis, Crohn's disease, or ulcerative colitis. No dose adjustment based on body weight is currently recommended.

Gender or race

The clearance of risankizumab was not significantly influenced by gender or race in adult subjects with plaque psoriasis, Crohn's disease or ulcerative colitis. No clinically meaningful differences in risankizumab exposure were observed in Chinese or Japanese subjects compared to Caucasian subjects in clinical pharmacokinetic studies in healthy volunteers.

5.3 Preclinical safety data

Nonclinical data revealed no special hazard for humans based on repeat-dose toxicity studies including safety pharmacology evaluations and an enhanced pre- and post- natal developmental toxicity study in cynomolgus monkeys at doses of up to 50 mg/kg/week, producing exposures 10 times the clinical exposures during induction at a dose of 600 mg intravenous every 4 weeks and 39 times the clinical exposures for maintenance when given 360 mg subcutaneously every 8 weeks for Crohn's disease. For ulcerative colitis, exposures were 5 times the clinical exposures during induction at a dose of 1 200 mg

intravenously every 4 weeks and 65 or 32 times the clinical exposures for maintenance when given 180 or 360 mg subcutaneously every 8 weeks.

Mutagenicity and carcinogenicity studies have not been conducted with risankizumab. In a 26-week chronic toxicology study in cynomolgus monkeys at doses of up to 50 mg/kg/week (7 times the clinical exposures during induction at a dose of 600 mg intravenous every 4 weeks and 28 times the clinical exposures for maintenance when given 360 mg subcutaneously every 8 weeks for Crohn's disease and 3 times the clinical exposures during induction at a dose of 1 200 mg intravenously every 4 weeks and 45 or 23 times the clinical exposures for maintenance when given 180 or 360 mg subcutaneously every 8 weeks for ulcerative colitis), there were no pre-neoplastic or neoplastic lesions observed and no adverse immunotoxicity or cardiovascular effects were noted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium acetate trihydrate
Acetic acid
Trehalose dihydrate
Polysorbate 20
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

2 years

Diluted solution for intravenous infusion

Chemical and physical in-use stability has been demonstrated for 20 hours at 2°C to 8°C (protected from light) or up to 8 hours at room temperature (protected from sunlight). Storage time at room temperature begins once the diluted solution has been prepared. The infusion should be completed within 8 hours after dilution in the infusion bag. Exposure to indoor light is acceptable during room temperature storage and administration.

From a microbiological point of view, the prepared infusion should be used immediately. If not used immediately, in-use storage time and conditions prior to use are the responsibility of the user and should not be longer than 20 hours at 2°C to 8°C.

Do not freeze.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after dilution of the medicinal product, see section 6.3

6.5 Nature and contents of container

10.0 mL concentrate solution for infusion in a glass vial closed with a coated bromobutyl rubber stopper.

Skyrizi is available in packs containing 1 vial pack.

6.6 Special precautions for disposal and other handling

The solutions should be visually inspected for particulate matter or discoloration prior to administration. The solution should be colourless to slightly yellow and clear to slightly opalescent. The liquid may contain tiny white or clear particles. The medicinal product and its dilutions should not be used if the solution is discoloured or cloudy, or if foreign particulate matter is present.

Instructions for dilution

This medicinal product should be prepared by a healthcare professional using aseptic technique. It must be diluted before administration.

The solution for infusion is prepared by dilution of the concentrate into an intravenous infusion bag or glass bottle containing 5% dextrose in water (D5W) or sodium chloride 9 mg/mL (0.9%) solution for infusion to a final concentration of approximately 1.2 mg/mL to 6 mg/mL. Refer to table below for dilution instructions based on patient's indication.

Indication	**Intravenous induction dose**	**Number of 600 mg/ 10 mL vials**	**Total volume of 5% dextrose or sodium chloride 9 mg/mL (0.9%) solution for infusion**
Crohn's disease	600 mg	1	100 mL, or 250 mL, or 500 mL
Ulcerative colitis	1 200 mg	2	250 mL, or 500 mL

Prior to the start of the intravenous infusion, the content of the intravenous infusion bag or glass bottle should be at room temperature.

Infuse the diluted solution over a period of at least one hour for the 600 mg dose; at least two hours for the 1 200 mg dose.

The solution in the vial and the dilutions should not be shaken.

Each vial is for single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 April 2019
Date of latest renewal: 5 January 2024

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 360 mg solution for injection in cartridge
Skyrizi 180 mg solution for injection in cartridge
Skyrizi 90 mg solution for injection in pre-filled syringe
Skyrizi 180 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Skyrizi 360 mg solution for injection in cartridge

Each cartridge contains 360 mg of risankizumab in 2.4 mL solution.

Skyrizi 180 mg solution for injection in cartridge

Each cartridge contains 180 mg of risankizumab in 1.2 mL solution.

Skyrizi 90 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 90 mg of risankizumab in 1 mL solution.

Skyrizi 180 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 180 mg of risankizumab in 1.2 mL solution.

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody produced in Chinese Hamster Ovary cells using recombinant DNA technology.

Excipients with known effect

180 mg and 360 mg solution for injection only

This medicinal product contains 0.24 mg of polysorbate 20 in each 180 mg dose and 0.48 mg of polysorbate 20 in each 360 mg dose.

90 mg solution for injection only

This medicinal product contains 164 mg sorbitol per 360 mg dose.

This medicinal product contains 0.8 mg of polysorbate 20 in each 360 mg dose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

Skyrizi 180 mg and 360 mg solution for injection in cartridge and 180 mg solution for injection in pre-filled syringe

The solution is colourless to yellow and clear to slightly opalescent.

Skyrizi 90 mg solution for injection in pre-filled syringe

The solution is colourless to slightly yellow and clear to slightly opalescent.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Crohn’s disease

Skyrizi is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy.

Ulcerative colitis

Skyrizi is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy.

4.2 Posology and method of administration

This medicinal product is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which Skyrizi is indicated.

Posology

Crohn’s disease

The recommended dose is 600 mg administered by intravenous infusion at week 0, week 4, and week 8, followed by 360 mg administered by subcutaneous injection at week 12, and every 8 weeks thereafter. Consideration should be given to discontinuing treatment in patients who have shown no evidence of therapeutic benefit by week 24.

For the posology of the initial intravenous dosing regimen, see section 4.2 of the Skyrizi 600 mg concentrate for solution for infusion Summary of Product Characteristics.

Ulcerative colitis

The recommended induction dose is 1 200 mg administered by intravenous infusion at week 0, week 4, and week 8. Starting at week 12 and every 8 weeks thereafter, the recommended maintenance dose is based on individual patient presentation:

- A dose of 180 mg administered by subcutaneous injection is recommended for patients with adequate improvement in disease activity after induction
- A dose of 360 mg administered by subcutaneous injection is recommended for patients with inadequate improvement in disease activity after induction

Consideration should be given to discontinuing treatment in patients who have shown no evidence of therapeutic benefit by week 24.

For the posology of the initial intravenous dosing regimen, see section 4.2 of the Skyrizi 600 mg concentrate for solution for infusion Summary of Product Characteristics.

Missed dose

If a dose is missed, the dose should be administered as soon as possible. Thereafter, dosing should be resumed at the regular scheduled time.

Special populations

Elderly

No dose adjustment is required (see section 5.2).
There is limited information in subjects aged ≥65 years.

Renal or hepatic impairment

No specific studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of Skyrizi. These conditions are generally not expected to have any significant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary (see section 5.2).

Paediatric population

The safety and efficacy of Skyrizi in children aged 0-17 years for the treatment of Crohn's disease and ulcerative colitis have not yet been established. Currently available data are described in section 5.1 and 5.2 but no recommendation on posology can be made.

Overweight patients

No dose adjustment is required (see section 5.2).

Method of administration

Skyrizi is administered by subcutaneous injection.

The injection should be administered in the thigh or abdomen. Skyrizi should not be injected into areas where the skin is tender, bruised, erythematous, indurated or damaged.

Skyrizi 180 mg and 360 mg solution for injection in cartridge

Patients may self-inject Skyrizi after training in subcutaneous injection technique with the on-body injector. Patients should be instructed to read section 7 'Instructions for use' provided in the package leaflet before administration.

Skyrizi 90 mg solution for injection in pre-filled syringe

This medicinal product should be administered by a healthcare professional.

Four pre-filled syringes should be injected to administer the full 360 mg dose. The four injections should be administered at different anatomic locations (see administration instructions provided with the package leaflet).

Skyrizi 180 mg solution for injection in pre-filled syringe

Patients may self-inject Skyrizi after training in subcutaneous injection technique with the pre-filled syringe. Patients should be instructed to read section 7 'Instructions for use' provided in the package leaflet before administration.

One pre-filled syringe should be injected to administer the 180 mg maintenance dose.

Two pre-filled syringes should be injected to administer the 360 mg maintenance dose. The two injections should be administered at different anatomic locations.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Clinically important active infections (e.g. active tuberculosis, see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infections

Risankizumab may increase the risk of infection.

In patients with a chronic infection, a history of recurrent infection, or known risk factors for infection, risankizumab should be used with caution. Treatment with risankizumab should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

Patients treated with risankizumab should be instructed to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops such an infection or is not responding to standard therapy for the infection, the patient should be closely monitored and risankizumab should not be administered until the infection resolves.

Tuberculosis

Prior to initiating treatment with risankizumab, patients should be evaluated for tuberculosis (TB) infection. Patients receiving risankizumab should be monitored for signs and symptoms of active TB. Anti-TB therapy should be considered prior to initiating risankizumab in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed.

Immunisations

Prior to initiating therapy with risankizumab, completion of all appropriate immunisations should be considered according to current immunisation guidelines. If a patient has received live vaccination (viral or bacterial), it is recommended to wait at least 4 weeks prior to starting treatment with risankizumab. Patients treated with risankizumab should not receive live vaccines during treatment and for at least 21 weeks after treatment (see section 5.2).

Hypersensitivity

Serious hypersensitivity reactions, including anaphylaxis, have been reported with use of risankizumab (see section 4.8). If a serious hypersensitivity reaction occurs, administration of risankizumab should be discontinued immediately and appropriate therapy initiated.

Excipients with known effect

Skyrizi 180 mg and 360 mg solution for injection in cartridge

Polysorbate

This medicinal product contains 0.24 mg of polysorbate 20 in each 180 mg dose and 0.48 mg of polysorbate 20 in each 360 mg dose. Polysorbates may cause allergic reactions.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per cartridge, that is to say essentially 'sodium-free'.

Skyrizi 90 mg solution for injection in pre-filled syringe

Polysorbate

This medicinal product contains 0.8 mg of polysorbate 20 in each 360 mg dose. Polysorbates may cause allergic reactions.

Sorbitol

This medicinal product contains 164 mg sorbitol per 360 mg dose.
The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per 360 mg dose, that is to say essentially 'sodium free'.

Skyrizi 180 mg solution for injection in pre-filled syringe

Polysorbate

This medicinal product contains 0.24 mg of polysorbate 20 in each dose 180 mg dose and 0.48 mg of polysorbate 20 in each 360 mg dose. Polysorbates may cause allergic reactions.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per 180 mg dose and 360 mg dose, that is to say essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

Risankizumab is not expected to undergo metabolism by hepatic enzymes or renal elimination. Interactions between risankizumab and inhibitors, inducers, or substrates of medicinal product metabolising enzymes are not expected and no dose adjustment is needed (see section 5.2).

Concomitant immunosuppressive therapy

The safety and efficacy of risankizumab in combination with immunosuppressants, including biologics, have not been evaluated.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 21 weeks after treatment.

Pregnancy

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of risankizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of risankizumab during pregnancy.

Breast-feeding

It is unknown whether risankizumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which decreases to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period. A decision should be made whether to discontinue/abstain from risankizumab therapy, taking into account the benefit of breast-feeding to the child and the benefit of risankizumab therapy to the woman.

Fertility

The effect of risankizumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Risankizumab has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions were upper respiratory infections (15.6% in Crohn's disease and 26.2% in ulcerative colitis).

Tabulated list of adverse reactions

Adverse reactions for risankizumab from clinical studies (Table 1) are listed by MedDRA system organ class and are based on the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: List of adverse reactions

System Organ Class	Frequency	Adverse reactions
Infections and infestations	Very common	Upper respiratory infections[a]
	Common	Tinea infections[b]
	Uncommon	Folliculitis
Immune system disorders	Rare	Anaphylactic reactions
Nervous system disorders	Common	Headache[c]
Skin and subcutaneous tissue disorders	Common	Pruritus Rash Eczema
	Uncommon	Urticaria
General disorders and administration site conditions	Common	Fatigue[d] Injection site reactions[e]

[a] Includes: respiratory tract infection (viral, bacterial or unspecified), sinusitis (including acute), rhinitis, nasopharyngitis, pharyngitis (including viral), tonsillitis, laryngitis, tracheitis

[b] Includes: tinea pedis, tinea cruris, body tinea, tinea versicolor, tinea manuum, onychomycosis, tinea infection

[c] Includes: headache, tension headache, sinus headache

[d] Includes: fatigue, asthenia, malaise

[e] Includes: injection site bruising, erythema, haematoma, haemorrhage, irritation, pain, pruritus, reaction, swelling, induration, hypersensitivity, nodule, rash, urticaria, vesicles, warmth; infusion site erythema, extravasation, reaction, swelling

Description of selected adverse reactions

Psoriasis

Infections

Over the entire psoriasis programme including long-term exposure to risankizumab, the rate of infections was 75.5 events per 100 subject-years. The majority of cases were non-serious and mild to moderate in severity and did not lead to discontinuation of risankizumab. The rate of serious infections was 1.7 events per 100 subject-years (see section 4.4).

Crohn's disease

Overall, the safety profile observed in patients with Crohn's disease treated with risankizumab was consistent with the safety profile observed in patients across indications.

Infections

The rate of infections in the pooled data from the 12-week induction studies was 83.3 events per 100 subject-years in subjects treated with risankizumab 600 mg intravenously compared to 117.7 events per 100 subject-years in placebo. The rate of serious infections was 3.4 events per 100 subject-years in subjects treated with risankizumab 600 mg intravenously compared to 16.7 events per 100 subject-years in placebo (see section 4.4).

The rate of infections in the 52-week maintenance study was 57.7 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 76.0 events per 100 subject-years in subjects who received placebo after risankizumab induction. The

rate of serious infections was 6.0 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 5.0 events per 100 subject-years in subjects who received placebo after risankizumab induction (see section 4.4).

Ulcerative colitis

Overall, the safety profile observed in patients with ulcerative colitis treated with risankizumab was consistent with the safety profile observed in patients across indications.

Infections

The rate of infections in the pooled data from the 12-week induction study was 78.3 events per 100 subject-years in subjects treated with risankizumab 1 200 mg intravenously compared to 74.2 events per 100 subject-years in placebo. The rate of serious infections was 3.0 events per 100 subject-years in subjects treated with risankizumab 1 200 mg intravenously compared to 5.4 events per 100 subject-years in placebo (see section 4.4).

The rate of infections in the 52-week maintenance study was 67.4 events per 100 subject-years in subjects treated with risankizumab 180 mg subcutaneously and 56.5 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 64.6 events per 100 subject-years in subjects who received placebo after risankizumab induction. The rate of serious infections was 1.1 events per 100 subject-years in subjects treated with risankizumab 180 mg subcutaneously and 0.6 events per 100 subject-years in subjects treated with risankizumab 360 mg subcutaneously after risankizumab induction compared to 2.3 events per 100 subject-years in subjects who received placebo after risankizumab induction (see section 4.4).

Immunogenicity

For subjects with Crohn's disease treated with risankizumab at the recommended intravenous induction and subcutaneous maintenance doses for up to 64 weeks in CD clinical trials, treatment-emergent anti-drug antibodies and neutralizing antibodies were detected in 3.4% (2/58) and 0% (0/58) of evaluated subjects, respectively.

For subjects with ulcerative colitis treated with risankizumab at the recommended intravenous induction and subcutaneous maintenance doses (180 mg or 360 mg) for up to 64 weeks in ulcerative colitis clinical trials, treatment-emergent anti-drug antibodies and neutralising antibodies were detected in 8.9% (8/90) and 6.7% (6/90) for the 180 mg subcutaneous dose, or 4.4% (4/91) and 2.2% (2/91) for the 360 mg subcutaneous dose, of evaluated subjects, respectively.

Antibodies to risankizumab including neutralizing antibodies were not associated with changes in clinical response or safety.

Elderly

There is limited safety information in subjects aged ≥65 years.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC18

Mechanism of action

Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds with high affinity to the p19 subunit of human interleukin 23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor complex. IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, risankizumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokines.

Pharmacodynamic effects

In a study of subjects with psoriasis, expression of genes associated with the IL-23/IL-17 axis was decreased in the skin after single doses of risankizumab. Reductions in epidermal thickness, infiltration of inflammatory cells, and expression of psoriatic disease markers were also observed in psoriatic lesions.

In a Phase 2 study of subjects with Crohn's disease, expression of genes associated with the IL-23/Th17 axis were decreased in gut tissue after multiple doses of risankizumab. Reductions in faecal calprotectin (FCP), serum C reactive protein (CRP) and IL-22 were also observed after multiple doses in Phase 3 induction studies in Crohn's patients. Decreases in FCP, CRP and serum IL-22 were maintained out to week 52 of the maintenance study.

In a Phase 2b/3 study of subjects with ulcerative colitis, statistically significant and clinically meaningful reduction from baseline was observed in the inflammatory biomarkers, FCP and CRP, and in the IL-23 pathway-associated biomarker, serum IL-22, at week 12 of the induction study. Decreases in FCP, CRP and serum IL-22 were maintained out to week 52 of the maintenance study.

Clinical efficacy and safety

Crohn's disease

The efficacy and safety of risankizumab were assessed in 1 419 subjects with moderately to severely active Crohn's disease in three multicentre, randomised, double-blind, placebo-controlled clinical studies. Enrolled subjects were 16 years of age or older with a Crohn's Disease Activity Index (CDAI) of 220 to 450, an average daily stool frequency (SF) ≥4 and/or average daily abdominal pain score (APS) ≥2, and a Simple Endoscopic Score for CD (SES-CD) of ≥6, or ≥4 for isolated ileal disease, excluding the narrowing component and confirmed by a central reviewer.

There were two 12-week intravenous induction studies (ADVANCE and MOTIVATE), which included a 12-week extension period for subjects who did not achieve SF/APS clinical response (≥ 30% decrease in SF and/or ≥ 30% decrease in APS and both not worse than baseline) at week 12. ADVANCE and MOTIVATE were followed by a 52-week randomised withdrawal study of subcutaneous maintenance treatment (FORTIFY) that enrolled subjects with SF/APS clinical response to intravenous induction treatment, representing at least 64 weeks of therapy.

ADVANCE and MOTIVATE

In studies ADVANCE and MOTIVATE, subjects were randomised to receive risankizumab at either 600 mg (recommended dose), 1 200 mg, or placebo, at week 0, week 4, and week 8.

In ADVANCE, 58% (491/850) subjects had failed or were intolerant to treatment with one or more biologic therapies (prior biologic failure), and 42% (359/850) had failed or were intolerant to therapy with conventional therapies but not biologic therapies (without prior biologic failure). In ADVANCE, among the subjects without prior biologic failure, (87%) 314/359 were naïve to biologic therapy and the remaining 13% had received a biologic but never failed or demonstrated intolerance. All patients in MOTIVATE had prior biologic failure.

In both studies, a greater proportion of subjects treated with risankizumab achieved the co-primary endpoints of clinical remission at week 12 and endoscopic response at week 12 compared to placebo. Enhanced SF/APS clinical response and clinical remission were significant as early as week 4 in subjects treated with risankizumab and continued to improve through week 12 (Table 2).

Table 2. Efficacy results in ADVANCE and MOTIVATE

	ADVANCE			**MOTIVATE**		
	Placebo intravenously (N=175) %	**Risankizumab 600 mg intravenously (N=336) %**	**Treatment difference[d] (95% CI)**	**Placebo intravenously (N=187) %**	**Risankizumab 600 mg intravenously (N=191) %**	**Treatment difference[d] (95% CI)**
Co-primary endpoints						
Clinical remission at week 12[e]	22%	43%	22% [14%, 30%][a]	19%	35%	15% [6%, 24%][b]
Endoscopic response at week 12[f]	12%	40%	28% [21%, 35%][a]	11%	29%	18% [10%, 25%][a]
Additional endpoints						
Enhanced SF/APS clinical response at week 4[g]	31%	46%	15% [6%, 23%][b]	32%	45%	14% [4%, 23%][c]
Enhanced SF/APS clinical response at week 12[g]	42%	63%	21% [12%, 30%][a]	39%	62%	23% [13%, 33%][a]
CDAI <150 at week 4	10%	18%	8% [1%, 14%][c]	11%	21%	10% [2%, 17%][c]
CDAI <150 at week 12	25%	45%	21% [12%, 29%][a]	20%	42%	22% [13%, 31%][a]
Mucosal healing at week 12[h]	(N=173) 8%	(N=336) 21%	14% [8%, 19%][a]	(N=186) 4%	(N=190) 14%	9% [4%, 15%][b]
Endoscopic remission at week 12[i]	9%	24%	15% [9%, 21%][a]	4%	19%	15% [9%, 21%][a]

[a] Statistically significant under multiplicity-control for risankizumab vs placebo comparison ($p<0.001$).
[b] Statistically significant under multiplicity-control for risankizumab vs placebo comparison ($p\leq0.01$).
[c] Nominal $p \leq 0.05$ risankizumab vs placebo comparison.
[d] Adjusted treatment difference.

[e] Clinical remission based on SF/APS: average daily SF ≤2.8 and not worse than baseline and average daily AP score ≤1 and not worse than baseline.
[f] Endoscopic response: greater than 50% decrease in SES-CD from baseline, or a decrease of at least 2 points for subjects with a baseline score of 4 and isolated ileal disease.
[g] Enhanced SF/APS clinical response: ≥60% decrease in average daily SF and/or ≥35% decrease in average daily AP score and both not worse than Baseline, and/or clinical remission.
[h] Mucosal healing: SES-CD ulcerated surface subscore of 0 in subjects with a subscore of ≥1 at Baseline.
[i] Endoscopic remission: SES-CD ≤4 and at least a 2 point reduction versus Baseline and no subscore greater than 1 in any individual variable.

At week 12, a higher proportion of subjects treated with risankizumab achieved a decrease of at least 100 points in baseline CDAI compared to placebo (ADVANCE, risankizumab =60%, placebo=37%, p<0.001; MOTIVATE, risankizumab =60%, placebo=30%, p<0.001).

At week 12, a higher proportion of subjects treated with risankizumab achieved both enhanced SF/APS clinical response and endoscopic response at week 12 compared to placebo (ADVANCE, risankizumab =31%, placebo=8%, p<0.001; MOTIVATE, risankizumab =21%, placebo=7%, p<0.001).

The results for the co-primary endpoints for the subgroups (without allowing for multiplicity) of subjects with and without prior biologic failure are presented in Table 3.

Table 3. Efficacy results at week 12 in subgroups of subjects with prior biologic treatment failure and subjects without prior biologic failure in ADVANCE

	ADVANCE		
	Placebo intravenously	**Risankizumab 600 mg**	**Treatment difference (95% CI)**
Clinical remission per SF/AP Score			
Prior biologic failure	23% (N=97)	41% (N=195)	18% [7%, 29%]
Without prior biologic failure	21% (N=78)	48% (N=141)	27% [15%, 39%]
Endoscopic response			
Prior biologic failure	11% (N=97)	33% (N=195)	21% [12%, 31%]
Without prior biologic failure	13% (N=78)	50% (N=141)	38% [27%, 49%]

In ADVANCE, a higher proportion of subjects treated with risankizumab with and without prior biologic failure achieved CDAI<150 compared to placebo (With prior biologic failure, risankizumab =42%, placebo=26%; Without prior biologic failure, risankizumab =49%, placebo=23%).

CD-related hospitalisations

Rates of CD-related hospitalisations through week 12 were lower in subjects treated with risankizumab compared to placebo (ADVANCE, risankizumab =3%, placebo=12%, p<0.001; MOTIVATE, risankizumab =3%, placebo=11%, p≤0.01).

FORTIFY

The maintenance study FORTIFY evaluated 462 subjects with SF/APS clinical response to 12 weeks of risankizumab intravenous induction treatment in studies ADVANCE and MOTIVATE. Subjects were randomised to continue to receive a maintenance regimen of risankizumab 360 mg subcutaneously (recommended dose), or risankizumab 180 mg subcutaneously every 8 weeks, or to

withdraw from risankizumab induction and receive placebo subcutaneously every 8 weeks for up to 52 weeks.

The co-primary endpoints were clinical remission at week 52 and, endoscopic response at week 52. Co-primary endpoints were also measured in subjects with and without prior biologic failure (see Table 4).

