

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fasenra 30 mg solution for injection in pre-filled syringe
Fasenra 30 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pre-filled syringe

Each pre-filled syringe contains 30 mg benralizumab* in 1 mL.

Pre-filled pen

Each pre-filled pen contains 30 mg benralizumab* in 1 mL.

*Benralizumab is a humanised monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection) in pre-filled syringe
Solution for injection (injection) in pre-filled pen (Fasenra Pen)

Clear to opalescent, colourless to yellow solution and may contain translucent or white to off-white particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Asthma

Fasenra is indicated as an add-on maintenance treatment in adult patients with severe eosinophilic asthma inadequately controlled despite high-dose inhaled corticosteroids plus long-acting β -agonists (see section 5.1).

Eosinophilic granulomatosis with polyangiitis (EGPA)

Fasenra is indicated as an add-on treatment for adult patients with relapsing or refractory eosinophilic granulomatosis with polyangiitis (see section 5.1).

4.2 Posology and method of administration

Fasenra treatment should be initiated by a physician experienced in the diagnosis and treatment of conditions for which benralizumab is indicated (see section 4.1).

After proper training in the subcutaneous injection technique and education about signs and symptoms of hypersensitivity reactions (see section 4.4), patients with no known history of anaphylaxis or their caregivers may administer Fasenra if their physician determines that it is appropriate, with medical follow-up as necessary. Self-administration should only be considered in patients already experienced with Fasenra treatment.

Posology

Fasenra is intended for long-term treatment. A decision to continue the therapy should be made at least annually based on disease severity, level of disease control and blood eosinophil counts.

Asthma

The recommended dose of benralizumab is 30 mg by subcutaneous injection every 4 weeks for the first 3 doses, and then every 8 weeks thereafter.

EGPA

The recommended dose of benralizumab is 30 mg by subcutaneous injection every 4 weeks.

Patients who develop life-threatening manifestations of EGPA should be evaluated for the need for continued therapy, as Fasenra has not been studied in this population.

Missed Dose

If an injection is missed on the planned date, dosing should resume as soon as possible on the indicated regimen; a double dose must not be administered.

Elderly

No dose adjustment is required for elderly patients (see section 5.2).

Renal and hepatic impairment

No dose adjustment is required for patients with renal or hepatic impairment (see section 5.2).

Paediatric population

The safety and efficacy of Fasenra in children and adolescents aged 6 to 17 years with asthma has not been established. Currently limited data in children 6 to 11 years old and data in adolescents aged 12 to 17 are described in sections 4.8, 5.1 and 5.2, but no recommendation on a posology can be made.

The safety and efficacy of Fasenra in children less than 6 years with asthma have not been established. No data are available.

The safety and efficacy of Fasenra in children and adolescents less than 18 years with EGPA have not been established.

Method of administration

This medicinal product is administered as a subcutaneous injection.

It should be injected into the thigh or abdomen. If the healthcare professional or caregiver administers the injection, the upper arm can also be used. It should not be injected into areas where the skin is tender, bruised, erythematous, or hardened.

Comprehensive instructions for administration using the pre-filled syringe/pre-filled pen are provided in the 'Instructions for Use'.

4.3 Contraindications

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

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.

Asthma exacerbations

Fasenra should not be used to treat acute asthma exacerbations.

Patients should be instructed to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment.

Corticosteroids

Abrupt discontinuation of corticosteroids after initiation of Fasenra therapy is not recommended. Reduction in corticosteroid doses, if appropriate, should be gradual and performed under the supervision of a physician.

Hypersensitivity reactions

Acute systemic reactions including anaphylactic reactions and hypersensitivity reactions (e.g. urticaria, papular urticaria, rash) have occurred following administration of benralizumab (see section 4.8). These reactions may occur within hours of administration, but in some instances have a delayed onset (i.e. days).

A history of anaphylaxis unrelated to benralizumab may be a risk factor for anaphylaxis following Fasenra administration (see section 4.3). In line with clinical practice, patients should be monitored for an appropriate time after administration of Fasenra.

In the event of a hypersensitivity reaction, Fasenra should be discontinued permanently and appropriate therapy should be initiated.