Table 4. Efficacy results in FORTIFY at week 52 (64 weeks from initiation of induction dose)

	FORTIFY		
	Risankizumab intravenous induction/ Placebo subcutaneously[f] (N=164) %	**Risankizumab intravenous induction/ Risankizumab 360 mg subcutaneously (N=141) %**	**Treatment difference (95% CI)**
Co-primary endpoints			
Clinical remission	40%	52%	15% [5%, 25%][a,g]
Prior biologic failure	34% (N=123)	48% (N=102)	14% [1%,27%]
Without prior biologic failure	56% (N=41)	62% (N=39)	5% [-16%,27%]
Endoscopic response	22%	47%	28% [19%, 37%][b,g]
Prior biologic failure	20% (N=123)	44% (N=102)	23% [11%, 35%]
Without prior biologic failure	27% (N=41)	54% (N=39)	27% [6%, 48%]
Additional endpoints			
Enhanced SF/APS clinical response	49%	59%	13% [2%, 23%][e,g]
Maintenance of clinical remission[h]	(N = 91) 51%	(N = 72) 69%	21% [6%, 35%][d,g]
Endoscopic remission	13%	39%	28% [20%, 37%][c,g]
Mucosal healing	(N = 162) 10%	(N = 141) 31%	22% [14%, 30%][c,g]

[a] Statistically significant under multiplicity-control for risankizumab vs placebo comparison ($p \leq 0.01$).
[b] Statistically significant under multiplicity-control for risankizumab vs placebo comparison ($p < 0.001$).
[c] Nominal $p < 0.001$ risankizumab vs placebo comparison without overall type I error control.
[d] Nominal $p \leq 0.01$ risankizumab vs placebo comparison without overall type I error control.
[e] Nominal $p \leq 0.05$ risankizumab vs placebo comparison without overall type I error control.
[f] The induction-only group consisted of subjects who achieved clinical response to risankizumab induction therapy and were randomised to receive placebo in the maintenance study (FORTIFY).
[g] Adjusted treatment difference.
[h] Maintenance of clinical remission: clinical remission at week 52 in subjects with clinical remission at week 0.

Deep remission (clinical remission and endoscopic remission) at week 52 was observed at higher rates in subjects treated with risankizumab intravenously / risankizumab subcutaneously compared to subjects who received risankizumab intravenously /placebo subcutaneously (28% vs. 10%, respectively, nominal $p < 0.001$).

At week 52, a higher proportion of subjects treated with risankizumab intravenously / risankizumab subcutaneously achieved CDAI < 150 compared to risankizumab intravenously /placebo subcutaneously (52% vs. 41%, respectively, nominal $p \leq 0.01$). A higher proportion of subjects treated with risankizumab intravenously/ risankizumab subcutaneously achieved a decrease of at least 100 points in baseline CDAI score compared to subjects treated with risankizumab intravenously /placebo subcutaneously (62% vs. 48%, respectively, nominal $p \leq 0.01$).

91 subjects who did not demonstrate SF/APS clinical response 12 weeks after risankizumab induction in studies ADVANCE and MOTIVATE received subcutaneous 360 mg dose of risankizumab at week 12 and week 20. Of these subjects, 64% (58/91) achieved SF/APS clinical response at week 24; 33 of the subjects achieving SF/APS clinical response enrolled in FORTIFY and continued receiving risankizumab 360 mg subcutaneously every 8 weeks for up to 52 weeks. Among these subjects, 55% (18/33) achieved clinical remission and 45% (15/33) achieved endoscopic response at week 52.

During FORTIFY, 30 subjects had loss of response to risankizumab 360 mg subcutaneously treatment and received rescue treatment with risankizumab (1 200 mg intravenous single dose, followed by 360 mg subcutaneously every 8 weeks). Of these subjects, 57% (17/30) achieved SF/APS clinical response at week 52. In addition, 20% (6/30) and 34% (10/29) of subjects achieved clinical remission and endoscopic response at week 52, respectively.

Health-related and quality of life outcomes

Health-related quality of life was assessed by the Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-Item Short Form Health Survey (SF-36). Improvement in fatigue was evaluated by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale. Work productivity was assessed by the Work Productivity and Activity Impairment CD (WPAI-CD) Questionnaire.

At week 12 of ADVANCE and MOTIVATE, subjects treated with risankizumab achieved clinically meaningful improvements from baseline in IBDQ total score, all IBDQ domain scores (bowel symptoms, systemic function, emotional function, and social function), SF-36 Physical and Mental Component Summary Score, FACIT-Fatigue and WPAI-CD compared to placebo. For WPAI-CD greater reductions in impairment while working, overall work impairment, and activity impairment were demonstrated in ADVANCE; and greater reduction in activity impairment was demonstrated in MOTIVATE. These improvements were maintained in subjects treated with risankizumab intravenously / risankizumab subcutaneously in FORTIFY through week 52.

Ulcerative colitis

The efficacy and safety of risankizumab was assessed in subjects with moderately to severely active ulcerative colitis in two multicentre, randomised, double-blind, placebo-controlled clinical studies. Enrolled subjects were ≥ 18 and ≤ 80 years of age with adapted Mayo Score (aMS) of 5 to 9 (using the Mayo scoring system, excluding Physician's Global Assessment) with an endoscopic subscore (ES) of 2 or 3 on screening endoscopy, confirmed by central review.

The 12-week intravenous induction study (INSPIRE) included a 12-week extension period for subjects who did not achieve clinical response [defined as a decrease from baseline in the aMS ≥ 2 points and ≥ 30% from baseline, and a decrease in rectal bleeding subscore (RBS) ≥ 1 or an absolute RBS ≤ 1] at Week 12. INSPIRE was followed by a 52-week randomised withdrawal study of subcutaneous maintenance treatment (COMMAND) that enrolled subjects with clinical response to 12 weeks of risankizumab intravenous induction treatment, representing at least 64 weeks of therapy.

INSPIRE

In study INSPIRE, 975 subjects were randomised and received either risankizumab 1 200 mg or placebo, at week 0, week 4, and week 8.

In INSPIRE, 52% (503/975) of subjects had failed (inadequate response or intolerance) one or more biologics therapies, JAK inhibitors, and/or S1P receptor modulators. Of these 503 subjects, 488 (97%) failed biologics and 90 (18%) failed JAK inhibitors.

Enrolled subjects were permitted to use a stable dose of oral corticosteroids (up to 20 mg/day prednisone or equivalent), immunomodulators, and aminosalicylates. At baseline in INSPIRE, 36% of

subjects received corticosteroids, 17% of subjects received immunomodulators and 73% of subjects received aminosalicylates. Patient disease activity was moderate (aMS ≤7) in 58% of subjects and severe (aMS >7) in 42% of subjects.

In INSPIRE, a significantly greater proportion of subjects treated with risankizumab achieved the primary endpoint of clinical remission per aMS [defined as stool frequency subscore (SFS) ≤ 1, and not greater than baseline, RBS = 0, and ES ≤ 1 without evidence of friability] at week 12 compared to placebo (Table 5). Results of the primary endpoint and key secondary endpoints are listed in Table 5.

Table 5. Efficacy results in INSPIRE at week 12

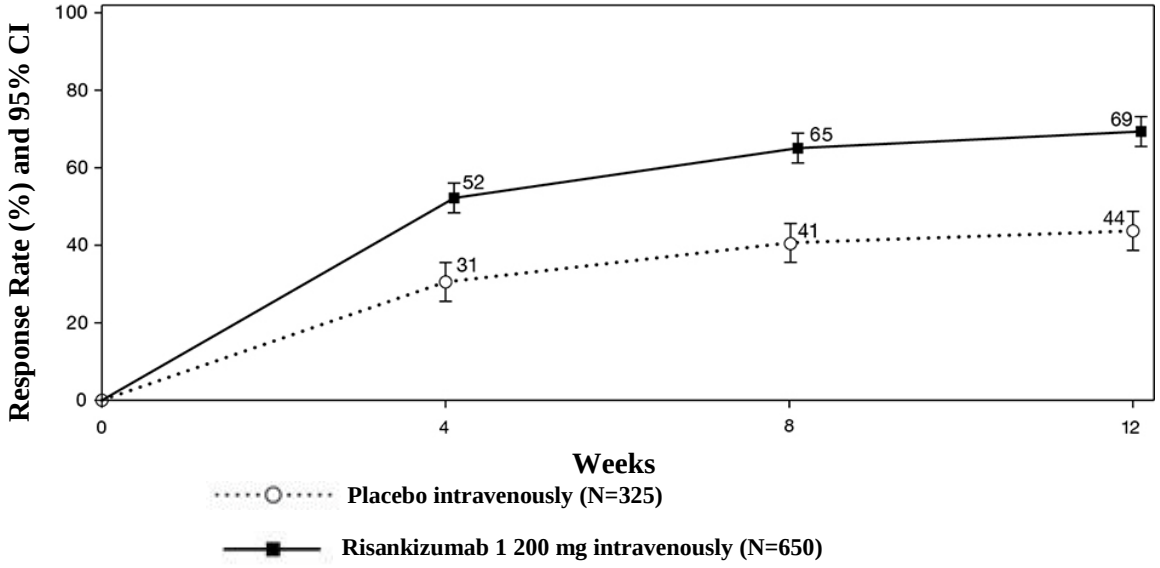
Endpoint	**Placebo intravenously (N=325) %**	**Risankizumab 1 200 mg intravenously (N=650) %**	**Treatment difference (95% CI)**
Disease activity and UC symptoms			
Clinical remission[ab]	6%	20%	14%[f] [10%, 18%]
With biologic and/or JAK inhibitor failure	4% (N=170)	11% (N=333)	7% [3%, 12%]
Without biologic and/or JAK inhibitor failure	8% (N=155)	30% (N=317)	21% [15%, 28%]
Clinical response[c]	36%	64%	29%[f] [22%, 35%]
With biologic and/or JAK inhibitor failure	31% (N=170)	55% (N=333)	24% [15%, 33%]
Without biologic and/or JAK inhibitor failure	41% (N=155)	74% (N=317)	33% [24%, 42%]
Endoscopic and histologic assessment			
Mucosal healing[d]	12%	37%	24%[f] [19%, 29%]
With biologic and/or JAK inhibitor failure	10% (N=170)	26% (N=333)	16% [9%, 22%]
Without biologic and/or JAK inhibitor failure	14% (N=155)	48% (N=317)	33% [26%, 41%]
Histologic-endoscopic mucosal healing[e]	8%	24%	17%[f] [12%, 21%]
With biologic and/or JAK inhibitor failure	7% (N=170)	16% (N=333)	9% [3%, 14%]
Without biologic and/or JAK inhibitor failure	8% (N=155)	33% (N=317)	25% [18%, 32%]

[a] Primary endpoint
[b] Clinical remission per aMS: SFS ≤ 1, and not greater than baseline, RBS = 0, and ES ≤ 1 without evidence of friability
[c] Clinical response per aMS: decrease from Baseline ≥ 2 points and ≥ 30%, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1
[d] ES ≤ 1 without the evidence of friability
[e] ES ≤ 1 without the evidence of friability and Geboes score ≤ 3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations or granulation tissue)
[f] $p < 0.00001$, adjusted treatment difference (95% CI)

Clinical disease activity and symptoms

The partial adapted Mayo score (paMS) is composed of SFS and RBS. Clinical response per paMS is defined as a decrease of ≥1 point and ≥30% from Baseline and a decrease in RBS ≥1 or an absolute RBS ≤1. The results of clinical response per paMS over time in INSPIRE are shown in Figure 1. Onset of efficacy was rapid with a greater proportion of subjects treated with risankizumab achieving clinical response as early as week 4 compared to placebo (52% vs 31%, respectively, p < 0.00001).

Figure 1. Proportion of subjects achieving clinical response per paMS over time in induction study INSPIRE



A significantly greater proportion of subjects treated with risankizumab compared to placebo had no abdominal pain (36% vs 26%, respectively, p < 0.01) and no bowel urgency (44% vs 28%, respectively, p < 0.00001) at week 12.

Other UC symptoms

Number of faecal incontinence episodes per week was reduced in a significantly greater amount in subjects treated with risankizumab compared to placebo at week 12 (change from baseline in risankizumab = -3.8, placebo = -2.2, p = 0.00003).

The proportion of subjects who had no nocturnal bowel movements was significantly greater in subjects treated with risankizumab compared to placebo at week 12 (67% vs 43%, respectively, p < 0.00001).

The proportion of subjects who had no tenesmus was significantly greater in subjects treated with risankizumab compared to placebo at week 12 (49% vs 30%, respectively, p < 0.00001).

Number of days with sleep interruption due to UC symptoms per week were reduced in a significantly greater amount in subjects treated with risankizumab compared to placebo at week 12 (change from baseline in risankizumab = -2.5, placebo = -1.5, p < 0.00001).

UC-related hospitalisations

Rates of UC-related hospitalisations through week 12 were significantly lower in subjects treated with risankizumab compared to placebo (1% vs 6%, respectively, p < 0.00001).

Extended treatment in week 12 non-responders

A total of 141 subjects who did not demonstrate clinical response at week 12 of risankizumab induction in INSPIRE received either subcutaneous 180 mg or 360 mg dose of risankizumab at week 12 and week 20. Of the 71 subjects who received risankizumab 180 mg subcutaneously and 70 subjects who received risankizumab 360 mg subcutaneously, 56% and 57% achieved clinical response at week 24, respectively.

COMMAND

The maintenance study COMMAND evaluated 548 subjects with clinical response after 12 weeks of risankizumab intravenous induction treatment in study INSPIRE. Subjects were randomised to receive a maintenance regimen of risankizumab 180 mg subcutaneously or 360 mg subcutaneously every 8 weeks, or to withdraw from risankizumab induction and receive placebo subcutaneously every 8 weeks for up to 52 weeks.

In COMMAND, 75% (411/548) of subjects had failed (inadequate response or intolerance) one or more biologics therapies, JAK inhibitors, and/or S1P receptor modulators prior to induction baseline. Of these 411 subjects, 407 (99%) failed biologics and 78 (19%) failed JAK inhibitors.

In COMMAND, a significantly greater proportion of the above 548 subjects treated with risankizumab 180 mg subcutaneously or risankizumab 360 mg subcutaneously achieved the primary endpoint of clinical remission per aMS at week 52 compared to placebo (see Table 6). Results of the primary endpoint and key secondary endpoints are listed in Table 6.

Table 6. Efficacy results in COMMAND at week 52 (64 weeks from initiation of induction dose)

Endpoint	**Risankizumab intravenous induction/ Placebo subcutaneously[+] (N=183) %**	**Risankizumab intravenous induction/ Risankizumab 180 mg subcutaneously (N=179) %**	**Risankizumab intravenous induction/ Risankizumab 360 mg subcutaneously (N=186) %**	**Treatment difference (97.5% CI)[++]**	
				Risankizumab intravenous induction/ Risankizumab 180 mg subcutaneously	**Risankizumab intravenous induction/ Risankizumab 360 mg subcutaneously**
Disease activity and UC symptoms					
Clinical remission[ab]	25%	40%	38%	16%[h] [6%, 27%]	14%[h] [4%, 24%]
With biologic and/or JAK inhibitor failure	23% (N=138)	37% (N=134)	29% (N=139)	13% [1%, 26%]	6% [-6%, 18%]
Without biologic and/or JAK inhibitor failure	31% (N=45)	51% (N=45)	62% (N=47)	20% [-3%, 43%]	31% [8%, 53%]
Maintenance of clinical remission[c]	40% (N=53)	70% (N=44)	50% (N=40)	29%[h] [7%, 51%]	13%[k] [-11%, 36%]
With biologic and/or JAK inhibitor failure	37% (N=35)	65% (N=26)	44% (N=25)	28% [0%, 56%]	7% [-22%, 36%]
Without biologic and/or JAK inhibitor failure	44% (N=18)	77% (N=18)	60% (N=15)	33% [-2%, 67%]	16% [-23%, 54%]
Corticosteroid-free clinical remission[d]	25%	40%	37%	16%[h] [6%, 26%]	14%[h] [3%, 24%]
With biologic and/or JAK inhibitor failure	23% (N=138)	36% (N=134)	29% (N=139)	13% [0%, 25%]	6% [-6%, 18%]

Without biologic and/or JAK inhibitor failure	31% (N=45)	51% (N=45)	60% (N=47)	20% [-3%, 43%]	28% [6%, 51%]
Clinical response[e]	52%	68%	62%	17%[i] [6%, 28%]	11%[j] [0%, 23%]
With biologic and/or JAK inhibitor failure	46% (N=138)	63% (N=134)	57% (N=139)	18% [4%, 31%]	11% [-2%, 25%]
Without biologic and/or JAK inhibitor failure	71% (N=45)	82% (N=45)	79% (N=47)	11% [-9%, 31%]	8% [-13%, 28%]
Endoscopic and histologic assessment					
Mucosal healing[f]	32%	51%	48%	20%[h] [9%, 31%]	17%[h] [7%, 28%]
With biologic and/or JAK inhibitor failure	30% (N=138)	48% (N=134)	39% (N=139)	17% [4%, 30%]	8% [-4%, 21%]
Without biologic and/or JAK inhibitor failure	36% (N=45)	60% (N=45)	76% (N=47)	24% [1%, 47%]	41% [19%, 62%]
Histologic-endoscopic mucosal healing[g]	23%	43%	42%	20%[h] [10%, 31%]	20%[h] [10%, 30%]
With biologic and/or JAK inhibitor failure	22% (N=138)	39% (N=134)	33% (N=139)	17% [5%, 29%]	11% [-1%, 23%]
Without biologic and/or JAK inhibitor failure	29% (N=45)	55% (N=45)	69% (N=47)	26% [3%, 49%]	40% [19%, 62%]

[+] The induction-only group consisted of subjects who achieved clinical response to risankizumab induction therapy and were randomised to receive placebo in the maintenance study (COMMAND).
[++] Adjusted difference for the overall treatment difference.
[a] Primary endpoint
[b] Clinical remission per aMS: SFS ≤ 1, and not greater than baseline, RBS = 0, and ES ≤ 1 without evidence of friability
[c] Clinical remission per aMS at Week 52 among subjects who achieved clinical remission at the end of induction treatment
[d] Clinical remission per aMS at Week 52 and corticosteroid-free for ≥90 days
[e] Clinical response per aMS: decrease from Baseline ≥ 2 points and ≥ 30%, and a decrease in RBS ≥ 1 or an absolute RBS ≤ 1
[f] ES of ≤ 1 without the evidence of friability
[g] ES ≤ 1 without the evidence of friability and Geboes score ≤ 3.1 (indicating neutrophil infiltration in <5% of crypts, no crypt destruction and no erosions, ulcerations or granulation tissue)
[h] Statistically significant under multiplicity-control for risankizumab vs placebo comparison ($p \leq 0.01$).
[i] Nominal $p \leq 0.01$ risankizumab vs placebo comparison
[j] Nominal $p \leq 0.05$ risankizumab vs placebo comparison
[k] $p = 0.2234$

Clinical disease activity and symptoms

A significantly greater proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously compared to risankizumab intravenously/placebo had no abdominal pain (47% vs 30%, respectively, $p < 0.001$) and no bowel urgency (54% vs 31%, respectively, $p < 0.00001$) at week 52. A greater proportion of subjects treated with risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo had no bowel urgency (49% vs 31%, respectively, $p < 0.001$) at week 52, and a numerically higher proportion of subjects had no abdominal pain compared to risankizumab intravenously/placebo (38% vs 30%, respectively, $p = 0.0895$) at week 52.

Other UC symptoms

The proportion of subjects who had no nocturnal bowel movements was greater in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo at week 52 (42% and 43% vs 30%, $p < 0.01$ and $p < 0.001$, respectively).

The proportion of subjects who had no tenesmus was greater in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo at week 52 (37% and 37% vs 23%, respectively, $p < 0.01$).

UC-related hospitalisations

Occurrence of UC-related hospitalisations through week 52 were numerically lower in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo (0.6 per 100 subject-years and 1.2 per 100 subject-years vs 3.1 per 100 subject-years, $p = 0.0949$ and $p = 0.2531$, respectively).

Endoscopic and histologic assessment

Endoscopic remission (normalisation of the endoscopic appearance of the mucosa) was defined as ES of 0. At week 12 of INSPIRE, a significantly greater proportion of subjects treated with risankizumab compared to placebo achieved endoscopic remission (11% vs 3%, respectively, $p < 0.00001$). At week 52 of COMMAND, a significantly greater proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo achieved endoscopic remission (23% and 24% vs 15%, respectively, $p < 0.05$).

Deep mucosal healing was defined as ES of 0 and Geboes score < 2.0 (indicating no neutrophil in crypts or lamina propria and no increase in eosinophil, no crypt destruction, and no erosions, ulcerations or granulation tissue). At week 12 of INSPIRE, a significantly greater proportion of subjects treated with risankizumab compared to placebo achieved deep mucosal healing (6% vs 1%, respectively, $p < 0.00001$). At week 52 of COMMAND, a numerically higher proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo achieved deep mucosal healing (13% and 16% vs 10%, $p = 0.2062$ and $p = 0.0618$, respectively).

In COMMAND, maintenance of mucosal healing at week 52 (ES $\leq$1 without friability) was seen in a greater proportion of subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously and risankizumab intravenously/risankizumab 360 mg subcutaneously compared to risankizumab intravenously/placebo among subjects who achieved mucosal healing at the end of induction (74% and 54% vs 47%, $p < 0.01$ and $p = 0.5629$, respectively).

Rescue treatment

During COMMAND, subjects who had loss of response to risankizumab subcutaneous treatment received rescue treatment with risankizumab (a single intravenous induction dose, followed by 360 mg subcutaneously every 8 weeks). Among these subjects, in the risankizumab 180 mg subcutaneously and risankizumab 360 mg subcutaneously treatment group, 85% (17/20) and 74% (26/35) achieved clinical response at week 52, respectively. In addition, 24% (6/25) and 35% (13/37) of subjects achieved clinical remission per aMS, and 38% (10/26) and 45% (17/38) of subjects achieved endoscopic improvement at week 52 in the risankizumab 180 mg subcutaneously and risankizumab 360 mg subcutaneously treatment group, respectively.

Week 24 responders

A total of 100 subjects did not demonstrate clinical response after 12 weeks of induction treatment, received either subcutaneous 180 mg (N=56) or 360 mg (N=44) dose of risankizumab at week 12 and week 20, demonstrated clinical response at week 24, and continued receiving risankizumab 180 mg or 360 mg subcutaneously every 8 weeks for up to 52 weeks in COMMAND. Among these subjects, 46% and 45% achieved clinical response per aMS at week 52, and 18% and 23% achieved clinical remission per aMS at week 52, for risankizumab 180 mg and 360 mg subcutaneously respectively.

Health-related and quality of life outcomes

Subjects treated with risankizumab achieved clinically meaningful improvements from baseline in the Inflammatory Bowel Disease Questionnaire (IBDQ) (bowel symptoms, systemic function, emotional function, and social function) compared to placebo. Changes from baseline in IBDQ total score at week 12 with risankizumab compared to placebo were 42.6 and 24.3, respectively. Changes from baseline in IBDQ total score at week 52 were 52.6, 50.3 and 35.0 in subjects treated with risankizumab intravenous/risankizumab 180 mg subcutaneously, risankizumab intravenous/risankizumab 360 mg subcutaneously and risankizumab intravenous/placebo, respectively.

Subjects receiving risankizumab experienced significantly greater improvement from baseline in fatigue, as measured by FACIT-F score at week 12 compared to placebo. Changes from baseline in FACIT-F score at week 12 with risankizumab compared to placebo were 7.9 and 3.3, respectively. Changes from baseline in FACIT-F score at week 52 were 10.9, 10.3 and 7.0 in subjects treated with risankizumab intravenously/risankizumab 180 mg subcutaneously, risankizumab intravenously/risankizumab 360 mg subcutaneously and risankizumab intravenously/placebo, respectively.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Skyrizi in one or more subsets of the paediatric population in the treatment of Crohn's disease and ulcerative colitis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetics of risankizumab was similar between plaque psoriasis and psoriatic arthritis, and between Crohn's disease and ulcerative colitis.

Absorption

Risankizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure across dose ranges of 18 to 360 mg and 0.25 to 1 mg/kg administered subcutaneously, and 200 to 1 800 mg and 0.01 to 5 mg/kg administered intravenously.

Following subcutaneous dosing of risankizumab, peak plasma concentrations were achieved between 3-14 days after dosing with an estimated absolute bioavailability of 74-89%. With dosing of 150 mg at week 0, week 4 and every 12 weeks thereafter, estimated steady-state peak and trough plasma concentrations are 12 and 2 µg/mL, respectively.

In subjects with Crohn's disease treated with 600 mg intravenous induction dose at weeks 0, 4, and 8 followed by 360 mg subcutaneous maintenance dose at week 12 and every 8 weeks thereafter, maximum median peak and trough concentrations are estimated to be 156 and 38.8 µg/mL respectively during the induction period (weeks 8-12) and steady-state median peak and trough concentrations are estimated to be 28.0 and 8.13 µg/mL respectively during the maintenance period (weeks 40-48).

In subjects with ulcerative colitis treated with 1 200 mg intravenous induction dose at weeks 0, 4, and 8 followed by 180 mg or 360 mg subcutaneous maintenance dose at week 12 and every 8 weeks thereafter, maximum median peak and trough concentrations are estimated to be 350 and 87.7 µg/mL respectively during the induction period (weeks 8-12) and steady-state median peak and trough concentrations are estimated to be 19.6 and 4.64 µg/mL for the 180 mg subcutaneous dose and 39.2 and 9.29 µg/mL for the 360 mg subcutaneous dose, respectively, during the maintenance period (weeks 40-48).

Distribution

The mean (±standard deviation) steady-state volume of distribution (V_{ss}) of risankizumab was 11.4 (±2.7) L in Phase 3 studies in subjects with psoriasis, indicating that the distribution of risankizumab is primarily confined to the vascular and interstitial spaces. In a typical 70 kg subject with Crohn's disease, V_{ss} was 7.68 L.

Biotransformation

Therapeutic IgG monoclonal antibodies are typically degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgGs. Risankizumab is not expected to be metabolised by cytochrome P450 enzymes.

Elimination

The mean (±standard deviation) systemic clearance (CL) of risankizumab was 0.3 (±0.1) L/day in Phase 3 studies in subjects with psoriasis. The mean terminal elimination half-life of risankizumab ranged from 28 to 29 days in Phase 3 studies in subjects with psoriasis. For a typical 70 kg subject with Crohn's disease, CL was 0.30 L/day and terminal elimination half-life was 21 days.

As an IgG1 monoclonal antibody, risankizumab is not expected to be filtered by glomerular filtration in the kidneys or to be excreted as an intact molecule in the urine.

Linearity/non-linearity

Risankizumab exhibited linear pharmacokinetics with approximately dose-proportional increases in systemic exposure (C_{max} and AUC) in the evaluated dose ranges of 18 to 360 mg or 0.25 to 1 mg/kg subcutaneous administration and 200 to 1800 mg and 0.01 to 5 mg/kg administered intravenously in healthy subjects or subjects with psoriasis, Crohn's disease or ulcerative colitis.

Interactions

Interaction studies were conducted in subjects with plaque psoriasis, Crohn's disease, or ulcerative colitis to assess the effect of repeated administration of risankizumab on the pharmacokinetics of cytochrome P450 (CYP) sensitive probe substrates. The exposure of caffeine (CYP1A2 substrate), warfarin (CYP2C9 substrate), omeprazole (CYP2C19 substrate), metoprolol (CYP2D6 substrate) and midazolam (CYP3A substrate) following risankizumab treatment were comparable to their exposures prior to risankizumab treatment, indicating no clinically meaningful interactions through these enzymes.

Population pharmacokinetic analyses indicated that risankizumab exposure was not impacted by concomitant medicinal products used by some subjects with plaque psoriasis during the clinical studies. Similar lack of impact by concomitant medicinal products was observed based on population pharmacokinetic analyses in Crohn's disease or ulcerative colitis.

Special populations

Paediatric population

The pharmacokinetics of risankizumab in paediatric subjects under 16 years of age has not been established. Of the 1 574 subjects with Crohn's disease exposed to risankizumab, 12 were 16 to 17 years old. Risankizumab exposures in 16 to 17 year-old subjects with Crohn's disease were similar to those in adults. Age was not found to have any significant impact on risankizumab exposures based on the population pharmacokinetic analyses.

Elderly

Of the 2 234 subjects with plaque psoriasis exposed to risankizumab, 243 were 65 years or older and 24 subjects were 75 years or older. Of the 1 574 subjects with Crohn's disease exposed to risankizumab, 72 were 65 years or older and 5 subjects were 75 years or older. Of the 1 512 subjects with ulcerative colitis exposed to risankizumab, 103 were 65 years or older and 8 subjects were 75 years or older. No overall differences in risankizumab exposure were observed between older and younger subjects who received risankizumab.

Patients with renal or hepatic impairment

No specific studies have been conducted to determine the effect of renal or hepatic impairment on the pharmacokinetics of risankizumab. Based on population pharmacokinetic analyses, serum creatinine levels, creatinine clearance, or hepatic function markers (ALT/AST/bilirubin) did not have a meaningful impact on risankizumab clearance in subjects with psoriasis, Crohn's disease, or ulcerative colitis.

As an IgG1 monoclonal antibody, risankizumab is mainly eliminated via intracellular catabolism and is not expected to undergo metabolism via hepatic cytochrome P450 enzymes or renal elimination.

Body weight

Risankizumab clearance and volume of distribution increase as body weight increases which may result in reduced efficacy in subjects with high body weight (>130 kg). However, this observation is based on a limited number of subjects with plaque psoriasis. Body weight had no clinically meaningful impact on risankizumab exposure or efficacy in psoriatic arthritis, Crohn's disease, or ulcerative colitis. No dose adjustment based on body weight is currently recommended.

Gender or race

The clearance of risankizumab was not significantly influenced by gender or race in adult subjects with plaque psoriasis, Crohn's disease or ulcerative colitis. No clinically meaningful differences in risankizumab exposure were observed in Chinese or Japanese subjects compared to Caucasian subjects in clinical pharmacokinetic studies in healthy volunteers.

5.3 Preclinical safety data

Nonclinical data revealed no special hazard for humans based on repeat-dose toxicity studies including safety pharmacology evaluations and an enhanced pre- and post- natal developmental toxicity study in cynomolgus monkeys at doses of up to 50 mg/kg/week, producing exposures 10 times the clinical exposures during induction at a dose of 600 mg intravenous every 4 weeks and 39 times the clinical exposures for maintenance when given 360 mg subcutaneously every 8 weeks for Crohn's disease. For ulcerative colitis, exposures were 5 times the clinical exposures during induction at a dose of 1 200 mg intravenously every 4 weeks and 65 or 32 times the clinical exposures for maintenance when given 180 or 360 mg subcutaneously every 8 weeks.

Mutagenicity and carcinogenicity studies have not been conducted with risankizumab. In a 26-week chronic toxicology study in cynomolgus monkeys at doses of up to 50 mg/kg/week (7 times the clinical exposures during induction at a dose of 600 mg intravenous every 4 weeks and 28 times the clinical exposures for maintenance when given 360 mg subcutaneously every 8 weeks for Crohn's disease and 3 times the clinical exposures during induction at a dose of 1 200 mg intravenously every 4 weeks and 45 or 23 times the clinical exposures for maintenance when given 180 or 360 mg subcutaneously every 8 weeks for ulcerative colitis), there were no pre-neoplastic or neoplastic lesions observed and no adverse immunotoxicity or cardiovascular effects were noted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Skyrizi 180 mg and 360 mg solution for injection in cartridge and Skyrizi 180 mg solution for injection in pre-filled syringe

Sodium acetate trihydrate
Acetic acid
Trehalose dihydrate
Polysorbate 20
Water for injections

Skyrizi 90 mg solution for injection in pre-filled syringe

Disodium succinate hexahydrate
Polysorbate 20
Sorbitol
Succinic acid
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.

The cartridge or pre-filled syringe(s) may be stored out of the refrigerator (up to a maximum of 25°C) for up to 24 hours.

Keep the cartridge or pre-filled syringe(s) in the outer carton in order to protect from light.

6.5 Nature and contents of container

Skyrizi 360 mg solution for injection in cartridge

A 360 mg solution in a single use cartridge made with cyclic olefin resin with coated chlorobutyl rubber septum and coated chlorobutyl rubber piston as product-contact materials, and a resin cap. The cartridge assembly is co-packed with an on-body injector (administration device). The fluid path within the on-body injector contains polyvinyl chloride tubing and a stainless steel 29-gauge needle. The on-body injector contains silver oxide-zinc batteries and an adhesive skin patch made from

polyester with an acrylic adhesive. The administration device is designed for use with the provided 360 mg cartridge.

Skyrizi 360 mg is available in packs containing 1 cartridge and 1 on-body injector.

Skyrizi 180 mg solution for injection in cartridge

A 180 mg solution in a single use cartridge made with cyclic olefin resin with coated chlorobutyl rubber septum and coated chlorobutyl rubber piston as product-contact materials, and a resin cap. The cartridge assembly is co-packed with an on-body injector (administration device). The fluid path within the on-body injector contains polyvinyl chloride tubing and a stainless steel 29-gauge needle. The on-body injector contains silver oxide-zinc batteries and an adhesive skin patch made from polyester with an acrylic adhesive. The administration device is designed for use with the provided 180 mg cartridge.

Skyrizi 180 mg is available in packs containing 1 cartridge and 1 on-body injector.

Skyrizi 90 mg solution for injection in pre-filled syringe

Pre-filled glass syringe with a fixed needle and needle cover, assembled in an automatic needle guard.

Skyrizi 90 mg is available in packs containing 4 pre-filled syringes.

Skyrizi 180 mg solution for injection in pre-filled syringe

Pre-filled glass syringe with a fixed needle and needle cover, assembled in an automatic needle guard.

Skyrizi 180 mg is available in packs containing 1 and 2 pre-filled syringes.

Not all presentations may be marketed.

6.6 Special precautions for disposal and other handling

Skyrizi 180 mg and 360 mg solution for injection in cartridge

Before injecting, the carton should be removed from the refrigerator and allowed to reach room temperature, out of direct sunlight, for 45 to 90 minutes without removing the cartridge from the carton.

Prior to use, a visual inspection of the cartridge is recommended. The solution is free from foreign particles and practically free from product-related particles. Skyrizi should not be used if the solution is cloudy or discoloured, or contains large particles. Do not shake the cartridge.

The solution should be colourless to yellow and clear to slightly opalescent.

Skyrizi 90 mg and 180 mg solution for injection in pre-filled syringe

Before injecting, the carton should be removed from the refrigerator and allow to reach room temperature out of direct sunlight, for 15 to 30 minutes without removing the pre-filled syringes from the carton.

Prior to use, a visual inspection of each pre-filled syringe is recommended. The solution may contain a few translucent to white product-related particles. Skyrizi should not be used if the solution is cloudy or discoloured, or contains large particles. Do not shake the pre-filled syringe.

The 90 mg solution for injection in pre-filled syringe should be colourless to slightly yellow and clear to slightly opalescent.

The 180 mg solution for injection in pre-filled syringe should be colourless to yellow and clear to slightly opalescent.

General precautions

Comprehensive instructions for use are provided in the package leaflet.

Each on-body injector with cartridge and pre-filled syringe are for single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

8. MARKETING AUTHORISATION NUMBER(S)

Skyrizi 360 mg solution for injection in cartridge

EU/1/19/1361/005

Skyrizi 180 mg solution for injection in cartridge

EU/1/19/1361/007

Skyrizi 90 mg solution for injection in pre-filled syringe

EU/1/19/1361/006

Skyrizi 180 mg solution for injection in pre-filled syringe

EU/1/19/1361/008
EU/1/19/1361/009

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 April 2019
Date of latest renewal: 5 January 2024

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

Boehringer Ingelheim Pharma GmbH & Co. KG
Birkendorfer Str. 65
88397 Biberach a.d.R.
GERMANY

and

AbbVie Bioresearch Center Inc.
100 Research Drive
Worcester
MA 01605
USA

and

AbbVie Biotechnology Ltd.
Road Number 2, Km 59.2
Barceloneta
Puerto Rico 00617
USA

and

AbbVie Operations Singapore PTE Ltd
23 Tuas South Avenue 6
Singapore 637022

Name and address of the manufacturer(s) responsible for batch release

AbbVie S.r.l.
148, Pontina Km 52 snc
04011
Campoverde di Aprilia (LT)
ITALY

and

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
GERMANY

and

AbbVie Biotechnology GmbH
Knollstrasse
67061 Ludwigshafen
GERMANY

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Periodic safety update reports (PSURs)

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.
An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 150 mg solution for injection in pre-filled pen
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg risankizumab in 1 mL.

3. LIST OF EXCIPIENTS

Excipients: sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pre-filled pen

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

Open here

For more information and support on Skyrizi go to www.skyrizi.eu or scan this code.
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

skyrizi 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 150 mg injection
risankizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 150 mg solution for injection in pre-filled syringe
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg risankizumab in 1 mL.

3. LIST OF EXCIPIENTS

Excipients: sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

Open here

For more information and support on Skyrizi go to www.skyrizi.eu or scan this code.
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

skyrizi 150 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

SYRINGE SLEEVE

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 150 mg solution for injection in pre-filled syringe
risankizumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

AbbVie (as logo)

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

For subcutaneous use

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 150 mg injection
risankizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 75 mg solution for injection in pre-filled syringe
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 75 mg risankizumab in 0.83 mL.

3. LIST OF EXCIPIENTS

Excipients: disodium succinate hexahydrate, succinic acid, sorbitol, polysorbate 20 and water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
2 pre-filled syringes
2 alcohol pads

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

Open here

For more information and support on Skyrizi go to www.skyrizi.eu or scan this code.
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

skyrizi 75 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN

NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 75 mg solution for injection in pre-filled syringe
risankizumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

AbbVie (as logo)

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

For subcutaneous use

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 75 mg injection
risankizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 600 mg concentrate for solution for infusion
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains 600 mg of risankizumab in 10 mL.

3. LIST OF EXCIPIENTS

Excipients: sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

concentrate for solution for infusion
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Intravenous use after dilution

For single use only.

Open

For more information and support on Skyrizi go to www.skyrizi.eu or scan this code.
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 600 mg sterile concentrate
risankizumab
IV use after dilution

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

AbbVie (as logo)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 360 mg solution for injection in cartridge
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each cartridge contains 360 mg of risankizumab in 2.4 mL.

3. LIST OF EXCIPIENTS

Excipients: sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 cartridge
1 on-body injector

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

Open here

For more information and support on Skyrizi go to www.skyrizi.eu or scan this code.
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the cartridge in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

skyrizi 360 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN

NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

CARTRIDGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 360 mg injection
risankizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

AbbVie (as logo)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 180 mg solution for injection in cartridge
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each cartridge contains 180 mg of risankizumab in 1.2 mL.

3. LIST OF EXCIPIENTS

Excipients: sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 cartridge
1 on-body injector

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

Open here

For more information and support on Skyrizi go to www.skyrizi.eu or scan this code.
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the cartridge in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

skyrizi 180 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN

NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

CARTRIDGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 180 mg injection
risankizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

AbbVie (as logo)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 90 mg solution for injection in pre-filled syringe
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 90 mg risankizumab in 1 mL.

3. LIST OF EXCIPIENTS

Excipients: disodium succinate hexahydrate, polysorbate 20, sorbitol, succinic acid and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
4 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 90 mg solution for injection in pre-filled syringe
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 90 mg risankizumab in 1 mL.

3. LIST OF EXCIPIENTS

Excipients: disodium succinate hexahydrate, polysorbate 20, sorbitol, succinic acid and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

Open here

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

SYRINGE SLEEVE

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 90 mg solution for injection in pre-filled syringe
risankizumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

AbbVie (as logo)

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

For subcutaneous use

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 90 mg injection
risankizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 180 mg solution for injection in pre-filled syringe
risankizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 180 mg risankizumab in 1.2 mL.

3. LIST OF EXCIPIENTS

Excipients: sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled syringe
2 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Subcutaneous use

For single use only.

Open here

For more information and support on Skyrizi go to www.skyrizi.eu or scan this code.
QR code to be included

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

Keep the pre-filled syringe(s) in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1361/008
EU/1/19/1361/009

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

skyrizi 180 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC

SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

SYRINGE SLEEVE (1- and 2-pack)

1. NAME OF THE MEDICINAL PRODUCT

Skyrizi 180 mg solution for injection in pre-filled syringe
risankizumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

AbbVie (as logo)

3. EXPIRY DATE

4. BATCH NUMBER

5. OTHER

For subcutaneous use

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Skyrizi 180 mg injection
risankizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Skyrizi 150 mg solution for injection in pre-filled pen
risankizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skyrizi is and what it is used for

Skyrizi contains the active substance risankizumab.

Skyrizi is used to treat the following inflammatory diseases:

- Plaque psoriasis
- Psoriatic arthritis

How Skyrizi works
This medicine works by stopping a protein in the body called ‘IL-23’, which causes inflammation.

Plaque psoriasis
Skyrizi is used to treat adults with moderate to severe plaque psoriasis. Skyrizi reduces inflammation and can therefore help reduce symptoms of plaque psoriasis such as burning, itching, pain, redness, and scaling.

Psoriatic arthritis
Skyrizi is used to treat adults with psoriatic arthritis. Psoriatic arthritis is a disease that causes inflamed joints and psoriasis. If you have active psoriatic arthritis, you may first be given other medicines. If these medicines do not work well enough, you will be given Skyrizi either alone or in combination with other medicines to treat your psoriatic arthritis.

Skyrizi reduces inflammation and can therefore help to reduce pain, stiffness, and swelling in and around your joints, pain and stiffness in your spine, psoriatic skin rash, psoriatic nail damage, and it may slow down damage to the bone and cartilage in your joints. These effects can ease your normal daily activities, reduce tiredness, and improve your quality of life.

2. What you need to know before you use Skyrizi

Do not use Skyrizi
- if you are allergic to risankizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an infection, including active tuberculosis, which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and during the use of Skyrizi:
- if you currently have an infection or if you have an infection that keeps coming back.
- if you have tuberculosis (TB).
- if you have recently received or plan to receive an immunisation (vaccine). You should not be given certain types of vaccines while using Skyrizi.

It is important to keep a record of the batch number of your Skyrizi.
Every time you get a new pack of Skyrizi, note down the date and the batch number (which is on the packaging after "Lot") and keep this information in a safe place.

Serious allergic reactions
Skyrizi can cause serious side effects, including serious allergic reactions ('anaphylaxis').
Tell your doctor or seek medical help immediately if you notice any signs of an allergic reaction while you are taking Skyrizi such as:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness
- severe itching of the skin, with a red rash or raised bumps

Children and adolescents
Skyrizi is not recommended for children and adolescents under 18 years of age. This is because Skyrizi has not been studied in this age group.

Other medicines and Skyrizi
Tell your doctor, pharmacist or nurse:
- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. You should not be given certain types of vaccines while using Skyrizi.

If you are not sure, talk to your doctor, pharmacist or nurse before and during the use of Skyrizi.

Pregnancy, contraception and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known how this medicine will affect the baby.

If you are a woman who can become pregnant, you should use contraception while using this medicine and for at least 21 weeks after your last dose of Skyrizi.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine.

Driving and using machines
Skyrizi is not likely to affect your driving and use of machines.

Skyrizi contains polysorbate and sodium
This medicine contains 0.2 mg of polysorbate 20 in each 150 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per pre-filled pen, that is to say essentially ‘sodium-free’.

3. How to use Skyrizi

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

This medicine is given as an injection under your skin (called a ‘subcutaneous injection’).

How much Skyrizi to use

Each dose is 150 mg given as a single injection. After the first dose, you will have the next dose 4 weeks later, and then every 12 weeks.

You and your doctor, pharmacist or nurse will decide if you should inject this medicine yourself. Do not inject yourself with this medicine unless you have been trained by your doctor, pharmacist or nurse. A caregiver may also give your injection after they have been trained.

Read section 7 ‘Instructions for use’ at the end of this leaflet before injecting Skyrizi yourself.

If you use more Skyrizi than you should
If you have used more Skyrizi than you should or the dose has been given sooner than prescribed, talk to your doctor.

If you forget to use Skyrizi
If you forget to use Skyrizi, inject a dose as soon as you remember. Talk to your doctor if you are not sure what to do.

If you stop using Skyrizi
Do not stop using Skyrizi without talking to your doctor first. If you stop treatment, your symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Allergic reactions – these may need urgent treatment. Tell your doctor or get emergency medical help straight away if you notice any of the following signs:

Serious allergic reactions (‘anaphylaxis’) are rare in people taking Skyrizi (may affect up to 1 in a 1 000 people). Signs include:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness

Talk to your doctor or get medical help immediately if you have the following symptoms.
Symptoms of a serious infection such as:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters

Your doctor will decide if you can keep using Skyrizi.

Other side effects
Tell your doctor, pharmacist or nurse if you get any of the following side effects

Very common: may affect more than 1 in 10 people
- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people
- feeling tired
- fungal skin infection
- injection site reactions (such as redness or pain)
- itching
- headache
- rash
- eczema

Uncommon: may affect up to 1 in 100 people
- small raised red bumps on the skin
- hives (urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Skyrizi

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the pen label and outer carton after 'EXP'.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Keep the pre-filled pen in the original carton in order to protect from light.

If needed, you may also store the pre-filled pen out of the refrigerator (up to a maximum of 25°C) for up to 24 hours in the original carton to protect from light.

Do not use this medicine if the liquid is cloudy or contains flakes or large particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Skyrizi contains
- The active substance is risankizumab. Each pre-filled pen contains 150 mg of risankizumab in 1 mL solution.
- The other ingredients are sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See section 2, "Skyrizi contains polysorbate and sodium".

What Skyrizi looks like and contents of the pack
Skyrizi is a clear and colourless to yellow liquid in a pre-filled pen. The liquid may contain tiny white or clear particles.

Each pack contains 1 pre-filled pen.

Marketing Authorisation Holder and Manufacturer

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

България
АбВи ЕООД
Тел: +359 2 90 30 430

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Eesti
AbbVie OÜ
Tel: +372 623 1011

Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10

France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Magyarország
AbbVie Kft.
Tel: +36 1 455 8600

Malta
V.J.Salomone Pharma Limited
Tel: +356 21220174

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Norge
AbbVie AS
Tlf: +47 67 81 80 00

Österreich
AbbVie GmbH
Tel: +43 1 20589-0

Polska
AbbVie Sp. z o.o.
Tel: +48 22 372 78 00

Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

Hrvatska
AbbVie d.o.o.
Tel: +385 (0)1 5625 501

Ireland
AbbVie Limited
Tel: +353 (0)1 4287900

Ísland
Vistor
Tel: +354 535 7000

Italia
AbbVie S.r.l.
Tel: +39 06 928921

Κύπρος
Lifepharma (Z.A.M.) Ltd
Τηλ: +357 22 34 74 40

Latvija
AbbVie SIA
Tel: +371 67605000

România
AbbVie S.R.L.
Tel: +40 21 529 30 35

Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060

Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777

Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200

Sverige
AbbVie AB
Tel: +46 (0)8 684 44 600

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu/

Detailed and updated information on this product is available by scanning the QR code included below or on the outer carton with a smartphone. The same information is also available at the following URL:
www.skyrizi.eu

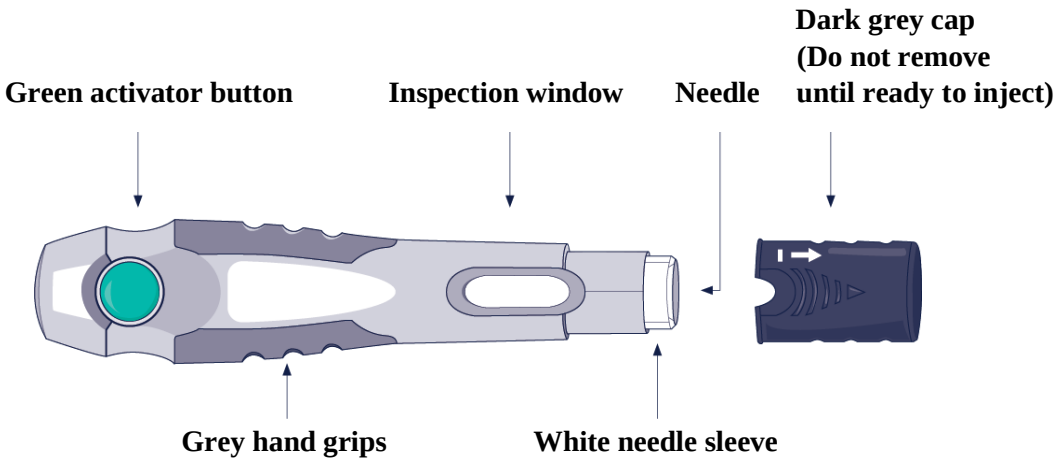
QR code to be included

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

7. Instructions for use

Please read all of section 7 before using Skyrizi

Skyrizi pre-filled pen



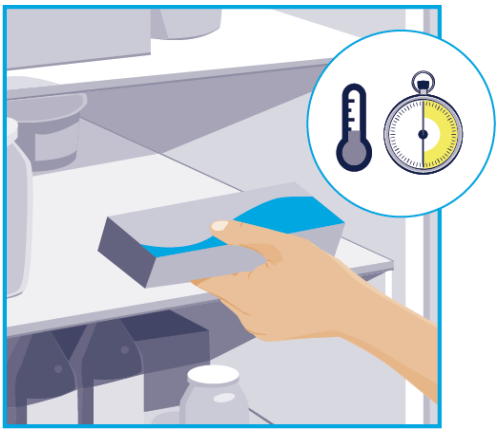
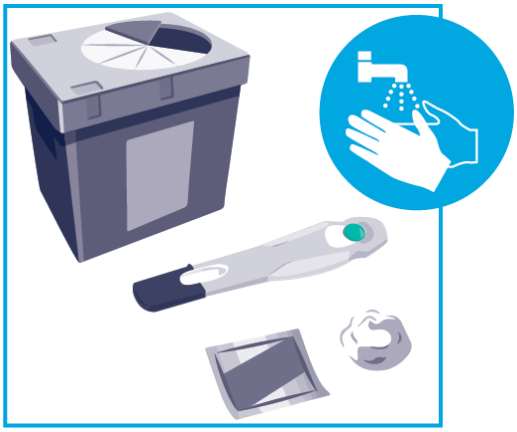
Important information to know before you inject Skyrizi

- You should receive training on how to inject Skyrizi before giving an injection. Talk to your doctor, pharmacist or nurse if you need help
- Mark the dates on your calendar so you know when to inject Skyrizi
- Keep Skyrizi in the original carton to protect the medicine from light until it is time to use it
- Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **30 to 90 minutes** before injecting
- **Do not** inject if the liquid in the inspection window is cloudy or contains flakes or large particles. The liquid should look clear to yellow and may contain tiny white or clear particles
- **Do not** shake the pen
- Wait to remove the dark grey cap until just before the injection

Return this medicine to the pharmacy

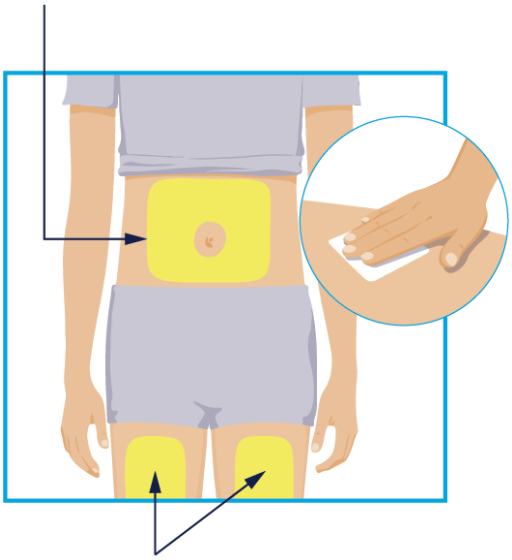
- if the expiry date (EXP) has passed
- if the liquid has ever been frozen (even if thawed)
- if the pen has been dropped or damaged
- if the carton perforations are broken

Follow the steps below each time you use Skyrizi

STEP 1 	Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **30 to 90 minutes** before injecting. • **Do not** remove the pen from the carton while allowing Skyrizi to reach room temperature • **Do not** warm Skyrizi in any other way. For example, **do not** warm it in a microwave or in hot water • **Do not** use the pen if liquid has been frozen, even if it has been thawed
STEP 2 	Place the following items on a clean, flat surface: • 1 pre-filled pen • 1 alcohol pad (not included in the carton) • 1 cotton ball or gauze pad (not included in the carton) • special disposal container (not included in the carton) Wash and dry your hands.