Parasitic (Helminth) infection

Eosinophils may be involved in the immunological response to some helminth infections. Patients with known helminth infections were excluded from participation in clinical trials. It is unknown if benralizumab may influence a patient's response against helminth infections.

Patients with pre-existing helminth infections should be treated before initiating therapy with benralizumab. If patients become infected, while receiving treatment and do not respond to anti-helminth treatment, therapy with benralizumab should be discontinued until infection resolves.

Organ threatening or life-threatening EGPA

Fasenra has not been studied in patients with active organ threatening or life-threatening manifestations of EGPA (see section 4.2).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. In a randomised, double-blind parallel-group study of 103 patients aged between 12 and 21 years with severe asthma, the humoral antibody responses induced by seasonal influenza virus vaccination do not appear to be affected by benralizumab treatment. An effect of benralizumab on the pharmacokinetics of co-administered medicinal products is not expected (see section 5.2).

Cytochrome P450 enzymes, efflux pumps and protein-binding mechanisms are not involved in the clearance of benralizumab. There is no evidence of IL-5R α expression on hepatocytes. Eosinophil depletion does not produce chronic systemic alterations of proinflammatory cytokines.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is a limited amount of data (less than 300 pregnancy outcomes) from the use of benralizumab in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Monoclonal antibodies, such as benralizumab, are transported across the placenta linearly as pregnancy progresses; therefore, potential exposure to the fetus is likely to be greater during the second and third trimester of pregnancy.

As a precautionary measure, it is preferable to avoid the use of Fasenra during pregnancy. Its administration to pregnant women should only be considered if the expected benefit to the mother is greater than any possible risk to the fetus.

Breast-feeding

It is unknown whether benralizumab or its metabolites are excreted in human or animal milk. A risk to the breast-fed child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from using Fasenra taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no fertility data in humans. Animal studies showed no adverse effects of benralizumab treatment on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The safety profile of benralizumab in asthma and EGPA are similar.

The most commonly reported adverse reactions during treatment in asthma are headache (8%) and pharyngitis (3%). The most commonly reported adverse reaction in EGPA is headache (17%). Cases of anaphylactic reaction of varied severity have been reported for benralizumab.

Tabulated list of adverse reactions

The following adverse reactions have been reported with benralizumab during clinical studies in asthma and EGPA and from post-marketing experience. The frequency of adverse reactions is defined using the following convention: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1\,000$ to $< 1/100$); rare ($\geq 1/10\,000$ to $< 1/1\,000$); very rare ($< 1/10\,000$); and not known (cannot be

estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1. Tabulated list of adverse reactions

MedDRA System organ class	Adverse reaction	Frequency
Infections and infestations	Pharyngitis ^a	Common
Immune system disorders	Hypersensitivity reactions ^b	Common
	Anaphylactic reaction	Not known
Nervous system disorders	Headache ^c	Common
General disorders and administration site conditions	Pyrexia	Common
	Injection site reaction ^d	

a. Pharyngitis was defined by the following grouped preferred terms: 'Pharyngitis', 'Pharyngitis bacterial', 'Viral pharyngitis', 'Pharyngitis streptococcal'.

b. Hypersensitivity reactions were defined by the following grouped preferred terms: 'Urticaria', 'Papular urticaria', and 'Rash'. For examples of the associated manifestations reported and a description of the time to onset, see section 4.4.

c. Very common in EGPA study.

d. See 'Description of selected adverse reaction'.

Description of selected adverse reaction

Injection site reactions

In placebo-controlled asthma studies, injection site reactions (e.g. pain, erythema, pruritus, papule) occurred at a rate of 2.2% in patients treated with the recommended benralizumab dose compared with 1.9% in patients treated with placebo. The events were transient in nature.

Long-term safety

In a 56-week extension trial (Trial 4) in patients with asthma from Trials 1, 2 and 3, 842 patients were treated with Fasenra at the recommended dose and remained in the trial. The overall safety profile was similar to the asthma trials described above. Additionally, in an open-label safety extension trial (Trial 5) in patients with asthma from previous trials, 226 patients were treated with Fasenra at the recommended dose for up to 43 months. Combined with the treatment period in previous studies, this corresponds to a median follow-up of 3.4 years (range 8.5 months – 5.3 years). The safety profile during this follow-up period was consistent with the known safety profile of Fasenra.