STEP 3

Areas to inject



Areas to inject

Choose from these 3 areas to inject:

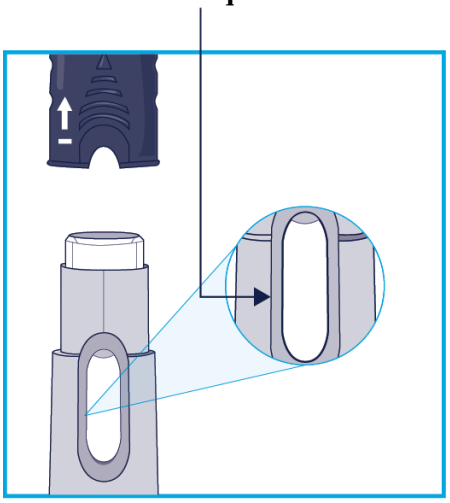
- front of left thigh
- front of right thigh
- your belly (abdomen) at least 5 cm from your belly button (navel)

Before the injection, wipe where you will inject in a circular motion with an alcohol pad.

- **Do not** touch or blow on the injection site after it is cleaned. Allow the skin to dry before injecting
- **Do not** inject through clothes
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, or has stretch marks
- **Do not** inject into areas affected by psoriasis

STEP 4

Check liquid



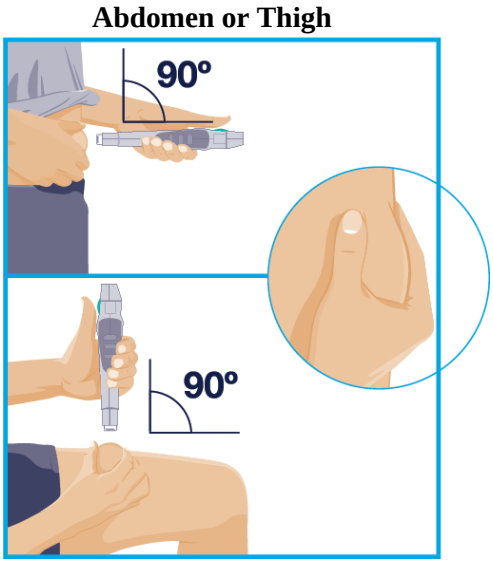
Hold the pen with the dark grey cap pointing up, as shown.

- Pull the dark grey cap straight off
- Throw the dark grey cap away

Check the liquid through the inspection window.

- It is normal to see bubbles in the liquid
- The liquid should look clear to yellow and may contain tiny white or clear particles
- **Do not** use if the liquid is cloudy or contains flakes or large particles

STEP 5



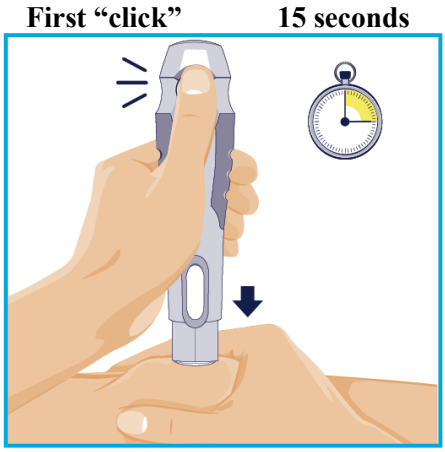
Hold the pen with your fingers on the grey hand grips.

Turn the pen so that the white needle sleeve points toward the injection site and you can see the green activator button.

Gently squeeze the skin at your injection site to make a raised area and hold it firmly.

Place the white needle sleeve straight (90º angle) against the raised injection site.

STEP 6



Hold the pen so that you can see the green activator button and inspection window.

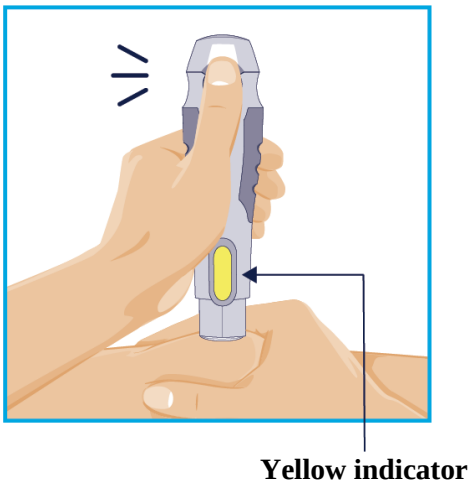
Push and keep pressing the pen down against the raised injection site.

- The pen will activate only if the white needle sleeve is pressed down against the injection site before pressing the green activator button

Press the green activator button and hold the pen for **15** seconds.

- A loud "click" means the start of the injection

STEP 7



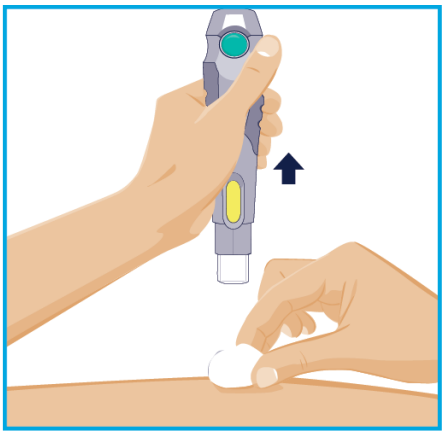
Keep pressing the pen down against the injection site.

The injection is complete when:

- the pen has made a second "click" **or**
- the yellow indicator has filled the inspection window

This takes **up to 15** seconds.

STEP 8



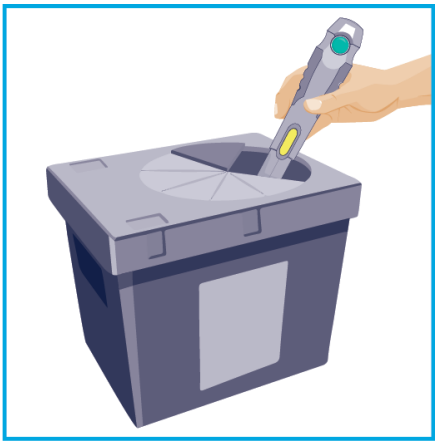
When the injection is complete, slowly pull the pen out from the skin.

The white needle sleeve will cover the needle tip and make another “click.”

After completing the injection, place a cotton ball or gauze pad on the skin at the injection site.

- **Do not** rub the injection site
- Slight bleeding at the injection site is normal

STEP 9



Throw away the used pen in a special disposal container straight after use.

- **Do not** throw away the used pen in the household waste
- Your doctor, pharmacist or nurse will tell you how to return the full special disposal container

Package leaflet: Information for the patient

Skyrizi 150 mg solution for injection in pre-filled syringe
risankizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skyrizi is and what it is used for

Skyrizi contains the active substance risankizumab.

Skyrizi is used to treat the following inflammatory diseases:

- Plaque psoriasis
- Psoriatic arthritis

How Skyrizi works
This medicine works by stopping a protein in the body called ‘IL-23’, which causes inflammation.

Plaque psoriasis
Skyrizi is used to treat adults with moderate to severe plaque psoriasis. Skyrizi reduces inflammation and can therefore help reduce symptoms of plaque psoriasis such as burning, itching, pain, redness, and scaling.

Psoriatic arthritis
Skyrizi is used to treat adults with psoriatic arthritis. Psoriatic arthritis is a disease that causes inflamed joints and psoriasis. If you have active psoriatic arthritis, you may first be given other medicines. If these medicines do not work well enough, you will be given Skyrizi either alone or in combination with other medicines to treat your psoriatic arthritis.

Skyrizi reduces inflammation and can therefore help to reduce pain, stiffness, and swelling in and around your joints, pain and stiffness in your spine, psoriatic skin rash, psoriatic nail damage, and it may slow down damage to the bone and cartilage in your joints. These effects can ease your normal daily activities, reduce tiredness, and improve your quality of life.

2. What you need to know before you use Skyrizi

Do not use Skyrizi
- if you are allergic to risankizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an infection, including active tuberculosis, which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and during the use of Skyrizi:
- if you currently have an infection or if you have an infection that keeps coming back.
- if you have tuberculosis (TB).
- if you have recently received or plan to receive an immunisation (vaccine). You should not be given certain types of vaccines while using Skyrizi.

It is important to keep a record of the batch number of your Skyrizi.
Every time you get a new pack of Skyrizi, note down the date and the batch number (which is on the packaging after "Lot") and keep this information in a safe place.

Serious allergic reactions
Skyrizi can cause serious side effects, including serious allergic reactions ('anaphylaxis').
Tell your doctor or seek medical help immediately if you notice any signs of an allergic reaction while you are taking Skyrizi such as:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness
- severe itching of the skin, with a red rash or raised bumps

Children and adolescents
Skyrizi is not recommended for children and adolescents under 18 years of age. This is because Skyrizi has not been studied in this age group.

Other medicines and Skyrizi
Tell your doctor, pharmacist or nurse:
- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. You should not be given certain types of vaccines while using Skyrizi.

If you are not sure, talk to your doctor, pharmacist or nurse before and during the use of Skyrizi.

Pregnancy, contraception and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known how this medicine will affect the baby.

If you are a woman who can become pregnant, you should use contraception while using this medicine and for at least 21 weeks after your last dose of Skyrizi.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine.

Driving and using machines
Skyrizi is not likely to affect your driving and use of machines.

Skyrizi contains polysorbate and sodium
This medicine contains 0.2 mg of polysorbate 20 in each 150 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per pre-filled syringe, that is to say essentially ‘sodium-free’.

3. How to use Skyrizi

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

This medicine is given as an injection under your skin (called a ‘subcutaneous injection’).

How much Skyrizi to use

Each dose is 150 mg given as a single injection. After the first dose, you will have the next dose 4 weeks later, and then every 12 weeks.

You and your doctor, pharmacist or nurse will decide if you should inject this medicine yourself. Do not inject yourself with this medicine unless you have been trained by your doctor, pharmacist or nurse. A caregiver may also give your injection after they have been trained.

Read section 7 ‘Instructions for use’ at the end of this leaflet before injecting Skyrizi yourself.

If you use more Skyrizi than you should
If you have used more Skyrizi than you should or the dose has been given sooner than prescribed, talk to your doctor.

If you forget to use Skyrizi
If you forget to use Skyrizi, inject a dose as soon as you remember. Talk to your doctor if you are not sure what to do.

If you stop using Skyrizi
Do not stop using Skyrizi without talking to your doctor first. If you stop treatment, your symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Allergic reactions – these may need urgent treatment. Tell your doctor or get emergency medical help straight away if you notice any of the following signs:

Serious allergic reactions (‘anaphylaxis’) are rare in people taking Skyrizi (may affect up to 1 in a 1 000 people). Signs include:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness

Talk to your doctor or get medical help immediately if you have the following symptoms.
Symptoms of a serious infection such as:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters

Your doctor will decide if you can keep using Skyrizi.

Other side effects
Tell your doctor, pharmacist or nurse if you get any of the following side effects

Very common: may affect more than 1 in 10 people
- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people
- feeling tired
- fungal skin infection
- injection site reactions (such as redness or pain)
- itching
- headache
- rash
- eczema

Uncommon: may affect up to 1 in 100 people
- small raised red bumps on the skin
- hives (urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Skyrizi

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the syringe label and outer carton after 'EXP'.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Keep the pre-filled syringe in the original carton in order to protect from light.

If needed, you may also store the pre-filled syringe out of the refrigerator (up to a maximum of 25°C) for up to 24 hours in the original carton to protect from light.

Do not use this medicine if the liquid is cloudy or contains flakes or large particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Skyrizi contains
- The active substance is risankizumab. Each pre-filled syringe contains 150 mg of risankizumab in 1 mL solution.
- The other ingredients are sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See section 2, "Skyrizi contains polysorbate and sodium".

What Skyrizi looks like and contents of the pack
Skyrizi is a clear and colourless to yellow liquid in a pre-filled syringe with needle guard. The liquid may contain tiny white or clear particles.

Each pack contains 1 pre-filled syringe.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer

AbbVie S.r.l.
04011 Campoverde di Aprilia
(Latina)
Italy

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

България
АбВи ЕООД
Тел: +359 2 90 30 430

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Magyarország
AbbVie Kft.
Tel: +36 1 455 8600

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Malta
V.J.Salomone Pharma Limited
Tel: +356 21220174

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Eesti
AbbVie OÜ
Tel: +372 623 1011

Norge
AbbVie AS
Tlf: +47 67 81 80 00

Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

Österreich
AbbVie GmbH
Tel: +43 1 20589-0

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10

France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Hrvatska
AbbVie d.o.o.
Tel: +385 (0)1 5625 501

Ireland
AbbVie Limited
Tel: +353 (0)1 4287900

Ísland
Vistor
Tel: +354 535 7000

Italia
AbbVie S.r.l.
Tel: +39 06 928921

Κύπρος
Lifepharma (Z.A.M.) Ltd
Τηλ: +357 22 34 74 40

Latvija
AbbVie SIA
Tel: +371 67605000

Polska
AbbVie Sp. z o.o.
Tel: +48 22 372 78 00

Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

România
AbbVie S.R.L.
Tel: +40 21 529 30 35

Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060

Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777

Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200

Sverige
AbbVie AB
Tel: +46 (0)8 684 44 600

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Detailed and updated information on this product is available by scanning the QR code included below or on the outer carton with a smartphone. The same information is also available at the following URL:
www.skyrizi.eu

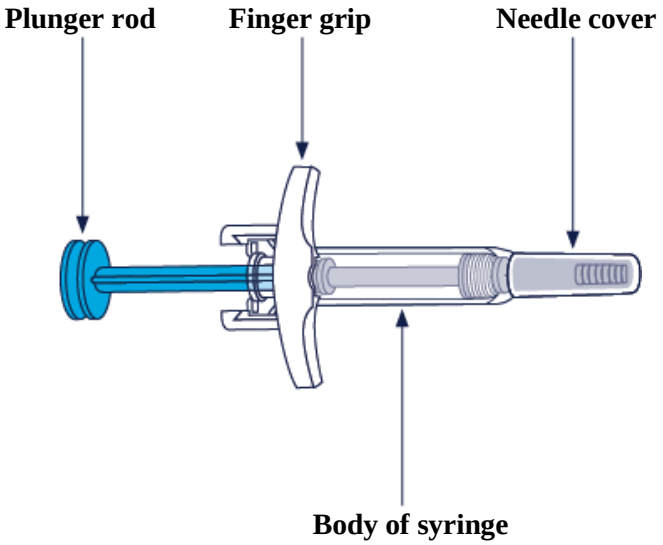
QR code to be included

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

7. Instructions for use

Please read all of section 7 before using Skyrizi

Skyrizi pre-filled syringe



Important information to know before you inject Skyrizi

- You should receive training on how to inject Skyrizi before giving an injection. Talk to your doctor, pharmacist or nurse if you need help
- Mark the dates on your calendar so you know when to inject Skyrizi
- Keep Skyrizi in the original carton to protect the medicine from light until it is time to use it
- **Do not** inject if the liquid is cloudy or contains flakes or large particles. The liquid should look clear to yellow and may contain tiny white or clear particles
- **Do not** shake the syringe
- Wait to remove the needle cover until just before the injection

Return this medicine to the pharmacy

- if the expiry date (EXP) has passed
- if the liquid has ever been frozen (even if thawed)
- if the syringe has been dropped or damaged
- if the carton perforations are broken

For a more comfortable injection: Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **15 to 30 minutes** before injecting.

- Skyrizi should not be warmed in any other way (for example, in a microwave or in hot water)
- Keep the syringe in the carton until ready to inject

Follow the steps below each time you use Skyrizi

STEP 1

Remove the pre-filled syringe from the cardboard sleeve by holding the finger grip.

- **Do not** hold or pull plunger rod when removing the pre-filled syringe from the sleeve

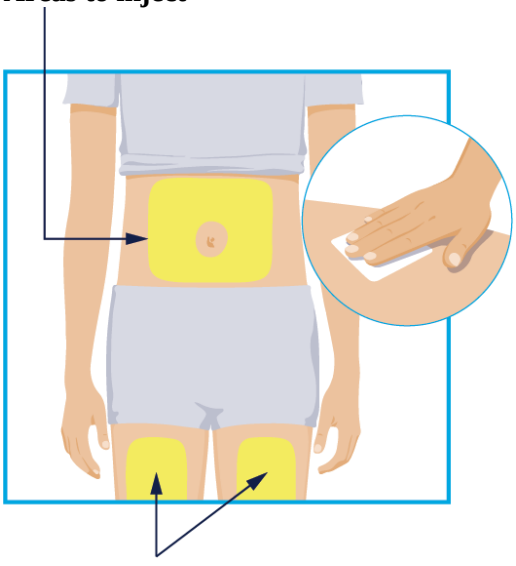
Place the following items on a clean, flat surface:

- 1 pre-filled syringe
- 1 alcohol pad (not included in the carton)
- 1 cotton ball or gauze pad (not included in the carton)
- special disposal container (not included in the carton)

Wash and dry your hands.

STEP 2

Areas to inject



Areas to inject

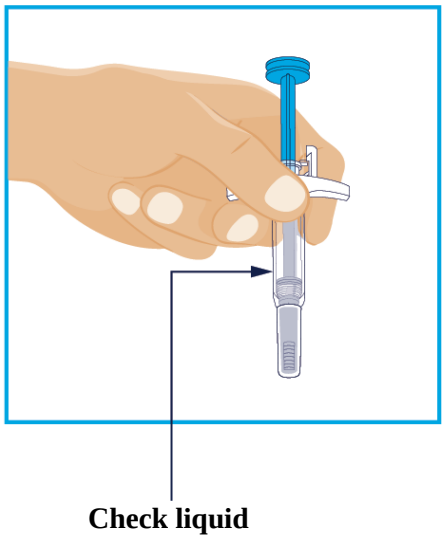
Choose from these 3 areas to inject:

- front of left thigh
- front of right thigh
- your belly (abdomen) at least 5 cm from your belly button (navel)

Before the injection, wipe where you will inject in a circular motion with an alcohol pad.

- **Do not** touch or blow on the injection site after it is cleaned. Allow the skin to dry before injecting
- **Do not** inject through clothes
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, or has stretch marks
- **Do not** inject into areas affected by psoriasis

STEP 3



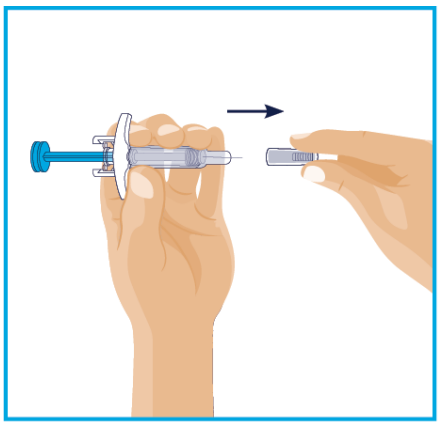
Check liquid

Hold the syringe with the covered needle pointing down, as shown.

Check the liquid in the syringe.

- It is normal to see bubbles in the window
- The liquid should look clear to yellow and may contain tiny white or clear particles
- **Do not** use if the liquid is cloudy or contains flakes or large particles

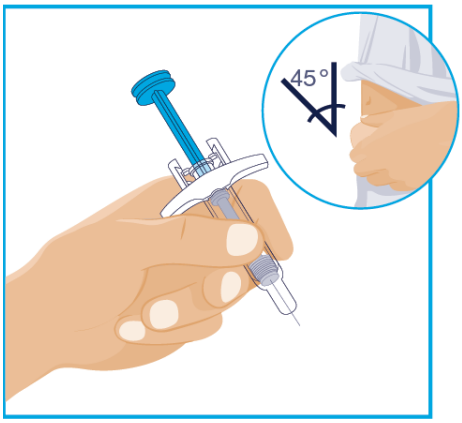
STEP 4



Removing the needle cover:

- Hold the syringe in one hand between the finger grip and needle cover
- With the other hand, gently pull the needle cover straight off
- **Do not** hold or pull the plunger rod when removing the needle cover
- You may see a drop of liquid at the end of the needle. This is normal
- Throw away the needle cover
- **Do not** touch the needle with your fingers or let the needle touch anything

STEP 5

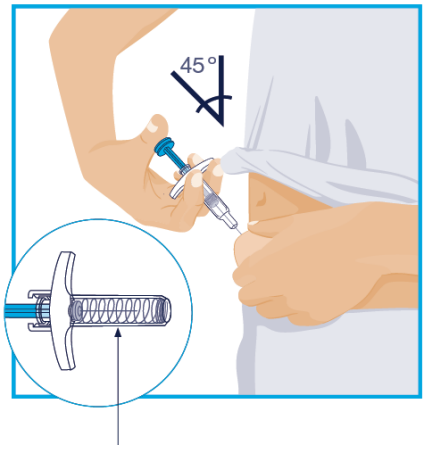


Hold the body of the syringe in one hand between the thumb and index finger, like you would a pencil.

Gently pinch the area of cleaned skin with your other hand and hold it firmly.

Insert the needle all the way into the skin at about a 45-degree angle using a quick, short movement. Keep the syringe steady at the same angle.

STEP 6



Needle guard

Slowly push the plunger rod all the way in until all of the liquid is injected.

Pull the needle out of the skin while keeping the syringe at the same angle.

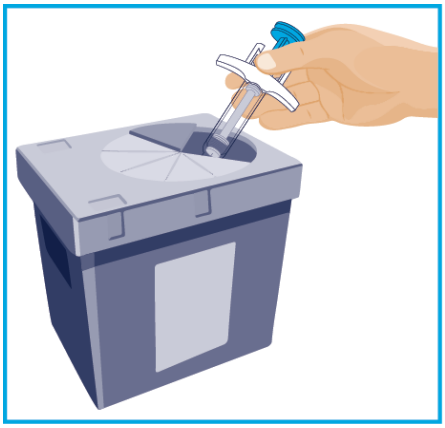
Slowly take your thumb off the plunger rod. The needle will then be covered by the needle guard.

- The needle guard will not activate unless all the liquid is injected
- Speak to your doctor, pharmacist or nurse if you think you have not given a full dose

Press a cotton ball or gauze pad where you have injected and hold for 10 seconds.

Do not rub the skin where you have injected. You may have slight bleeding from where you injected. This is normal.

STEP 7



Throw away the used syringe in a special disposal container straight after use.

- **Do not** throw away the used syringe in the household waste
- Your doctor, pharmacist or nurse will tell you how to return the full special disposal container

Package leaflet: Information for the patient

Skyrizi 75 mg solution for injection in pre-filled syringe
risankizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skyrizi is and what it is used for

Skyrizi contains the active substance risankizumab.

Skyrizi is used to treat the following inflammatory diseases:

- Plaque psoriasis
- Psoriatic arthritis

How Skyrizi works
This medicine works by stopping a protein in the body called ‘IL-23’, which causes inflammation.

Plaque psoriasis
Skyrizi is used to treat adults with moderate to severe plaque psoriasis. Skyrizi reduces inflammation and can therefore help reduce symptoms of plaque psoriasis such as burning, itching, pain, redness, and scaling.

Psoriatic arthritis
Skyrizi is used to treat adults with psoriatic arthritis. Psoriatic arthritis is a disease that causes inflamed joints and psoriasis. If you have active psoriatic arthritis, you may first be given other medicines. If these medicines do not work well enough, you will be given Skyrizi either alone or in combination with other medicines to treat your psoriatic arthritis.

Skyrizi reduces inflammation and can therefore help to reduce pain, stiffness, and swelling in and around your joints, pain and stiffness in your spine, psoriatic skin rash, psoriatic nail damage, and it may slow down damage to the bone and cartilage in your joints. These effects can ease your normal daily activities, reduce tiredness, and improve your quality of life.

2. What you need to know before you use Skyrizi

Do not use Skyrizi
- if you are allergic to risankizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an infection, including active tuberculosis, which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and during the use of Skyrizi:
- if you currently have an infection or if you have an infection that keeps coming back.
- if you have tuberculosis (TB).
- if you have recently received or plan to receive an immunisation (vaccine). You should not be given certain types of vaccines while using Skyrizi.

It is important to keep a record of the batch number of your Skyrizi.
Every time you get a new pack of Skyrizi, note down the date and the batch number (which is on the packaging after "Lot") and keep this information in a safe place.

Serious allergic reactions
Skyrizi can cause serious side effects, including serious allergic reactions ('anaphylaxis').
Tell your doctor or seek medical help immediately if you notice any signs of an allergic reaction while you are taking Skyrizi such as:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness
- severe itching of the skin, with a red rash or raised bumps

Children and adolescents
Skyrizi is not recommended for children and adolescents under 18 years of age. This is because Skyrizi has not been studied in this age group.

Other medicines and Skyrizi
Tell your doctor, pharmacist or nurse:
if you are using, have recently used or might use any other medicines.
if you have recently had or are going to have a vaccination. You should not be given certain types of vaccines while using Skyrizi.

If you are not sure, talk to your doctor, pharmacist or nurse before and during the use of Skyrizi.

Pregnancy, contraception and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known how this medicine will affect the baby.

If you are a woman who can become pregnant, you should use contraception while using this medicine and for at least 21 weeks after your last dose of Skyrizi.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine.

Driving and using machines
Skyrizi is not likely to affect your driving and use of machines.

Skyrizi contains sorbitol, polysorbate and sodium
This medicine contains 68 mg sorbitol per 150 mg dose.

This medicine contains 0.34 mg of polysorbate 20 in each 150 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per 150 mg dose, that is to say essentially 'sodium-free'.

3. How to use Skyrizi

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

This medicine is given as 2 injections under your skin (called 'subcutaneous injections').

How much Skyrizi to use

The dose is 150 mg given as two 75 mg injections.

	How much?	**When?**
1st dose	150 mg (**two** 75 mg injections)	When your doctor tells you
2nd dose	150 mg (**two** 75 mg injections)	4 weeks after 1st dose
Further doses	150 mg (**two** 75 mg injections)	Every 12 weeks starting after 2nd dose

You and your doctor, pharmacist or nurse will decide if you should inject this medicine yourself. Do not inject yourself with this medicine unless you have been trained by your doctor, pharmacist or nurse. A caregiver may also give your injections after they have been trained.

Read section 7 'Instructions for use' at the end of this leaflet before injecting Skyrizi yourself.

If you use more Skyrizi than you should
If you have used more Skyrizi than you should or the dose has been given sooner than prescribed, talk to your doctor.

If you forget to use Skyrizi
If you forget to use Skyrizi, inject a dose as soon as you remember. Talk to your doctor if you are not sure what to do.

If you stop using Skyrizi
Do not stop using Skyrizi without talking to your doctor first. If you stop treatment, your symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Allergic reactions – these may need urgent treatment. Tell your doctor or get emergency medical help straight away if you notice any of the following signs:

Serious allergic reactions ('anaphylaxis') are rare in people taking Skyrizi (may affect up to 1 in a 1 000 people). Signs include:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness

Talk to your doctor or get medical help immediately if you have the following symptoms.
Symptoms of a serious infection such as:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters

Your doctor will decide if you can keep using Skyrizi.

Other side effects
Tell your doctor, pharmacist or nurse if you get any of the following side effects

Very common: may affect more than 1 in 10 people
- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people
- feeling tired
- fungal skin infection
- injection site reactions (such as redness or pain)
- itching
- headache
- rash
- eczema

Uncommon: may affect up to 1 in 100 people
- small raised red bumps on the skin
- hives (urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Skyrizi

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the syringe label and outer carton after 'EXP'.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Keep the pre-filled syringes in the original carton in order to protect from light.

Do not use this medicine if the liquid is cloudy or contains flakes or large particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Skyrizi contains
- The active substance is risankizumab. Each pre-filled syringe contains 75 mg of risankizumab in 0.83 mL solution.
- The other ingredients are disodium succinate hexahydrate, succinic acid, sorbitol, polysorbate 20 and water for injections. See section 2, "Skyrizi contains sorbitol, polysorbate and sodium".

What Skyrizi looks like and contents of the pack
Skyrizi is a clear and colourless to slightly yellow liquid in a pre-filled syringe with needle guard. The liquid may contain tiny white or clear particles.

Each pack contains 2 pre-filled syringes and 2 alcohol pads.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer

AbbVie S.r.l.
04011 Campoverde di Aprilia
(Latina)
Italy

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

България
АбВи ЕООД
Тел:+359 2 90 30 430

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Magyarország
AbbVie Kft.
Tel:+36 1 455 8600

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Malta
V.J.Salomone Pharma Limited
Tel: +356 21220174

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Eesti
AbbVie OÜ
Tel: +372 623 1011

Norge
AbbVie AS
Tlf: +47 67 81 80 00

Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10

France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Hrvatska
AbbVie d.o.o.
Tel: + 385 (0)1 5625 501

Ireland
AbbVie Limited
Tel: +353 (0)1 4287900

Ísland
Vistor
Tel: +354 535 7000

Italia
AbbVie S.r.l.
Tel: +39 06 928921

Κύπρος
Lifepharma (Z.A.M.) Ltd
Τηλ: +357 22 34 74 40

Latvija
AbbVie SIA
Tel: +371 67605000

Österreich
AbbVie GmbH
Tel: +43 1 20589-0

Polska
AbbVie Sp. Z o.o.
Tel: +48 22 372 78 00

Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

România
AbbVie S.R.L.
Tel: +40 21 529 30 35

Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060

Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777

Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200

Sverige
AbbVie AB
Tel: +46 (0)8 684 44 600

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

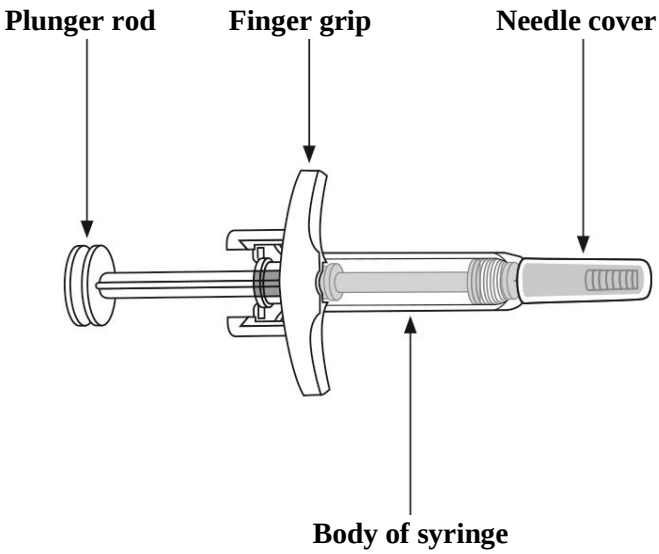
Detailed and updated information on this product is available by scanning the QR code included below or on the outer carton with a smartphone. The same information is also available at the following URL:
www.skyrizi.eu

QR code to be included

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

7. Instructions for use

Please read all of section 7 before using Skyrizi



Important information to know before you inject Skyrizi

- You should receive training on how to inject Skyrizi before giving an injection. Talk to your doctor, pharmacist or nurse if you need help
- Mark the dates on your calendar so you know when to inject Skyrizi
- Keep Skyrizi in the original carton to protect the medicine from light until it is time to use it
- **Do not** inject if the liquid is cloudy or contains flakes or large particles. The liquid should look clear to slightly yellow and may contain tiny white or clear particles
- **Do not** shake the syringe
- Wait to remove the needle cover until just before the injection

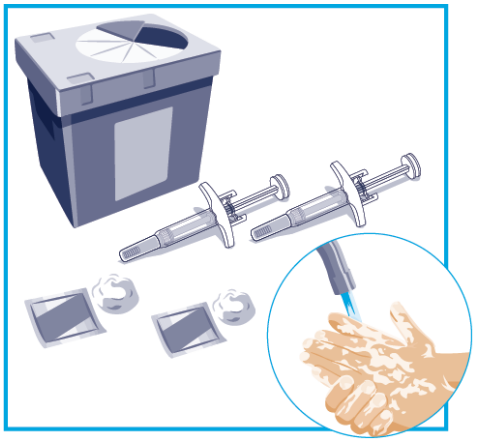
Return this medicine to the pharmacy

- if the expiry date (EXP) has passed
- if the liquid has ever been frozen (even if thawed)
- if the syringe has been dropped or damaged
- if the syringe paper tray cover is broken or missing

For a more comfortable injection: Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **15 to 30 minutes** before injecting.

- Skyrizi should not be warmed in any other way (for example, in a microwave or in hot water)
- Keep the syringes in the carton until ready to inject

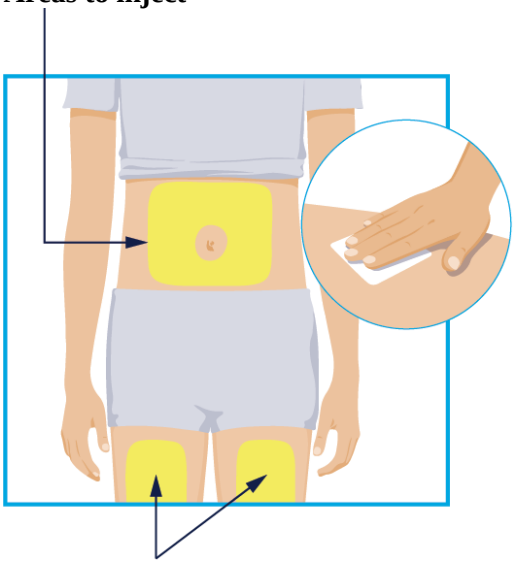
Follow the steps below each time you use Skyrizi

<table>
<tr>
<td>STEP 1
  </td>
<td>Place the following items on a clean, flat surface:
• 2 pre-filled syringes and 2 alcohol pads (included in the carton)
• 2 cotton balls or gauze pads (not included in the carton)
• Special disposal container (not included in the carton)

Wash and dry your hands.

Start with one syringe for the first injection.

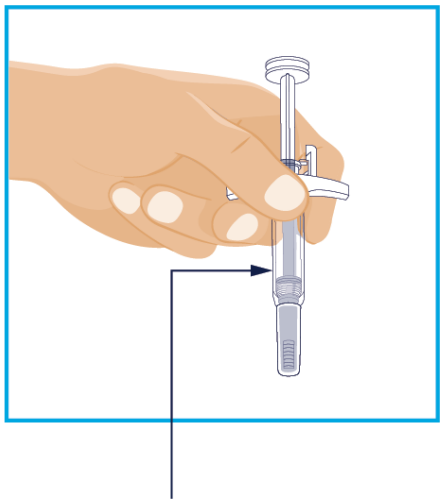
For a full dose, 2 injections are required, one after the other.</td>
</tr>
<tr>
<td>STEP 2

Areas to inject
 
</td>
<td>Choose from these 3 areas to inject:
• front of left thigh
• front of right thigh
• your belly (abdomen) at least 5 cm from your belly button (navel)

For the second syringe, inject at least 3 cm away from the first injection. Do not inject into the same place.

Before each injection, wipe where you will inject in a circular motion with an alcohol pad.
• Do not touch or blow on the injection site after it is cleaned. Allow the skin to dry before injecting
• Do not inject through clothes
• Do not inject into skin that is sore, bruised, red, hard, scarred, or has stretch marks
• Do not inject into areas affected by psoriasis</td>
</tr>
</table>

STEP 3



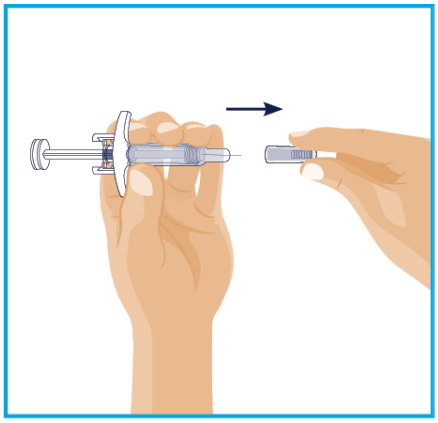
Check liquid

Hold the syringe with the covered needle pointing down, as shown.

Check the liquid in the syringe.

- It is normal to see bubbles in the window
- The liquid should look clear to slightly yellow and may contain tiny white or clear particles
- **Do not** use if the liquid is cloudy or contains flakes or large particles

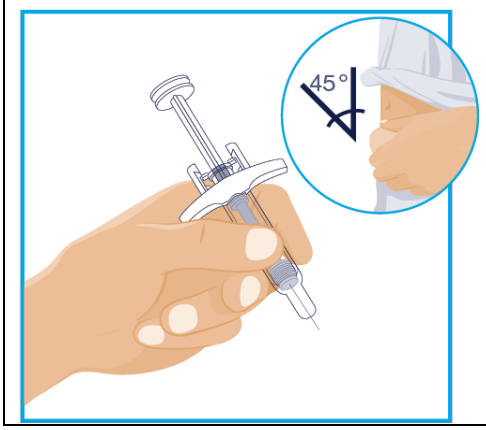
STEP 4



Removing the needle cover:

- Hold the syringe in one hand between the finger grip and needle cover
- With the other hand, gently pull the needle cover straight off
- **Do not** hold or pull the plunger rod when removing the needle cover
- You may see a drop of liquid at the end of the needle. This is normal
- Throw away the needle cover
- **Do not** touch the needle with your fingers or let the needle touch anything

STEP 5

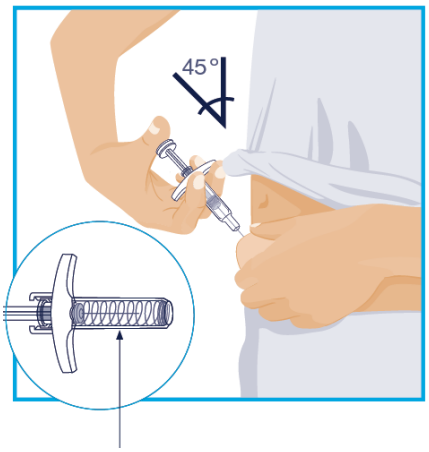


Hold the body of the syringe in one hand between the thumb and index finger, like you would a pencil.

Gently pinch the area of cleaned skin with your other hand and hold it firmly.

Insert the needle all the way into the skin at about a 45-degree angle using a quick, short movement. Keep the syringe steady at the same angle.

STEP 6



Needle guard

Slowly push the plunger rod all the way in until all of the liquid is injected.

Pull the needle out of the skin while keeping the syringe at the same angle.

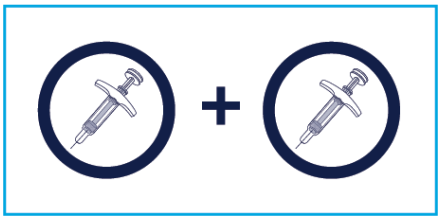
Slowly take your thumb off the plunger rod. The needle will then be covered by the needle guard.

- The needle guard will not activate unless all the liquid is injected
- Speak to your doctor, pharmacist or nurse if you think you have not given a full dose

Press a cotton ball or gauze pad where you have injected and hold for 10 seconds.

Do not rub the skin where you have injected. You may have slight bleeding from where you injected. This is normal

STEP 7

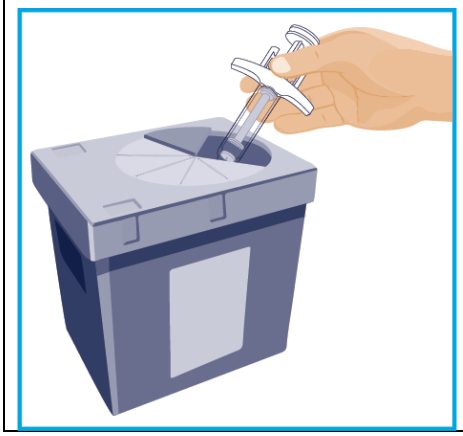


2 Injections Required

For a full dose, two injections are needed, one after the other.

- Repeat Steps 2 through 6 with the second syringe
- Inject the second syringe straight after the first injection but at least 3 cm away from the first injection

STEP 8



Throw away used syringes in a special disposal container straight after use.

- **Do not** throw away used syringes in the household waste
- Your doctor, pharmacist or nurse will tell you how to return the full special disposal container

Package leaflet: Information for the patient

Skyrizi 600 mg concentrate for solution for infusion
risankizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skyrizi is and what it is used for

Skyrizi contains the active substance risankizumab.

Skyrizi is used to treat adult patients with:
- moderate to severe Crohn's disease
- moderate to severe ulcerative colitis

How Skyrizi works

This medicine works by stopping a protein in the body called 'IL-23', which causes inflammation.

Crohn's disease
Crohn's disease is an inflammatory disease of the digestive tract. If you have active Crohn's disease you will first be given other medicines. If these medicines do not work well enough, you will be given Skyrizi to treat your Crohn's disease.

Ulcerative colitis
Ulcerative colitis is an inflammatory disease of the large bowel. If you have active ulcerative colitis you will first be given other medicines. If these medicines do not work well enough or if you cannot take these medicines, you will be given Skyrizi to treat your ulcerative colitis.

Skyrizi reduces the inflammation and can therefore help to reduce the signs and symptoms of your disease.

2. What you need to know before you are given Skyrizi

You should not be given Skyrizi
- if you are allergic to risankizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an infection, including active tuberculosis, which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and during the use of Skyrizi:
- if you currently have an infection or if you have an infection that keeps coming back.
- if you have tuberculosis (TB).
- if you have recently received or plan to receive an immunisation (vaccine). You should not be given certain types of vaccines while using Skyrizi.

It is important that your doctor or nurse keep a record of the batch number of your Skyrizi.
Every time you get a new pack of Skyrizi, your doctor or nurse must note down the date and the batch number (which is on the packaging after "Lot").

Serious allergic reactions
Skyrizi can cause serious side effects, including serious allergic reactions ('anaphylaxis').
Tell your doctor or seek medical help immediately if you notice any signs of an allergic reaction while you are taking Skyrizi such as:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness
- severe itching of the skin, with a red rash or raised bumps

Children and adolescents
Skyrizi is not recommended for children and adolescents under 18 years of age. This is because the use of Skyrizi has not been confirmed in this age group.

Other medicines and Skyrizi
Tell your doctor, pharmacist or nurse:
- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. You should not be given certain types of vaccines while using Skyrizi.

If you are not sure, talk to your doctor, pharmacist or nurse before and during the use of Skyrizi.

Pregnancy, contraception and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known how this medicine will affect the baby.

If you are a woman who can become pregnant, you should use contraception while using this medicine and for at least 21 weeks after your last dose of Skyrizi.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine.

Driving and using machines
Skyrizi is not likely to affect your driving and use of machines.

Skyrizi contains polysorbate and sodium
This medicine contains 2 mg of polysorbate 20 in each 600 mg dose and 4 mg of polysorbate 20 in each 1 200 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per 600 mg dose and 1 200 mg dose, that is to say essentially 'sodium-free'.

3. How Skyrizi will be given

You will begin treatment with Skyrizi with a starting dose which will be given by your doctor or nurse through a drip in your arm (intravenous infusion).

Starting doses

	How much?	**When?**
Crohn's disease	600 mg	When your doctor tells you
	600 mg	4 weeks after 1st dose
	600 mg	4 weeks after 2nd dose

	How much?	**When?**
Ulcerative colitis	1 200 mg	When your doctor tells you
	1 200 mg	4 weeks after 1st dose
	1 200 mg	4 weeks after 2nd dose

Afterwards, you will receive Skyrizi as an injection under your skin. See package leaflet for Skyrizi 90 mg pre-filled syringe, 180 mg and 360 mg solution for injection in cartridge, and 180 mg pre-filled syringe.

Maintenance doses

	How much?		**When?**
Crohn's disease	1st maintenance dose	360 mg	4 weeks after the last starting dose (at week 12)
	Further doses	360 mg	Every 8 weeks, starting after the 1st maintenance dose

	How much?		**When?**
Ulcerative colitis	1st maintenance dose	180 mg or 360 mg	4 weeks after the last starting dose (at week 12)
	Further doses	180 mg or 360 mg	Every 8 weeks, starting after the 1st maintenance dose

If you forget to use Skyrizi
If you forget or miss the appointment for any of your doses, contact your doctor to reschedule your appointment as soon as you remember.

If you stop using Skyrizi
Do not stop using Skyrizi without talking to your doctor first. If you stop treatment, your symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Allergic reactions – these may need urgent treatment. Tell your doctor or get emergency medical help straight away if you notice any of the following signs:

Serious allergic reactions ('anaphylaxis') are rare in people taking Skyrizi (may affect up to 1 in a 1 000 people). Signs include:
- difficulty breathing or swallowing

- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness

Talk to your doctor or get medical help immediately if you have the following symptoms.
Symptoms of a serious infection such as:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters

Your doctor will decide if you can keep using Skyrizi.

Other side effects
Tell your doctor, pharmacist or nurse if you get any of the following side effects

Very common: may affect more than 1 in 10 people
- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people
- feeling tired
- fungal skin infection
- injection site reactions (such as redness or pain)
- itching
- headache
- rash
- eczema

Uncommon: may affect up to 1 in 100 people
- small raised red bumps on the skin
- hives (urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Skyrizi

Skyrizi 600 mg concentrate for solution for infusion is given in a hospital or clinic and patients should not need to store or handle it.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial label and outer carton after 'EXP'.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Keep the vial in the original carton in order to protect from light.

Do not shake the Skyrizi vial. Prolonged vigorous shaking can damage the medicine.

Do not use this medicine if the liquid is cloudy or contains flakes or large particles.

Each vial is for single use only.

Do not throw away any medicines via wastewater or household waste. These measures will help protect the environment.

6. Contents of the pack and other information

What Skyrizi contains

- The active substance is risankizumab. Each vial contains 600 mg of risankizumab in 10 mL solution.
- The other ingredients are sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See section 2, "Skyrizi contains polysorbate and sodium".

What Skyrizi looks like and contents of the pack

Skyrizi is a clear and colourless to slightly yellow liquid in a vial. The liquid may contain tiny white or clear particles.

Each pack contains 1 vial.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer

AbbVie S.r.l.
04011 Campoverde di Aprilia
(Latina)
Italy

or

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

България
АбВи ЕООД
Тел: +359 2 90 30 430

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Eesti
AbbVie OÜ
Tel: +372 623 1011

Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10

France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Hrvatska
AbbVie d.o.o.
Tel: +385 (0)1 5625 501

Ireland
AbbVie Limited
Tel: +353 (0)1 4287900

Ísland
Vistor
Tel: +354 535 7000

Italia
AbbVie S.r.l.
Tel: +39 06 928921

Κύπρος
Lifepharma (Z.A.M.) Ltd
Τηλ: +357 22 34 74 40

Latvija
AbbVie SIA
Tel: +371 67605000

Magyarország
AbbVie Kft.
Tel: +36 1 455 8600

Malta
V.J.Salomone Pharma Limited
Tel: +356 21220174

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Norge
AbbVie AS
Tlf: +47 67 81 80 00

Österreich
AbbVie GmbH
Tel: +43 1 20589-0

Polska
AbbVie Sp. z o.o.
Tel: +48 22 372 78 00

Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

România
AbbVie S.R.L.
Tel: +40 21 529 30 35

Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060

Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777

Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200

Sverige
AbbVie AB
Tel: +46 (0)8 684 44 600

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Detailed and updated information on this product is available by scanning the QR code included below or on the outer carton with a smartphone. The same information is also available at the following URL: www.skyrizi.eu

QR code to be included

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

The following information is intended for healthcare professionals only

Traceability

In order to improve the traceability of biological medicinal products, the tradename and the batch number of the administered product should be clearly recorded.

Instructions for use

1. This medicinal product should be prepared by a healthcare professional using aseptic technique.

2. It must be diluted before administration.

3. The solution for infusion is prepared by dilution of the concentrate into an infusion bag or glass bottle containing 5% dextrose in water (D5W) or sodium chloride 9 mg/mL (0.9%) solution for infusion to a final concentration of approximately 1.2 mg/mL to 6 mg/mL. Refer to table below for dilution instructions based on patient's indication.

Indication	**Intravenous induction dose**	**Number of 600 mg/ 10 mL vials**	**Total volume of 5% dextrose or sodium chloride 9 mg/mL (0.9%) solution for infusion**
Crohn's disease	600 mg	1	100 mL, or 250 mL, or 500 mL
Ulcerative colitis	1 200 mg	2	250 mL, or 500 mL

4. The solution in the vial and dilutions should not be shaken.

5. Prior to the start of the intravenous infusion, the content of the infusion bag or glass bottle should be at room temperature.

6. Infuse the diluted solution over a period of at least one hour for the 600 mg dose; at least two hours for the 1 200 mg dose.

7. The vial solution should not be administered concomitantly in the same intravenous line with other medicinal products.

Each vial is for single use only and any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Storage of diluted solution

Chemical and physical in-use stability has been demonstrated for 20 hours at 2°C to 8°C (protected from light) or up to 8 hours at room temperature (protected from sunlight). Storage time at room temperature begins once the diluted solution has been prepared. The infusion should be completed within 8 hours after dilution in the infusion bag. Exposure to indoor light is acceptable during room temperature storage and administration.

From a microbiological point of view, the prepared infusion should be used immediately. If not used immediately, in-use storage time and conditions prior to use are the responsibility of the user and should not be longer than 20 hours at 2°C to 8°C. Do not freeze.

Package leaflet: Information for the patient

Skyrizi 180 mg solution for injection in cartridge
Skyrizi 360 mg solution for injection in cartridge
risankizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skyrizi is and what it is used for

Skyrizi contains the active substance risankizumab.

Skyrizi is used to treat adult patients with:
- moderate to severe Crohn's disease
- moderate to severe ulcerative colitis

How Skyrizi works

This medicine works by stopping a protein in the body called 'IL-23', which causes inflammation.

Crohn's disease
Crohn's disease is an inflammatory disease of the digestive tract. If you have active Crohn's disease you will first be given other medicines. If these medicines do not work well enough, you will be given Skyrizi to treat your Crohn's disease.