Paediatric population

There are limited data in paediatric patients. There were 108 adolescents aged 12 to 17 with asthma enrolled in the phase 3 trials (Trial 1: n=53, Trial 2: n=55). Of these, 46 received placebo, 40 received benralizumab every 4 weeks for 3 doses, followed by every 8 weeks thereafter, and 22 received benralizumab every 4 weeks. Adolescent patients aged 12 to 17 (n=86) from Trials 1 and 2 continued the treatment with benralizumab in Trial 4 for up to 108 weeks. The frequency, type and severity of adverse reactions in the adolescent population were observed to be similar to those seen in adults.

In an open-label, uncontrolled pharmacokinetic and pharmacodynamic study of 48 weeks duration in a limited number of paediatric patients (n=28) with uncontrolled severe asthma, the safety profile for patients aged 6 to 11 years old was similar to the adult and adolescent population (see section 4.2).

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

Doses of up to 200 mg were administered subcutaneously in clinical trials to patients with eosinophilic asthma without evidence of dose-related toxicities.

There is no specific treatment for an overdose with benralizumab. If overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for obstructive airway diseases, other systemic drugs for obstructive airway diseases, ATC code: R03DX10

Mechanism of action

Benralizumab is an anti-eosinophil, humanised afucosylated, monoclonal antibody (IgG1, kappa). It specifically binds to the alpha subunit of the human interleukin-5 receptor (IL-5R α). The IL-5 receptor is specifically expressed on the surface of eosinophils and basophils. The absence of fucose in the Fc domain of benralizumab results in high affinity for Fc γ RIII receptors on immune effector cells such as natural killer (NK) cells. This leads to apoptosis of eosinophils and basophils through enhanced antibody-dependent cell-mediated cytotoxicity (ADCC), which reduces eosinophilic inflammation.

Pharmacodynamic effects

Effect on blood eosinophils

In patients with asthma, treatment with benralizumab results in near complete depletion of blood eosinophils within 24 hours following the first dose which is maintained throughout treatment. The depletion of blood eosinophils is accompanied by a reduction in serum eosinophil granule proteins (eosinophil derived neurotoxin [EDN] and eosinophil cationic protein [ECP]) and a reduction in blood basophils.

In patients with EGPA, depletion of blood eosinophils was consistent with the effect observed in asthma trials. Blood eosinophil depletion was seen at the first observed time point, 1 week of treatment, and was maintained throughout the 52-week treatment period.

Effect on eosinophils in the airway mucosa

The effect of benralizumab on eosinophils in the airway mucosa in asthmatic patients with elevated sputum eosinophil counts (at least 2.5%) was evaluated in a 12-week, phase 1, randomised, double-blind, placebo-controlled clinical study with benralizumab 100 or 200 mg administered subcutaneously. In this study, there was a median reduction from baseline in airway mucosa eosinophils of 96% in the benralizumab-treated group compared to a 47% reduction in the placebo group (p=0.039).

Clinical efficacy

Asthma

The efficacy of benralizumab was evaluated in 3 randomised, double-blind, parallel-group, placebo-controlled clinical trials between 28 to 56 weeks duration, in patients aged 12 to 75 years.

In these studies, benralizumab was administered at a dose of 30 mg once every 4 weeks for the first 3 doses, and then every 4 or 8 weeks thereafter as add-on to background treatment and was evaluated in comparison with placebo.

The two exacerbation trials, SIROCCO (Trial 1) and CALIMA (Trial 2), enrolled a total of 2 510 patients with severe uncontrolled asthma, 64% females, with a mean age of 49 years. Patients had a history of 2 or more asthma exacerbations requiring oral or systemic corticosteroid treatment (mean of 3) in the past 12 months, Asthma Control Questionnaire-6 (ACQ-6) score of 1.5 or more at screening, and reduced lung function at baseline (mean predicted pre-bronchodilator forced expiratory volume in 1 second [FEV₁] of 57.5%), despite regular treatment with high-dose inhaled corticosteroid (ICS) (Trial 1) or with medium or high-dose ICS (Trial 2) and a long-acting β -agonist (LABA); at least one additional controller was administered to 51% and 41% of these patients, respectively.