Ulcerative colitis
Ulcerative colitis is an inflammatory disease of the large bowel. If you have active ulcerative colitis you will first be given other medicines. If these medicines do not work well enough or if you cannot take these medicines, you will be given Skyrizi to treat your ulcerative colitis.

Skyrizi reduces the inflammation and can therefore help to reduce the signs and symptoms of your disease.

2. What you need to know before you use Skyrizi

Do not use Skyrizi
- if you are allergic to risankizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an infection, including active tuberculosis, which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and during the use of Skyrizi:
- if you currently have an infection or if you have an infection that keeps coming back.
- if you have tuberculosis (TB).
- if you have recently received or plan to receive an immunisation (vaccine). You should not be given certain types of vaccines while using Skyrizi.

It is important to keep a record of the batch number of your Skyrizi.
Every time you get a new pack of Skyrizi, note down the date and the batch number (which is on the packaging after "Lot") and keep this information in a safe place.

Serious allergic reactions
Skyrizi can cause serious side effects, including serious allergic reactions ('anaphylaxis').
Tell your doctor or seek medical help immediately if you notice any signs of an allergic reaction while you are taking Skyrizi such as:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness
- severe itching of the skin, with a red rash or raised bumps

Children and adolescents
Skyrizi is not recommended for children and adolescents under 18 years of age. This is because the use of Skyrizi has not been confirmed in this age group.

Other medicines and Skyrizi
Tell your doctor, pharmacist or nurse:
- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. You should not be given certain types of vaccines while using Skyrizi.

If you are not sure, talk to your doctor, pharmacist or nurse before and during the use of Skyrizi.

Pregnancy, contraception and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known how this medicine will affect the baby.

If you are a woman who can become pregnant, you should use contraception while using this medicine and for at least 21 weeks after your last dose of Skyrizi.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine.

Driving and using machines
Skyrizi is not likely to affect your driving and use of machines.

Skyrizi contains polysorbate and sodium
This medicine contains 0.24 mg of polysorbate 20 in each 180 mg dose and 0.48 mg of polysorbate 20 in each 360 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per cartridge, that is to say essentially 'sodium-free'.

3. How to use Skyrizi

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

This medicine is given as an injection under your skin (called a 'subcutaneous injection').

How much Skyrizi to use

You will begin treatment with Skyrizi with a starting dose which will be given by your doctor or nurse through a drip in your arm (intravenous infusion).

Starting doses

	How much?	**When?**
Crohn's disease	600 mg	When your doctor tells you
	600 mg	4 weeks after 1st dose
	600 mg	4 weeks after 2nd dose

	How much?	**When?**
Ulcerative colitis	1 200 mg	When your doctor tells you
	1 200 mg	4 weeks after 1st dose
	1 200 mg	4 weeks after 2nd dose

Afterwards, you will receive Skyrizi as an injection under your skin.

Maintenance doses

	How much?		**When?**
Crohn's disease	1st maintenance dose	360 mg	4 weeks after the last starting dose (at week 12)
	Further doses	360 mg	Every 8 weeks, starting after the 1st maintenance dose

	How much?		**When?**
Ulcerative colitis	1st maintenance dose	180 mg or 360 mg	4 weeks after the last starting dose (at week 12)
	Further doses	180 mg or 360 mg	Every 8 weeks, starting after the 1st maintenance dose

You and your doctor, pharmacist or nurse will decide if you should inject this medicine yourself. Do not inject yourself with this medicine unless you have been trained by your doctor, pharmacist or nurse. A caregiver may also give your injection after they have been trained.

Read section 7 'Instructions for use' at the end of this leaflet before injecting Skyrizi yourself.

If you use more Skyrizi than you should
If you have used more Skyrizi than you should or the dose has been given sooner than prescribed, talk to your doctor.

If you forget to use Skyrizi
If you forget to use Skyrizi, inject a dose as soon as you remember. Talk to your doctor if you are not sure what to do.

If you stop using Skyrizi
Do not stop using Skyrizi without talking to your doctor first. If you stop treatment, your symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Allergic reactions – these may need urgent treatment. Tell your doctor or get emergency medical help straight away if you notice any of the following signs:

Serious allergic reactions (‘anaphylaxis’) are rare in people taking Skyrizi (may affect up to 1 in a 1 000 people). Signs include:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness

Talk to your doctor or get medical help immediately if you have the following symptoms.
Symptoms of a serious infection such as:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters

Your doctor will decide if you can keep using Skyrizi.

Other side effects
Tell your doctor, pharmacist or nurse if you get any of the following side effects

Very common: may affect more than 1 in 10 people
- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people
- feeling tired
- fungal skin infection
- injection site reactions (such as redness or pain)
- itching
- headache
- rash
- eczema

Uncommon: may affect up to 1 in 100 people
- small raised red bumps on the skin
- hives (urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting

system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Skyrizi

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the cartridge label and outer carton after 'EXP'.

Store in a refrigerator (2°C - 8°C). Do not freeze.

If needed, you may also store the cartridge out of the refrigerator (up to a maximum of 25°C) for up to 24 hours.

Keep the cartridge in the original carton in order to protect from light.

Do not use this medicine if the liquid is cloudy or contains flakes or large particles.

Each on-body injector with cartridge is for single use only.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Skyrizi contains
The active substance is risankizumab.

Skyrizi 180 mg solution for injection in cartridge
- Each cartridge contains 180 mg of risankizumab in 1.2 mL solution.
- The other ingredients are sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See section 2, "Skyrizi contains polysorbate and sodium".

Skyrizi 360 mg solution for injection in cartridge
- Each cartridge contains 360 mg of risankizumab in 2.4 mL solution.
- The other ingredients are sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See section 2, "Skyrizi contains polysorbate and sodium".

What Skyrizi looks like and contents of the pack
Skyrizi is a clear and colourless to yellow liquid in a cartridge. The liquid may contain tiny white or clear particles.

Each pack contains 1 cartridge and 1 on-body injector.

Marketing Authorisation Holder and Manufacturer

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

България
АбВи ЕООД
Тел: +359 2 90 30 430

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Eesti
AbbVie OÜ
Tel: +372 623 1011

Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10

France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Hrvatska
AbbVie d.o.o.
Tel: +385 (0)1 5625 501

Ireland
AbbVie Limited
Tel: +353 (0)1 4287900

Ísland
Vistor
Tel: +354 535 7000

Italia
AbbVie S.r.l.
Tel: +39 06 928921

Κύπρος

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Magyarország
AbbVie Kft.
Tel: +36 1 455 8600

Malta
V.J.Salomone Pharma Limited
Tel: +356 21220174

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Norge
AbbVie AS
Tlf: +47 67 81 80 00

Österreich
AbbVie GmbH
Tel: +43 1 20589-0

Polska
Abbvie Sp. z o.o.
Tel: +48 22 372 78 00

Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

România
AbbVie S.R.L.
Tel: +40 21 529 30 35

Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060

Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777

Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200

Sverige

Lifepharma (Z.A.M.) Ltd
Τηλ: +357 22 34 74 40

AbbVie AB
Tel: +46 (0)8 684 44 600

Latvija
AbbVie SIA
Tel: +371 67605000

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Detailed and updated information on this product is available by scanning the QR code included below or on the outer carton with a smartphone. The same information is also available at the following URL: www.skyrizi.eu

QR code to be included

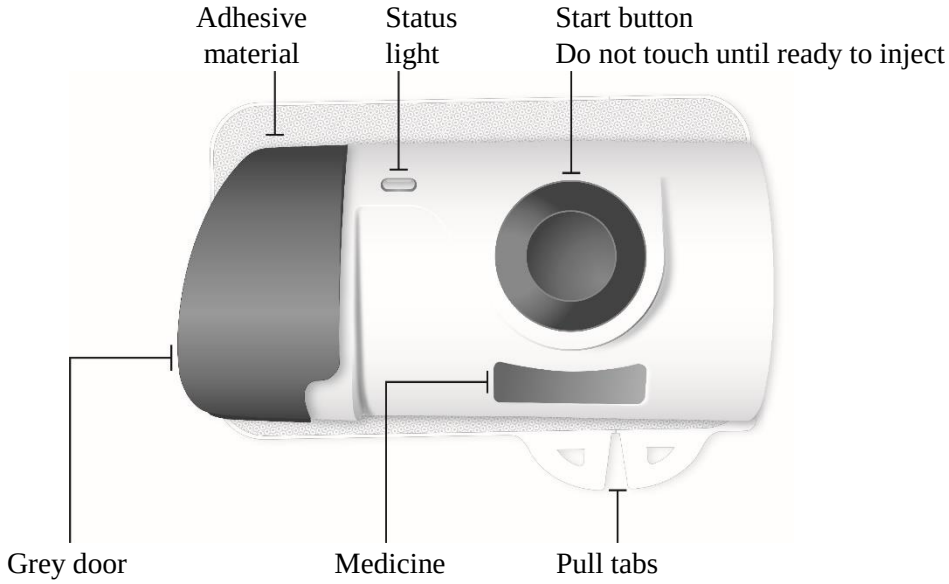
To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

7. Instructions for use

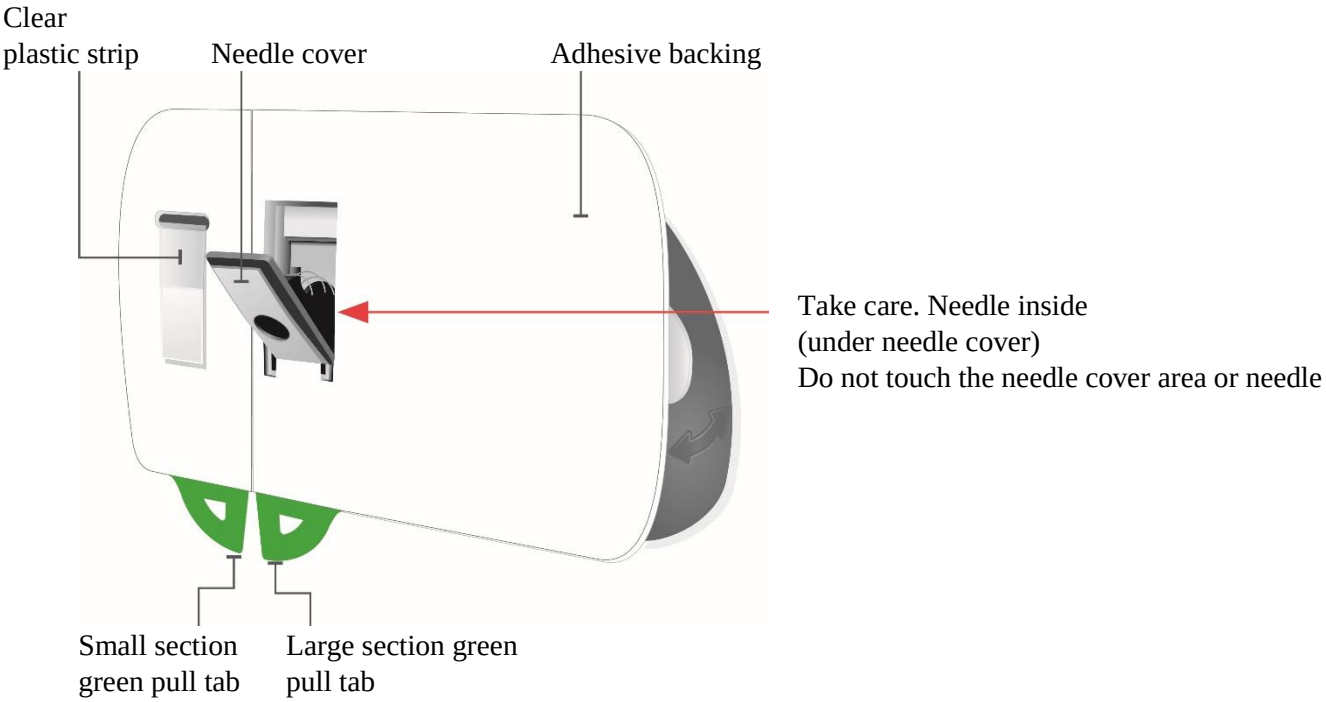
Please read all of section 7 before using Skyrizi

Skyrizi on-body injector

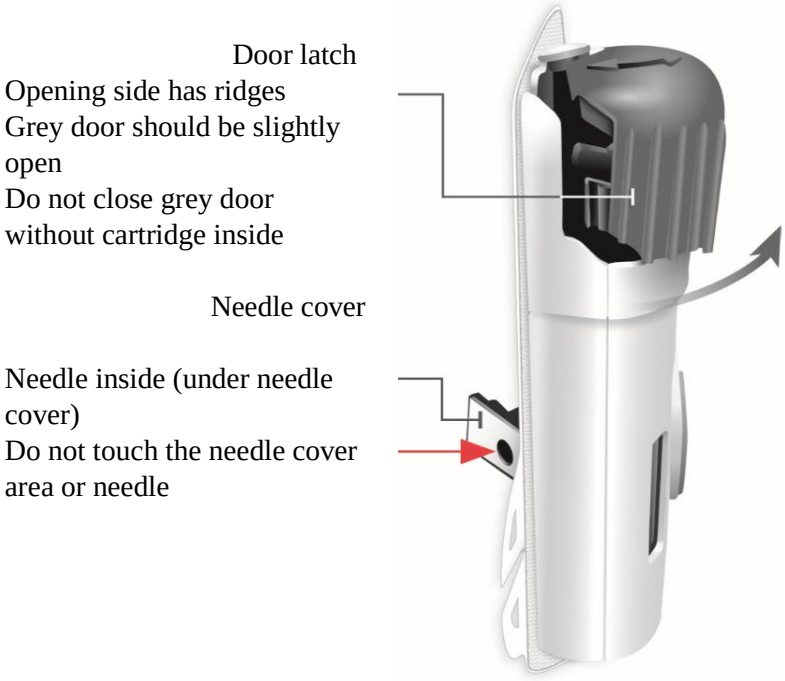
Front view



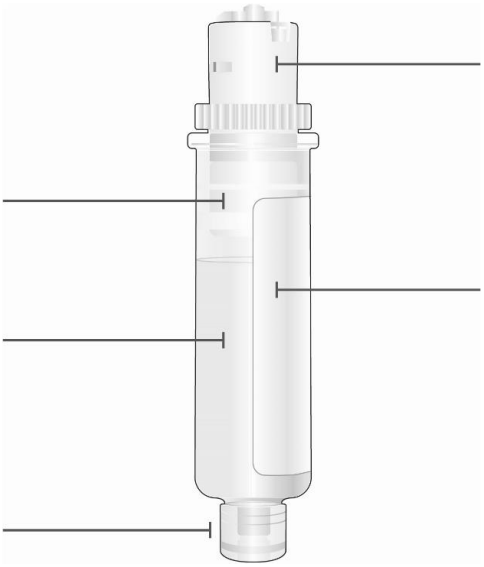
Back view



Side view



Cartridge



Important information to know before you inject Skyrizi

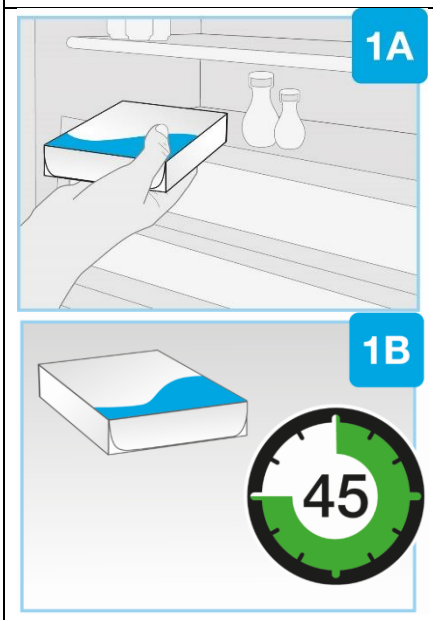
- You should receive training on how to inject Skyrizi before giving an injection. Talk to your doctor, pharmacist or nurse if you need help
- Mark the dates on your calendar so you know when to inject Skyrizi
- The single use on-body injector is designed for use with Skyrizi cartridge only
- Keep Skyrizi in the original carton to protect the medicine from light until it is time to use it
- Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, **for at least 45 up to 90 minutes** before injecting
    - The on-body injector will not work if Skyrizi is not left at room temperature to warm for at least 45 minutes
- **Do not** let the on-body injector get wet with water or any other liquids
- **Do not** touch the start button until you place the on-body injector loaded with the cartridge onto your skin and are ready to inject
    - You can only press the start button **one** time
- Physical activity should be limited during the injection process. Moderate physical activities can be done, such as walking, reaching and bending
- **Do not** delay in injecting the medicine after loading the cleaned cartridge into the on-body injector. Waiting will dry out the medicine and the on-body injector will not work afterwards
- **Do not** inject if the liquid in the inspection window is cloudy or contains flakes or large particles. The liquid should look clear to yellow and may contain tiny white or clear particles
- **Do not** shake the carton, cartridge or on-body injector
- **Do not** re-use the cartridge or the on-body injector

Return this medicine to the pharmacy

- if the expiry date (EXP) has passed
- if the liquid has ever been frozen (even if thawed)
- if the cartridge or on-body injector has been dropped or damaged
- if the carton perforations are broken
- if the white paper tray cover is broken or missing

Follow the steps below each time you use Skyrizi

STEP 1 - Get ready



Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **at least 45 up to 90 minutes** before injecting.

- The on-body injector will not work if Skyrizi is not left at room temperature to warm for at least 45 minutes
- Check expiry date (EXP) on the carton. Do not use Skyrizi if the expiry date (EXP) has passed
- **Do not** remove the cartridge or on-body injector from the carton while allowing Skyrizi to reach room temperature
- **Do not** warm Skyrizi in any other way. For example, **do not** warm it in a microwave or in hot water

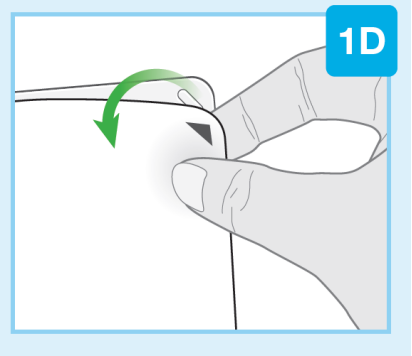
Special disposal container

Gather all supplies and wash your hands

Place the following items on a clean, flat surface.

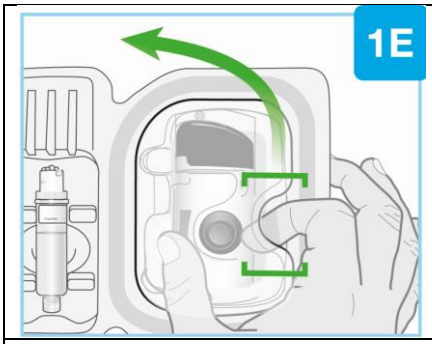
- plastic tray containing 1 on-body injector and 1 cartridge
- 2 alcohol pads (not included in the carton)
- 1 cotton ball or gauze pad (not included in the carton)
- special disposal container (not included in the carton)

Wash and dry your hands.



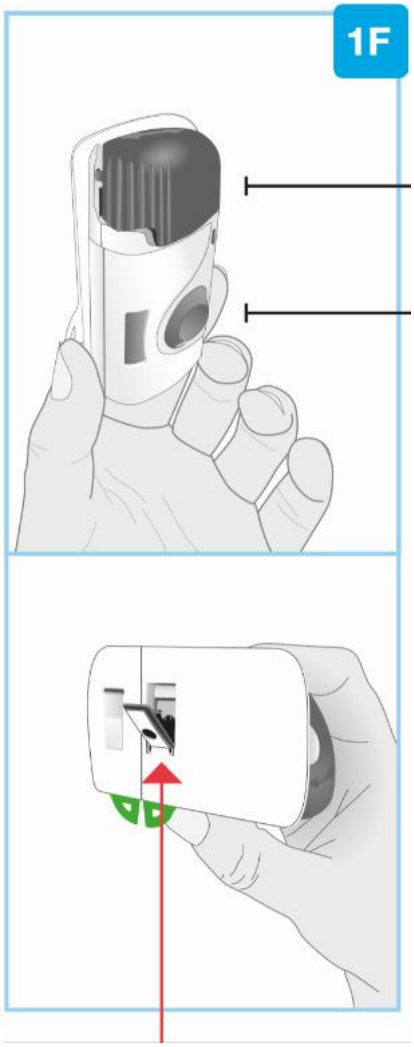
Remove the white paper tray seal

- Locate the black arrow
- Peel away the white paper tray seal from the plastic tray



Lift the plastic cover

- Locate the rounded opening on the top cover
- Insert your index finger in the opening and place your thumb on the opposite side
- Lift the cover to remove and set it aside
- **Do not** touch the grey start button until it is time to inject. It can only be pressed **one** time



Needle inside
(under needle cover)

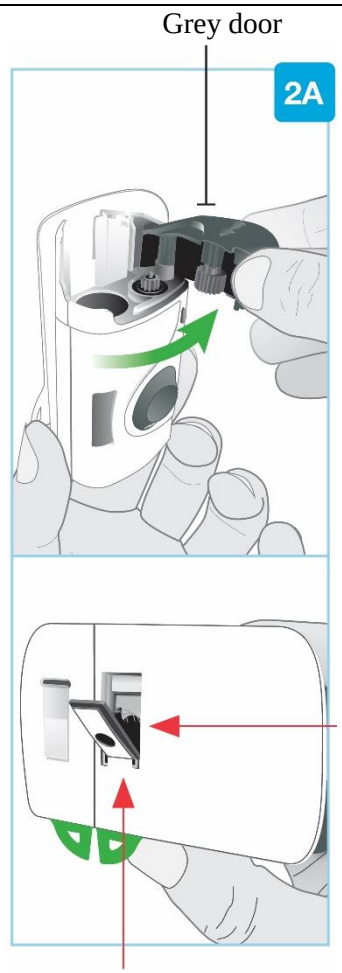
Inspect the on-body injector

- Check that the on-body injector is intact and not damaged
- The grey door should be slightly open
- If the grey door does not open, press in firmly on the grey door ridges (left side of door) and swing open the door
- **Do not** close the grey door before the cartridge is loaded
- **Do not** use on-body injector if you drop it, discover missing pieces, or if it's damaged
- **Do not** touch the grey start button until it is time to inject. It can be pressed **one** time only
- **Do not** touch the needle cover area or needle

If the grey start button is pressed before placing it on your body, the on-body injector can no longer be used. If this happens, speak to your doctor, pharmacist or nurse.

Proceed to the next step.

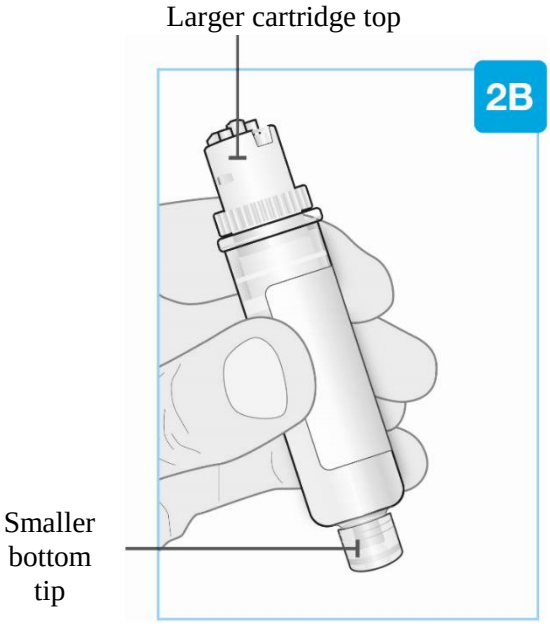
STEP 2 - Set up on-body injector



Fully open the grey door

- Avoid touching the needle cover area on the back of the on-body injector. The needle is behind the needle cover
- Swing the grey door all the way to the right to open it
- If the grey door does not open, press in firmly on the grey door ridges (left side of door) and swing open the door
- **Do not** close the grey door before the cartridge is loaded
- **Do not** touch the grey start button until it is time to inject. It can only be pressed **one** time

Put the on-body injector aside.



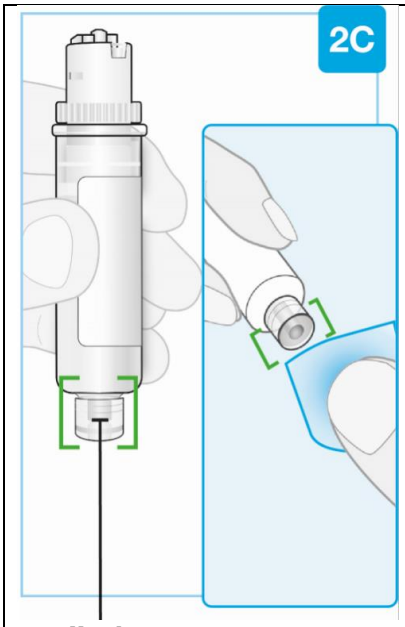
Inspect the cartridge

- **Do not** twist or remove cartridge top

Carefully remove the cartridge from the plastic tray.

Check the cartridge

- The liquid should look clear to yellow and may contain tiny white or clear particles. It is normal to see one or more bubbles
- **Do not** use if the liquid is cloudy, discoloured, or contains flakes or large particles
- The cartridge parts and the clear plastic are not cracked or broken
- **Do not** use if the liquid has been frozen (even if thawed).
- **Do not** use the cartridge if you drop it, discover missing pieces, or it is damaged.



Smaller bottom tip

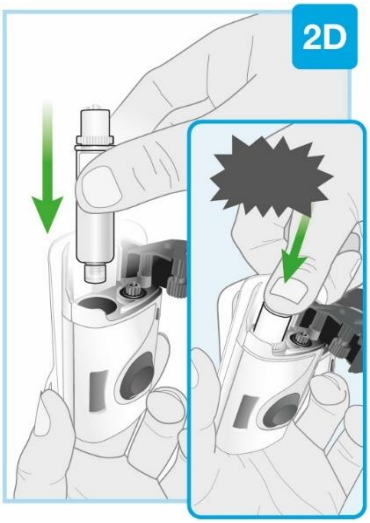
Clean centre of smaller bottom tip

Clean the smaller bottom tip of the cartridge
Locate the smaller bottom tip of the cartridge.

- Clean smaller bottom tip of the cartridge with an alcohol pad. Make sure to use the alcohol pad to clean the centre of the smaller bottom tip of the cartridge
- **Do not** touch the smaller bottom tip of the cartridge after cleaning

Insert straight

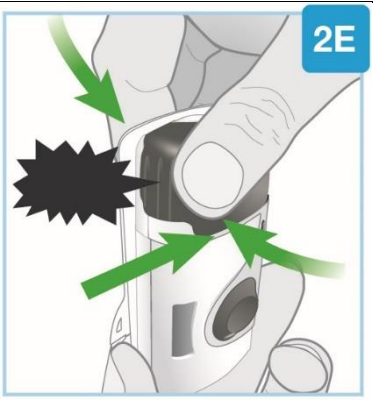
‘click’



Load the cleaned cartridge into the on-body injector

- **Do not** twist or remove the cartridge top
- **Do not** touch the grey start button until it is time to inject. It can only be pressed **one** time
- Insert the smaller bottom tip of the cartridge into the on-body injector first
- Firmly push down on the cartridge top until you hear a ‘click’ and it is fully inserted
- After loading the cartridge, you may see a few drops of medicine on the back of the on-body injector. This is normal

Make sure to proceed to the next step without delay after inserting the cartridge. Waiting will dry out the medicine and the on-body injector will not work afterwards.



‘snap’

No gaps

Confirm cartridge is inserted and close the grey door

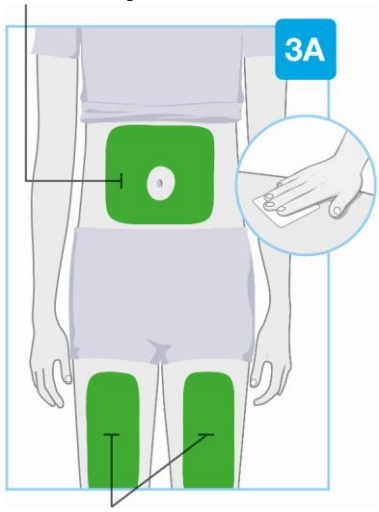
- Confirm the cartridge is fully inserted
- **Do not** close the grey door if the cartridge is not fully inserted or is missing
- Swing the grey door to the left, then squeeze firmly and listen for the grey door to ‘snap’ shut. No gaps should exist between the grey door and the on-body injector
- The grey door should stay locked after loading the cartridge

Do not touch the grey start button until it is time to inject. It can only be pressed **one** time.

Proceed without delay to the next step.

STEP 3 - Prepare to inject

Areas to inject



Areas to inject

Choose and clean your injection site

Choose from these 3 areas to inject:

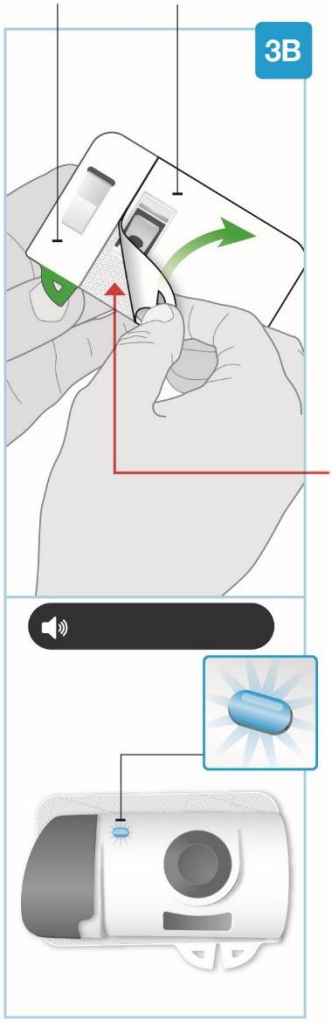
- front of left thigh
- front of right thigh
- your belly (abdomen) at least 5 cm from your belly button (navel)

Do not inject into areas of the skin that naturally fold or bulge because the on-body injector could fall off during wear.

Before the injection, wipe where you will inject in a circular motion with an alcohol pad.

- **Do not** touch or blow on the injection site after it is cleaned. Allow the skin to dry before placing the on-body injector on the skin
- **Do not** inject through clothes
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, or has stretch marks, moles or excessive hair. You can trim the excessive hair from the injection site

Small section Large section



Needle inside (under needle cover)

Activated injector
Status light flashing blue

‘beep-beep-beep’

Peel both tabs to expose skin adhesive
Turn the on-body injector over to find both green pull tabs

- Avoid touching the needle cover (needle inside)

Peel away the large section using the green pull tab to expose the skin adhesive.

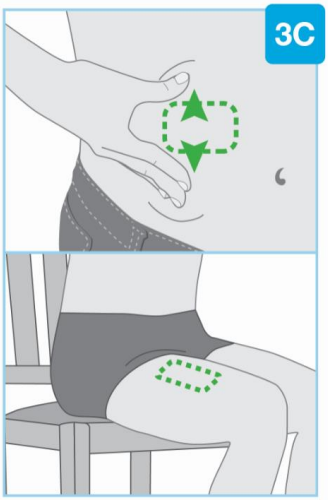
Peel away the small section using the green pull tab to expose the skin adhesive. This will remove the clear plastic strip, activating the on-body injector.

- Check the status light when the on-body injector beeps
- The status light will flash blue when the on-body injector is activated
- If the status light does not flash blue, speak to your doctor, pharmacist or nurse
- **Do not** press the grey start button yet
- **Do not** touch the needle cover or the needle
- **Do not** pull the adhesive material off on-body injector or allow the sticky side to fold and stick to itself

The Skyrizi on-body injector must be placed on the skin and injection must be started within 30 minutes after removing the green pull tabs or it will not work. Make sure to proceed to next step without delay.

‘beep-beep-beep-beep-beep’

If the status light flashes red and beeps, the on-body injector is not working properly. Do not continue to use it.
Speak to your doctor, pharmacist or nurse for assistance.
If the on-body injector is attached to your body, carefully remove it from your skin.



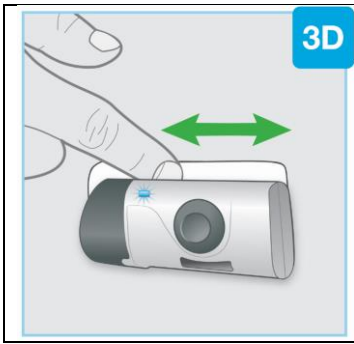
Prepare the on-body injector for placement

- For the belly (abdomen), move and hold the skin to create a firm, flat surface for injection at least 5 cm from your belly button (navel). Make sure to sit up straight to avoid skin folds and bulges
- You do not need to pull the skin flat for the front of left thigh or right thigh

Make sure to place the on-body injector so that you can see the blue status light.

Place the on-body injector on your skin

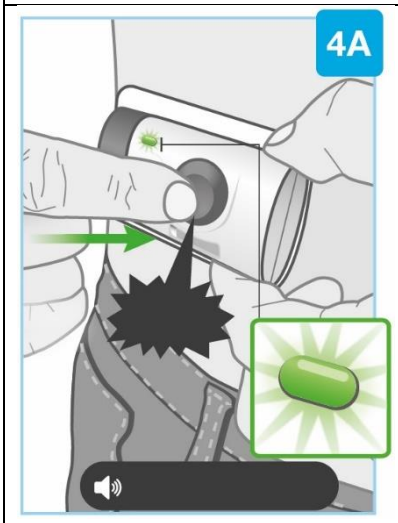
- When the blue light flashes, the on-body injector is ready. Place the on-body injector onto the cleaned skin with the status light visible



- **Do not** place the on-body injector on clothes. Only place on bare skin
- Run your finger around the adhesive material to secure it
- **Do not** move or adjust the on-body injector after it has been placed on your skin

Proceed without delay to the next step.

STEP 4 - Inject Skyrizi

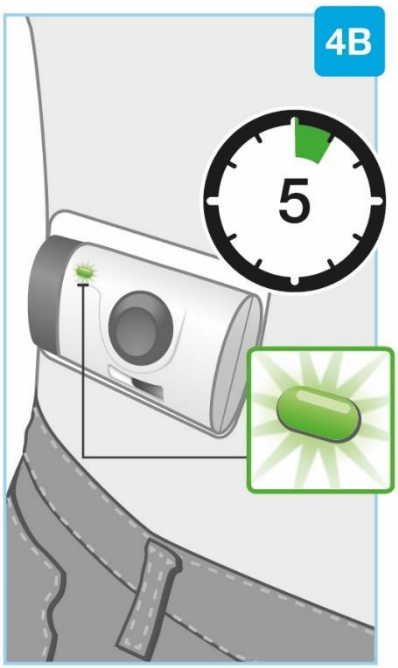


‘click’
‘beep-beep-beep’

Start injection

- **Do not** touch the grey start button until you place the on-body injector loaded with the cartridge onto your skin and are ready to inject. You can only press the start button **one** time
- Firmly press the grey start button until you hear a "click". Then release the grey start button
- You may feel a needle pinch
- Check the status light when the on-body injector beeps
- After starting the injection, the status light will continuously flash green
- After starting the injection, you will hear pumping sounds as the on-body injector delivers the medicine

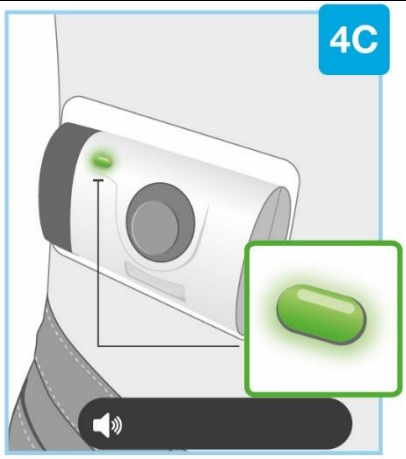
Do not continue to use the on-body injector if status light flashes red and beeps. Carefully remove from skin if the status light flashes red. If this happens, speak to your doctor, pharmacist or nurse.



Wait for the injection to finish

- It may take up to 5 minutes to complete the full dose of medicine. The on-body injector will automatically stop when the injection is finished
- During the injection, the status light will continue to flash green
- During the injection, you will hear pumping sounds as the on-body injector continues delivering the medicine
- During the injection, moderate physical activities can be done, such as walking, reaching and bending

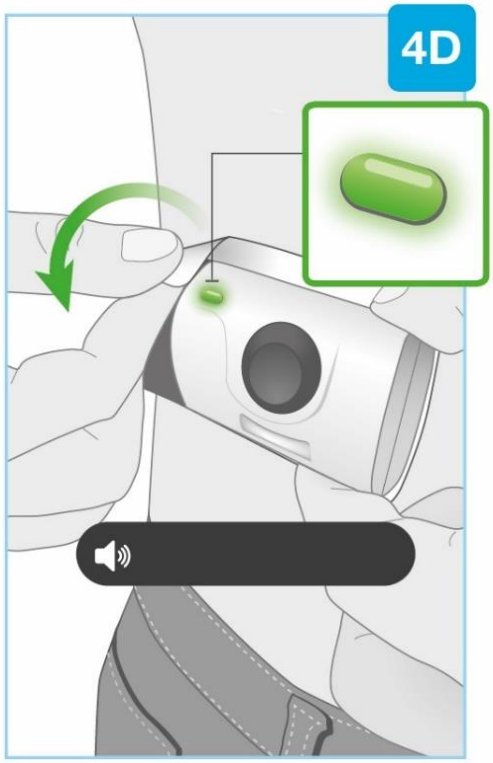
Do not continue to use the on-body injector if the status light flashes red and beeps. Carefully remove it from the skin if the status light flashes red. If this happens, speak to your doctor, pharmacist or nurse.



‘beep-beep-beep’

Injection is complete when

- The on-body injector stops on its own
- You hear a beep and the status light changes to solid green. If the status light has changed to solid green, this means that the injection is complete



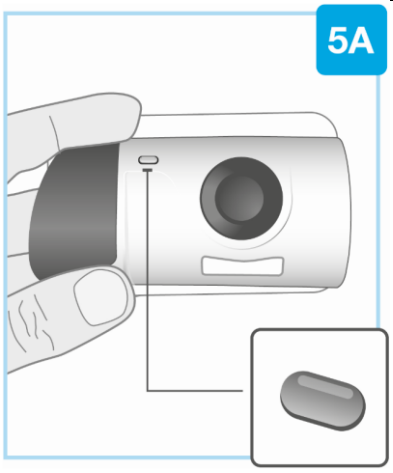
'beep-beep-beep'

Remove the on-body injector

- **Do not** remove the on-body injector if the status light is still flashing green and the injection is not finished
- **Do not** put your fingers on the back side of the on-body injector when removing it from your skin
- When the injection is done, grab the corner of the adhesive to carefully peel the on-body injector from the skin
- Avoid touching the needle cover or needle on the back of the on-body injector
- After removing the on-body injector, you will hear several beeps and the status light will turn off
- The needle cover will cover the needle when the on-body injector is removed from the skin
- It is normal to see a few small drops of liquid on your skin after removing the on-body injector
- Press a cotton ball or gauze pad over the injection site on your skin and hold for 10 seconds
- **Do not** rub the injection site
- Slight bleeding at the injection site is normal

Proceed to the next step.

STEP 5 - Finish



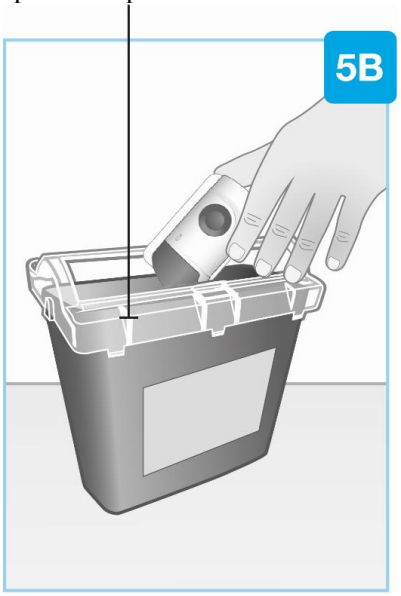
Check the on-body injector

Inspect the medicine window and status light.

Check to see that the white plunger fills the entire medicine window and the solid green light turns off, letting you know that all the medicine has been injected.

- If the white plunger does not fill the window, speak to your doctor, pharmacist or nurse

Special disposal container



Disposal

Throw away the used on-body injector in a special disposal container straight after use.

- The on-body injector contains batteries, electronics, and a needle
- Leave the cartridge in the on-body injector
- **Do not** throw away the used on-body injector in the household waste
- Your doctor, pharmacist or nurse will tell you how to return the full special disposal container. There may be local guidelines for disposal

Package leaflet: Information for the patient

Skyrizi 90 mg solution for injection in pre-filled syringe
risankizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skyrizi is and what it is used for

Skyrizi contains the active substance risankizumab.

Skyrizi is used to treat adult patients with moderate to severe Crohn's disease.

How Skyrizi works

This medicine works by stopping a protein in the body called 'IL-23', which causes inflammation.

Crohn's disease is an inflammatory disease of the digestive tract. If you have active Crohn's disease you will first be given other medicines. If these medicines do not work well enough, you will be given Skyrizi to treat your Crohn's disease.

Skyrizi reduces the inflammation and can therefore help to reduce the signs and symptoms of your disease.

2. What you need to know before you are given Skyrizi

You should not be given Skyrizi
- if you are allergic to risankizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an infection, including active tuberculosis, which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and during the use of Skyrizi
- if you currently have an infection or if you have an infection that keeps coming back.
- if you have tuberculosis (TB).
- if you have recently received or plan to receive an immunisation (vaccine). You should not be given certain types of vaccines while using Skyrizi.

It is important that your doctor or nurse keep a record of the batch number of your Skyrizi.
Every time you get a new pack of Skyrizi, your doctor or nurse must note down the date and the batch number (which is on the packaging after "Lot").

Serious allergic reactions
Skyrizi can cause serious side effects, including serious allergic reactions ('anaphylaxis').
Tell your doctor or seek medical help immediately if you notice any signs of an allergic reaction while you are taking Skyrizi such as:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness
- severe itching of the skin, with a red rash or raised bumps

Children and adolescents
Skyrizi is not recommended for children and adolescents under 18 years of age. This is because the use of Skyrizi has not been confirmed in this age group.

Other medicines and Skyrizi
Tell your doctor, pharmacist or nurse
- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. You should not be given certain types of vaccines while using Skyrizi.

If you are not sure, talk to your doctor, pharmacist or nurse before and during the use of Skyrizi.

Pregnancy, contraception and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known how this medicine will affect the baby.

If you are a woman who can become pregnant, you should use contraception while using this medicine and for at least 21 weeks after your last dose of Skyrizi.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine.

Driving and using machines
Skyrizi is not likely to affect your driving and use of machines.

Skyrizi contains sorbitol, polysorbate and sodium
This medicine contains 164 mg sorbitol per 360 mg dose.

This medicine contains 0.8 mg of polysorbate 20 in each 360 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per 360 mg dose, that is to say essentially 'sodium-free'.

3. How Skyrizi will be given

You will begin treatment with Skyrizi with a starting dose which will be given by your doctor or nurse through a drip in your arm (intravenous infusion).

Starting doses

	How much?	When?
Starting doses	600 mg	When your doctor tells you
	600 mg	4 weeks after 1st dose
	600 mg	4 weeks after 2nd dose

Afterwards, you will receive Skyrizi as an injection under your skin (called a 'subcutaneous injection') This will be given by your doctor or nurse as four injections under your skin as described below. Alternatively Skyrizi may be administered by an on-body injector.

Maintenance doses

	How much?	When?
1st maintenance dose	360 mg (4 injections of 90 mg)	4 weeks after the last starting dose (at week 12)
Further doses	360 mg (4 injections of 90 mg)	Every 8 weeks, starting after the 1st maintenance dose

If you forget to use Skyrizi
If you forget or miss the appointment for any of your doses, contact your doctor to reschedule your appointment as soon as you remember.

If you stop using Skyrizi
Do not stop using Skyrizi without talking to your doctor first. If you stop treatment, your symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Allergic reactions – these may need urgent treatment. Tell your doctor or get emergency medical help straight away if you notice any of the following signs:

Serious allergic reactions ('anaphylaxis') are rare in people taking Skyrizi (may affect up to 1 in a 1 000 people). Signs include:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness

Talk to your doctor or get medical help immediately if you have the following symptoms.
Symptoms of a serious infection such as:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters

Your doctor will decide if you can keep using Skyrizi.

Other side effects
Tell your doctor, pharmacist or nurse if you get any of the following side effects

Very common: may affect more than 1 in 10 people
- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people
- feeling tired
- fungal skin infection
- injection site reactions (such as redness or pain)
- itching
- headache
- rash
- eczema

Uncommon: may affect up to 1 in 100 people
- small raised red bumps on the skin
- hives (urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Skyrizi

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the syringe label and outer carton after 'EXP'.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Keep the pre-filled syringes in the original carton in order to protect from light.

Do not use this medicine if the liquid is cloudy or contains flakes or large particles.

Each pre-filled syringe is for single use only.

Do not throw away any medicines via wastewater or household waste. These measures will help protect the environment.

6. Contents of the pack and other information

What Skyrizi contains
- The active substance is risankizumab. Each pre-filled syringe contains 90 mg of risankizumab in 1 mL solution.
- The other ingredients are disodium succinate hexahydrate, polysorbate 20, sorbitol, succinic acid and water for injections. See section 2, "Skyrizi contains sorbitol, polysorbate and sodium".

What Skyrizi looks like and contents of the pack
Skyrizi is a clear and colourless to slightly yellow liquid in a pre-filled syringe with needle guard. The liquid may contain tiny white or clear particles.

Each pack contains 4 pre-filled syringes.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer

AbbVie S.r.l.
04011 Campoverde di Aprilia
(Latina)
Italy

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

България
АбВи ЕООД
Тел: +359 2 90 30 430

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Eesti
AbbVie OÜ
Tel: +372 623 1011

Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10

France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Magyarország
AbbVie Kft.
Tel: +36 1 455 8600

Malta
V.J.Salomone Pharma Limited
Tel: +356 21220174

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Norge
AbbVie AS
Tlf: +47 67 81 80 00

Österreich
AbbVie GmbH
Tel: +43 1 20589-0

Polska
AbbVie Sp. z o.o.
Tel: +48 22 372 78 00

Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

Hrvatska
AbbVie d.o.o.
Tel: +385 (0)1 5625 501

Ireland
AbbVie Limited
Tel: +353 (0)1 4287900

Ísland
Vistor
Tel: +354 535 7000

Italia
AbbVie S.r.l.
Tel: +39 06 928921

Κύπρος
Lifepharma (Z.A.M.) Ltd
Τηλ: +357 22 34 74 40

Latvija
AbbVie SIA
Tel: +371 67605000

România
AbbVie S.R.L.
Tel: +40 21 529 30 35

Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060

Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777

Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200

Sverige
AbbVie AB
Tel: +46 (0)8 684 44 600

This leaflet was last revised in

Other sources of information

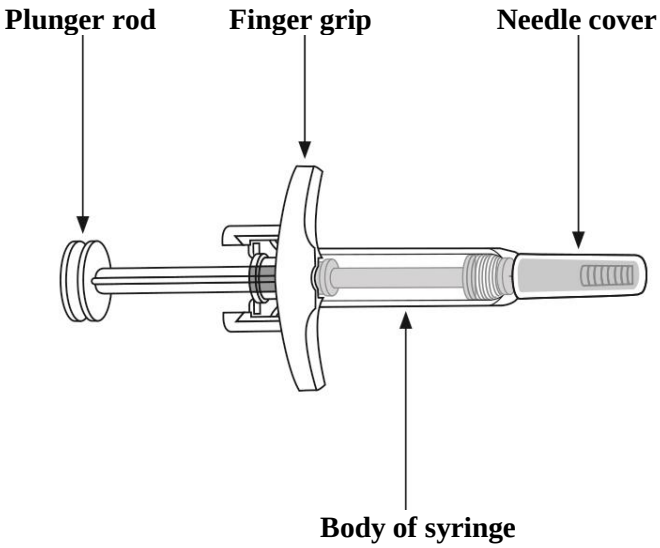
Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

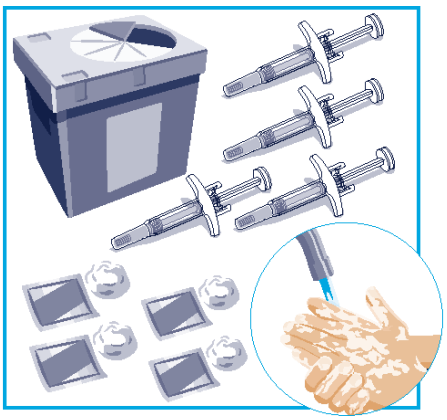
The following information is intended for healthcare professionals only

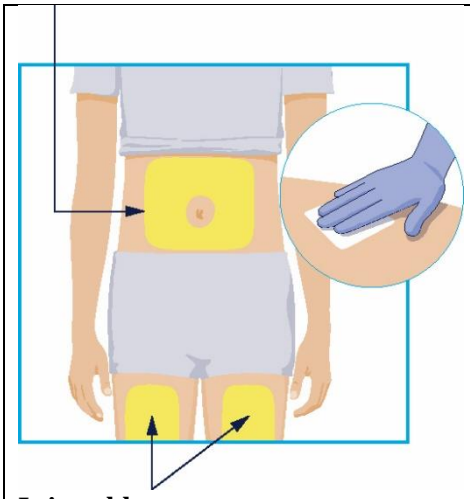
Traceability
In order to improve the traceability of biological medicinal products, the tradename and the batch number of the administered product should be clearly recorded.

Skyrizi pre-filled syringe



Instructions for use
This medicinal product should be administered by a healthcare professional.
Administer each pre-filled syringe subcutaneously as follows:

STEP 1 	Before injecting, remove the carton from the refrigerator without removing the pre-filled syringes from the carton. • **Do not** use this medicinal product if the carton seal is broken or missing, or if any of the components are damaged. Allow Skyrizi to reach room temperature out of direct sunlight (15 to 30 minutes). **Do not** shake the pre-filled syringes. Place the following items on a clean, flat surface: • 4 pre-filled syringes and 4 alcohol pads (not included in the carton) • 4 cotton balls or gauze pads (not included in the carton) • Special disposal container (not included in the carton) Wash and dry your hands. **For a full dose, 4 injections are required, one after the other.**
STEP 2 **Injectable areas**	Choose an injection site. • Inject one pre-filled syringe after the other in the following anatomic location(s): o front of left thigh or right thigh



Injectable areas

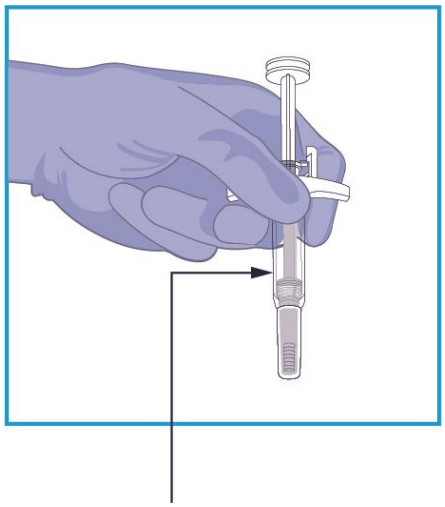
- abdomen (belly) at least 5 cm from the navel (belly button)

- Use a new injection site for each injection.
- For each syringe, inject at least 3 cm away from the previous injection. **Do not** inject into the same place.

Before each injection, wipe where you will inject in a circular motion with an alcohol pad.

- **Do not** inject into areas where the skin is tender, bruised, erythematous, indurated or affected by any lesions.

STEP 3



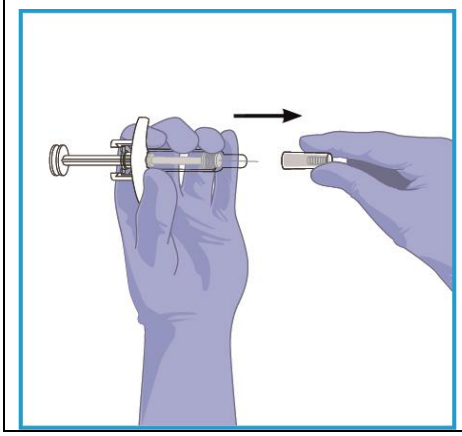
Check liquid

Hold the syringe with the covered needle pointing down, as shown.

Check the liquid in the syringe.

- It is normal to see bubbles in the window
- The liquid should look clear to slightly yellow and may contain tiny white or clear particles
- **Do not** use if the liquid is cloudy or contains flakes or large particles

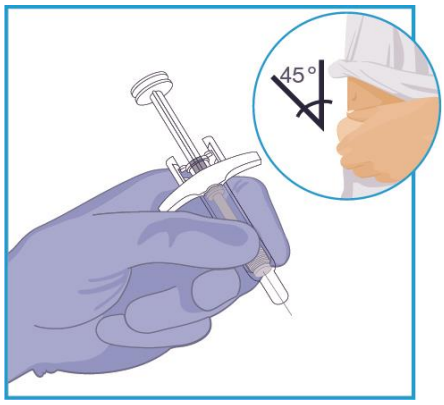
STEP 4



Removing the needle cover:

- Hold the syringe in one hand between the finger grip and needle cover
- With the other hand, gently pull the needle cover straight off
- **Do not** hold or pull the plunger rod when removing the needle cover
- You may see a drop of liquid at the end of the needle. This is normal
- Throw away the needle cover
- **Do not** touch the needle with your fingers or let the needle touch anything

STEP 5



Hold the body of the syringe in one hand between the thumb and index finger, like you would a pencil.

Gently pinch the area of cleaned skin with your other hand and hold it firmly.

Insert the needle all the way into the skin at about a 45-degree angle using a quick, short movement. Keep the syringe steady at the same angle.

Slowly push the plunger rod all the way in until all of the liquid is injected.

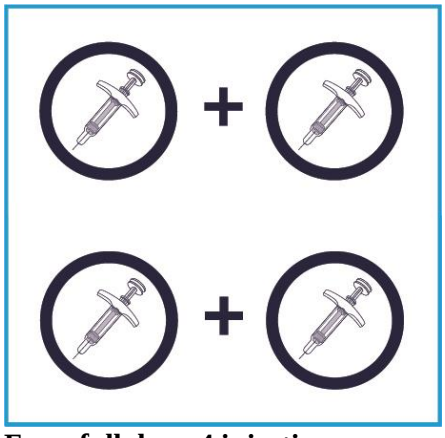
Pull the needle out of the skin while keeping the syringe at the same angle.

Slowly take your thumb off the plunger rod. The needle will then be covered by the needle guard.

The needle guard will not activate unless all the liquid is injected.

Press a cotton ball or gauze pad where you have injected and hold for 10 seconds.

STEP 6



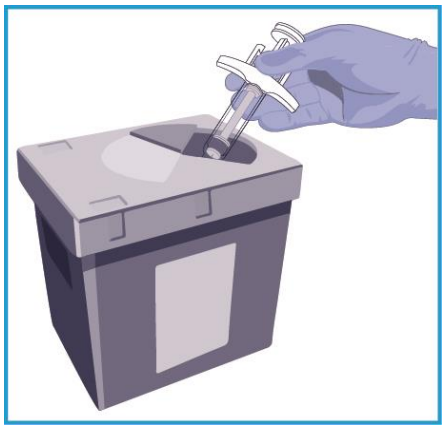
For a full dose, 4 injections are required

Use **four** 90 mg pre-filled syringes to subcutaneously administer the maintenance dose of 360 mg.

- Repeat Steps 2 through 5 with the subsequent syringes.

If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time.

STEP 7



Each pre-filled syringe is for single use only and any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Package leaflet: Information for the patient

Skyrizi 180 mg solution for injection in pre-filled syringe
risankizumab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skyrizi is and what it is used for

Skyrizi contains the active substance risankizumab.

Skyrizi is used to treat adult patients with:
- moderate to severe Crohn's disease
- moderate to severe ulcerative colitis

How Skyrizi works

This medicine works by stopping a protein in the body called 'IL-23', which causes inflammation.

Crohn's disease
Crohn's disease is an inflammatory disease of the digestive tract. If you have active Crohn's disease you will first be given other medicines. If these medicines do not work well enough, you will be given Skyrizi to treat your Crohn's disease.

Ulcerative colitis
Ulcerative colitis is an inflammatory disease of the large bowel. If you have active ulcerative colitis you will first be given other medicines. If these medicines do not work well enough or if you cannot take these medicines, you will be given Skyrizi to treat your ulcerative colitis.

Skyrizi reduces the inflammation and can therefore help to reduce the signs and symptoms of your disease.

2. What you need to know before you use Skyrizi

Do not use Skyrizi
- if you are allergic to risankizumab or any of the other ingredients of this medicine (listed in section 6).

- if you have an infection, including active tuberculosis, which your doctor thinks is important.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and during the use of Skyrizi
- if you currently have an infection or if you have an infection that keeps coming back.
- if you have tuberculosis (TB).
- if you have recently received or plan to receive an immunisation (vaccine). You should not be given certain types of vaccines while using Skyrizi.

It is important to keep a record of the batch number of your Skyrizi.
Every time you get a new pack of Skyrizi, note down the date and the batch number (which is on the packaging after "Lot") and keep this information in a safe place.

Serious allergic reactions
Skyrizi can cause serious side effects, including serious allergic reactions ('anaphylaxis').
Tell your doctor or seek medical help immediately if you notice any signs of an allergic reaction while you are taking Skyrizi such as:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness
- severe itching of the skin, with a red rash or raised bumps

Children and adolescents
Skyrizi is not recommended for children and adolescents under 18 years of age. This is because the use of Skyrizi has not been confirmed in this age group.

Other medicines and Skyrizi
Tell your doctor, pharmacist or nurse
- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. You should not be given certain types of vaccines while using Skyrizi.

If you are not sure, talk to your doctor, pharmacist or nurse before and during the use of Skyrizi.

Pregnancy, contraception and breast-feeding
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. This is because it is not known how this medicine will affect the baby.

If you are a woman who can become pregnant, you should use contraception while using this medicine and for at least 21 weeks after your last dose of Skyrizi.

If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine.

Driving and using machines
Skyrizi is not likely to affect your driving and use of machines.

Skyrizi contains polysorbate and sodium
This medicine contains 0.24 mg of polysorbate 20 in each dose 180 mg dose and 0.48 mg of polysorbate 20 in each 360 mg dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per 180 mg dose and 360 mg dose, that is to say essentially 'sodium-free'.

3. How to use Skyrizi

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

This medicine is given as 1 or 2 injections under your skin (called 'subcutaneous injections').

How much Skyrizi to use

You will begin treatment with Skyrizi with a starting dose which will be given by your doctor or nurse through a drip in your arm (intravenous infusion).

Starting doses

	How much?	**When?**
Crohn's disease	600 mg	When your doctor tells you
	600 mg	4 weeks after 1st dose
	600 mg	4 weeks after 2nd dose

Ulcerative colitis	**How much?**	**When?**
	1 200 mg	When your doctor tells you
	1 200 mg	4 weeks after 1st dose
	1 200 mg	4 weeks after 2nd dose

Afterwards, you will receive Skyrizi as an injection under your skin (called a 'subcutaneous injection')

Maintenance doses

	How much?		**When?**
Crohn's disease	1st maintenance dose	360 mg (2 injections of 180 mg)	4 weeks after the last starting dose (at week 12)
	Further doses	360 mg (2 injections of 180 mg)	Every 8 weeks, starting after the 1st maintenance dose

	How much?		**When?**
Ulcerative colitis	1st maintenance dose	180 mg (1 injection of 180 mg) or 360 mg (2 injections of 180 mg)	4 weeks after the last starting dose (at week 12)
	Further doses	180 mg (1 injection of 180 mg) or 360 mg (2 injections of 180 mg)	Every 8 weeks, starting after the 1st maintenance dose

You and your doctor, pharmacist or nurse will decide if you should inject this medicine yourself. Do not inject yourself with this medicine unless you have been trained by your doctor, pharmacist or nurse. A caregiver may also give your injection after they have been trained.

Read section 7 'Instructions for use' at the end of this leaflet before injecting Skyrizi yourself.

If you use more Skyrizi than you should
If you have used more Skyrizi than you should or the dose has been given sooner than prescribed, talk to your doctor.

If you forget to use Skyrizi
If you forget to use Skyrizi, inject a dose as soon as you remember. Talk to your doctor if you are not sure what to do.

If you stop using Skyrizi
Do not stop using Skyrizi without talking to your doctor first. If you stop treatment, your symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Allergic reactions – these may need urgent treatment. Tell your doctor or get emergency medical help straight away if you notice any of the following signs:

Serious allergic reactions (‘anaphylaxis’) are rare in people taking Skyrizi (may affect up to 1 in a 1 000 people). Signs include:
- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- low blood pressure, which can cause dizziness or light-headedness

Talk to your doctor or get medical help immediately if you have the following symptoms.
Symptoms of a serious infection such as:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters

Your doctor will decide if you can keep using Skyrizi.

Other side effects
Tell your doctor, pharmacist or nurse if you get any of the following side effects

Very common: may affect more than 1 in 10 people
- upper respiratory infections with symptoms such as sore throat and stuffy nose

Common: may affect up to 1 in 10 people
- feeling tired
- fungal skin infection
- injection site reactions (such as redness or pain)
- itching
- headache
- rash
- eczema

Uncommon: may affect up to 1 in 100 people
- small raised red bumps on the skin
- hives (urticaria)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Skyrizi

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the syringe label and outer carton after 'EXP'.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Keep the pre-filled syringe(s) in the original carton in order to protect from light.

If needed, you may also store the pre-filled syringe(s) out of the refrigerator (up to a maximum of 25°C) for up to 24 hours in the original carton to protect from light.

Do not use this medicine if the liquid is cloudy or contains flakes or large particles.

Each pre-filled syringe is for single use only.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Skyrizi contains

- The active substance is risankizumab. Each pre-filled syringe contains 180 mg of risankizumab in 1.2 mL solution.
- The other ingredients are sodium acetate trihydrate, acetic acid, trehalose dihydrate, polysorbate 20 and water for injections. See section 2, "Skyrizi contains polysorbate and sodium".

What Skyrizi looks like and contents of the pack

Skyrizi is a clear and colourless to yellow liquid in a pre-filled syringe with needle guard. The liquid may contain tiny white or clear particles.

Each pack contains 1 or 2 pre-filled syringes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

Manufacturer

AbbVie Biotechnology GmbH
Knollstrasse
67061 Ludwigshafen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
AbbVie SA
Tél/Tel: +32 10 477811

България
АбВи ЕООД
Тел: +359 2 90 30 430

Česká republika
AbbVie s.r.o.
Tel: +420 233 098 111

Danmark
AbbVie A/S
Tlf: +45 72 30-20-28

Deutschland
AbbVie Deutschland GmbH & Co. KG
Tel: 00800 222843 33 (gebührenfrei)
Tel: +49 (0) 611 / 1720-0

Eesti
AbbVie OÜ
Tel: +372 623 1011

Ελλάδα
AbbVie ΦΑΡΜΑΚΕΥΤΙΚΗ Α.Ε.
Τηλ: +30 214 4165 555

España
AbbVie Spain, S.L.U.
Tel: +34 91 384 09 10

France
AbbVie
Tél: +33 (0) 1 45 60 13 00

Hrvatska
AbbVie d.o.o.
Tel: +385 (0)1 5625 501

Ireland
AbbVie Limited
Tel: +353 (0)1 4287900

Ísland
Vistor
Tel: +354 535 7000

Italia
AbbVie S.r.l.
Tel: +39 06 928921

Κύπρος
Lifepharma (Z.A.M.) Ltd

Lietuva
AbbVie UAB
Tel: +370 5 205 3023

Luxembourg/Luxemburg
AbbVie SA
Belgique/Belgien
Tél/Tel: +32 10 477811

Magyarország
AbbVie Kft.
Tel: +36 1 455 8600

Malta
V.J.Salomone Pharma Limited
Tel: +356 21220174

Nederland
AbbVie B.V.
Tel: +31 (0)88 322 2843

Norge
AbbVie AS
Tlf: +47 67 81 80 00

Österreich
AbbVie GmbH
Tel: +43 1 20589-0

Polska
AbbVie Sp. z o.o.
Tel: +48 22 372 78 00

Portugal
AbbVie, Lda.
Tel: +351 (0)21 1908400

România
AbbVie S.R.L.
Tel: +40 21 529 30 35

Slovenija
AbbVie Biofarmacevtska družba d.o.o.
Tel: +386 (1)32 08 060

Slovenská republika
AbbVie s.r.o.
Tel: +421 2 5050 0777

Suomi/Finland
AbbVie Oy
Puh/Tel: +358 (0)10 2411 200

Sverige
AbbVie AB

Τηλ: +357 22 34 74 40

Tel: +46 (0)8 684 44 600

Latvija
AbbVie SIA
Tel: +371 67605000

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Detailed and updated information on this product is available by scanning the QR code included below or on the outer carton with a smartphone. The same information is also available at the following URL:
www.skyrizi.eu

QR code to be included

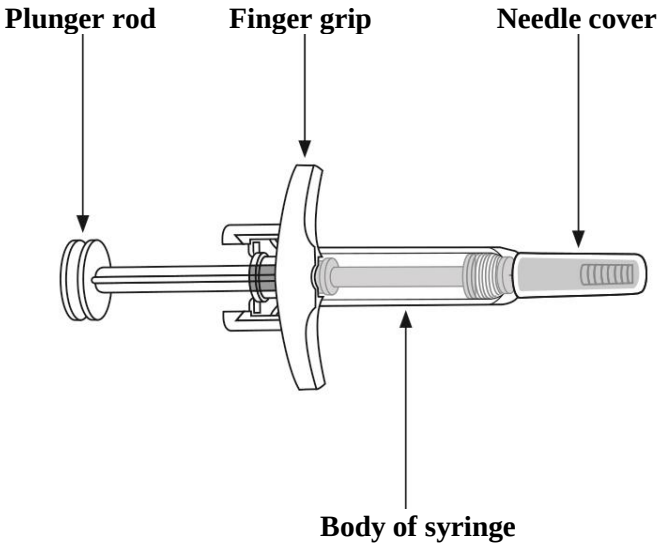
To listen to or request a copy of this leaflet in <Braille>, <large print> or <audio>, please contact the local representative of the Marketing Authorisation Holder.

---

7. Instructions for use

Please read all of section 7 before using Skyrizi

Skyrizi pre-filled syringe



Important information to know before you inject Skyrizi

- You should receive training on how to inject Skyrizi before giving an injection. Talk to your doctor, pharmacist or nurse if you need help
- Mark the dates on your calendar so you know when to inject Skyrizi
- Keep Skyrizi in the original carton to protect the medicine from light until it is time to use it
- **Do not** inject if the liquid is cloudy or contains flakes or large particles. The liquid should look clear to yellow and may contain tiny white or clear particles
- **Do not** shake the syringe(s)

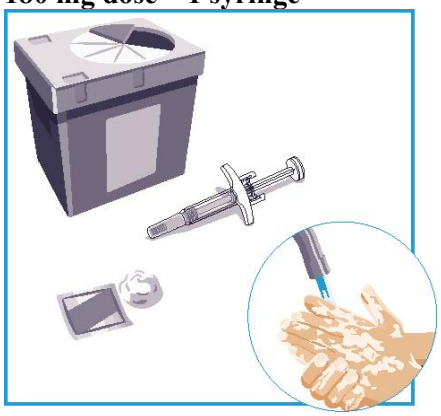
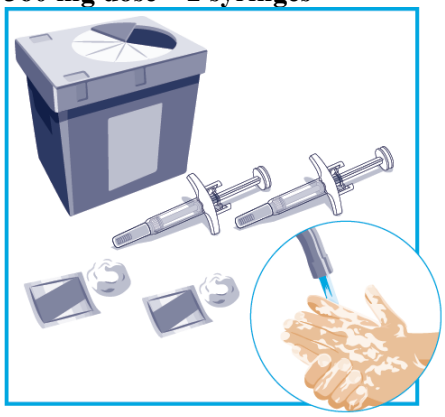
- Wait to remove the needle cover until just before the injection

Return this medicine to the pharmacy
- if the expiry date (EXP) has passed
- if the liquid has ever been frozen (even if thawed)
- if the syringe has been dropped or damaged
- if the carton perforations are broken

For a more comfortable injection: Take the carton out of the refrigerator and leave it at room temperature, out of direct sunlight, for **15 to 30 minutes** before injecting.
- Skyrizi should not be warmed in any other way (for example, in a microwave or in hot water)
- Keep the syringe in the carton until ready to inject

Follow the steps below each time you use Skyrizi

<table>
<tr>
<td>STEP 1

180 mg dose – 1 syringe
 
360 mg dose – 2 syringes
  </td>
<td>Place the following items on a clean, flat surface:

• 1 or 2 pre-filled syringe(s) and 1 or 2 alcohol pad(s) (not included in the carton)
• 1 or 2 cotton ball(s) or gauze pad(s) (not included in the carton)
• Special disposal container (not included in the carton)

Wash and dry your hands.

For the 180 mg dose

1 injection is required.

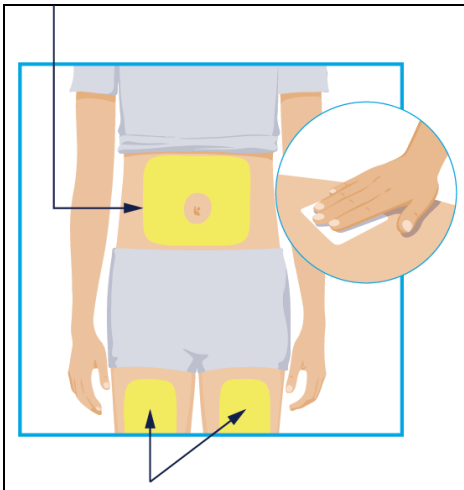
For the 360 mg dose

2 injections are required, one after the other.

Start with one syringe for the first injection.</td>
</tr>
<tr>
<td>STEP 2

Areas to inject</td>
<td>Choose from these 3 areas to inject:
• front of left thigh
• front of right thigh
• belly (abdomen) at least 5 cm from the belly button (navel)

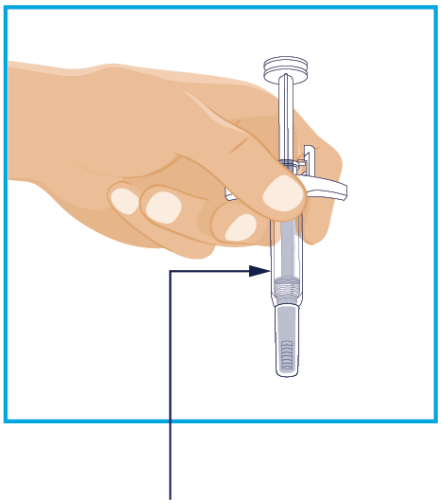
Before injecting, wipe where you will inject in a circular motion with an alcohol pad.</td>
</tr>
</table>

<table>
<tr>
<td> 
Areas to inject</td>
<td>

Do not touch or blow on the injection site after it is cleaned. Allow the skin to dry before injecting.
Do not inject through clothes
Do not inject into skin that is sore, bruised, red, hard, scarred, or has stretch marks.

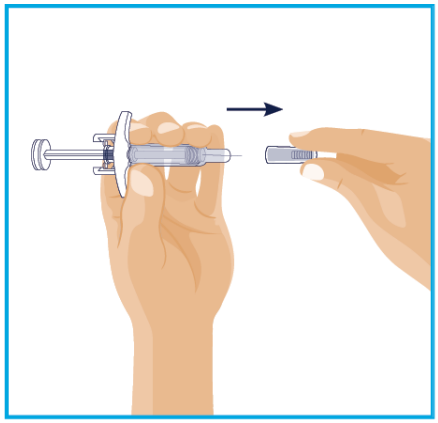
For the 360 mg dose

Use a new injection site for each injection.
For the second syringe, inject at least 3 cm away from the first injection. Do not inject into the same place.

</td>
</tr>
<tr>
<td>STEP 3
 
Check liquid</td>
<td>Hold the syringe with the covered needle pointing down, as shown.

Check the liquid in the syringe.

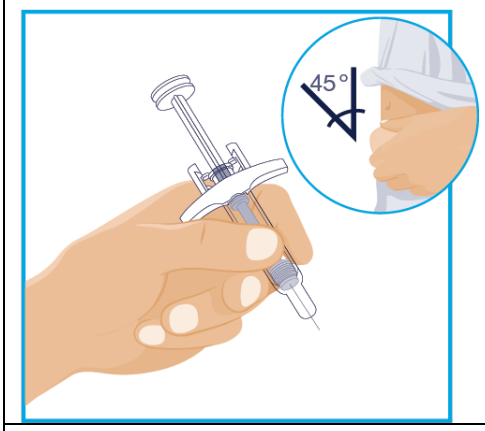
It is normal to see bubbles in the window
The liquid should look clear to yellow and may contain tiny white or clear particles
Do not use if the liquid is cloudy or contains flakes or large particles

</td>
</tr>
<tr>
<td>STEP 4
  </td>
<td>Removing the needle cover:

Hold the syringe in one hand between the finger grip and needle cover
With the other hand, gently pull the needle cover straight off
Do not hold or pull the plunger rod when removing the needle cover
You may see a drop of liquid at the end of the needle. This is normal
Throw away the needle cover
Do not touch the needle with your fingers or let the needle touch anything

</td>
</tr>
</table>

STEP 5

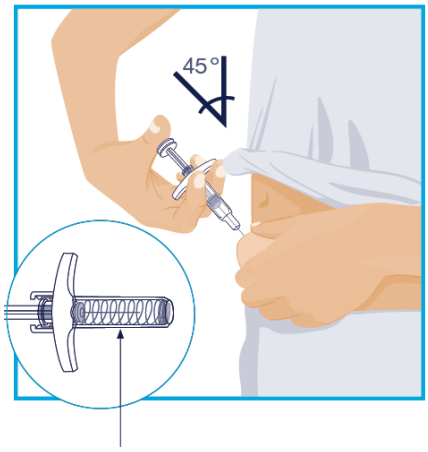


Hold the body of the syringe in one hand between the thumb and index finger, like you would a pencil.

Gently pinch the area of cleaned skin with your other hand and hold it firmly.

Insert the needle all the way into the skin at about a 45-degree angle using a quick, short movement. Keep the syringe steady at the same angle.

STEP 6



Needle guard

Slowly push the plunger rod all the way in until all of the liquid is injected.

Pull the needle out of the skin while keeping the syringe at the same angle.

Slowly take your thumb off the plunger rod. The needle will then be covered by the needle guard.

- The needle guard will not activate unless all the liquid is injected.
- Speak to your doctor, pharmacist or nurse if you think you have not given a full dose.

Press a cotton ball or gauze pad where you have injected and hold for 10 seconds.

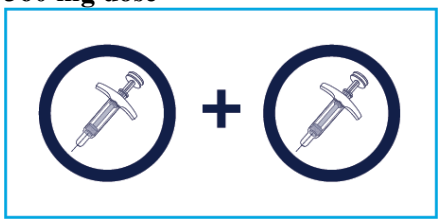
Do not rub the skin where you have injected. You may have slight bleeding from where you injected. This is normal.

STEP 7

180 mg dose

1 injection is required

360 mg dose

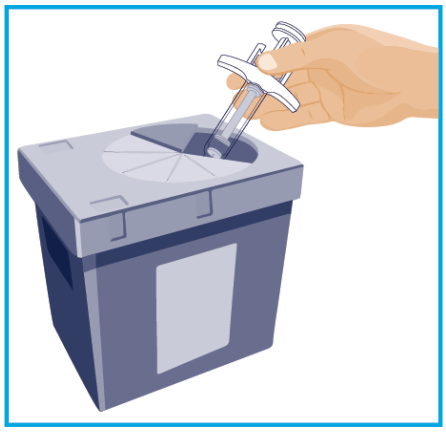


2 injections are required

For the 180 mg dose
1 injection is required.

For the 360 mg dose
2 injections are required

- Repeat Steps 2 through 6 with the second syringe.
- Inject the second syringe straight after the first injection but at least 3 cm away from the first injection.

STEP 8 	Throw away used syringes in a special disposal container right away after use. • **Do not** throw away used syringes in the household waste • Your doctor, pharmacist or nurse will tell you how to return the full special disposal container