For the oral corticosteroid (OCS) reduction trial ZONDA (Trial 3), a total of 220 asthma patients (61% female; mean age of 51 years) were enrolled; they were treated with daily OCS (8 to 40 mg per day; median of 10 mg) in addition to regular use of high-dose ICS and LABA with at least one additional controller to maintain asthma control in 53% of the cases. The trial included an 8-week run-in period during which the OCS was titrated to the minimum effective dose without losing asthma control. Patients had blood eosinophil counts ≥ 150 cells/ μ L and a history of at least one exacerbation in the past 12 months.

While 2 dose regimens were studied in Trials 1, 2, and 3, the recommended dose regimen is benralizumab administered every 4 weeks for the first 3 doses, then every 8 weeks thereafter (see section 4.2) as no additional benefit was observed by more frequent dosing. The results summarised below are those for the recommended dose regimen.

Exacerbation trials

The primary endpoint was the annual rate of clinically significant asthma exacerbations in patients with baseline blood eosinophil counts ≥ 300 cells/ μ L who were taking high-dose ICS and LABA. Clinically significant asthma exacerbation was defined as worsening of asthma requiring use of oral/systemic corticosteroids for at least 3 days, and/or emergency department visits requiring use of oral/systemic corticosteroids and/or hospitalisation. For patients on maintenance OCS, this was defined as a temporary increase in stable oral/systemic corticosteroids for at least 3 days or a single depo-injectable dose of corticosteroids.

In both trials, patients receiving benralizumab experienced significant reductions in annual exacerbation rates compared to placebo in patients with blood eosinophils ≥ 300 cells/ μ L. In addition, change from baseline in mean FEV₁ showed benefit as early as 4 weeks, which was maintained through to end of treatment (Table 2).

Reductions in exacerbation rates were observed irrespective of baseline eosinophil count; however, increasing baseline eosinophil counts was identified as a potential predictor of improved treatment response particularly for FEV₁.

Table 2. Results of annual exacerbation rate and lung function at end of treatment of Trial 1 and 2 by eosinophil count

	Trial 1		Trial 2	
	Benralizumab	Placebo	Benralizumab	Placebo
Blood eosinophil count ≥ 300 cells/μL^a	n=267	n=267	n=239	n=248
Clinically significant exacerbations				
Rate	0.74	1.52	0.73	1.01

	Trial 1		Trial 2	
	Benralizumab	Placebo	Benralizumab	Placebo
Difference	-0.78		-0.29	
Rate ratio (95% CI)	0.49 (0.37, 0.64)		0.72 (0.54, 0.95)	
p-value	<0.001		0.019	
Pre-bronchodilator FEV ₁ (L)				
Mean baseline	1.660	1.654	1.758	1.815
Improvement from baseline	0.398	0.239	0.330	0.215
Difference (95% CI)	0.159 (0.068, 0.249)		0.116 (0.028, 0.204)	
p-value	0.001		0.010	
Blood eosinophil count <300 cells/μL ^b	n=131	n=140	n=125	n=122
Clinically significant exacerbations				
Rate	1.11	1.34	0.83	1.38
Difference	-0.23		-0.55	
Rate ratio (95% CI)	0.83 (0.59, 1.16)		0.60 (0.42, 0.86)	
Pre-bronchodilator FEV ₁ (L)				
Mean change	0.248	0.145	0.140	0.156
Difference (95% CI)	0.102 (-0.003, 0.208)		-0.015 (-0.127, 0.096)	

a. Intent-to-treat population (patients on high-dose ICS and blood eosinophils ≥ 300 cells/μL).

b. Not powered to detect a treatment difference in patients with blood eosinophils <300 cells/μL.

Across Trials 1 and 2 combined, there was a numerically greater exacerbation rate reduction and greater improvements in FEV₁ with increasing baseline blood eosinophils.

The rate of exacerbations requiring hospitalisation and/or emergency room visits for patients receiving benralizumab compared to placebo for Trial 1 were 0.09 versus 0.25 (rate ratio 0.37, 95% CI: 0.20, 0.67, $p \leq 0.001$) and for Trial 2 were 0.12 versus 0.10 (rate ratio 1.23, 95% CI: 0.64, 2.35, $p=0.538$). In Trial 2, there were too few events in the placebo treatment arm to draw conclusions for exacerbations requiring hospitalisation or emergency room visits.

In both Trials 1 and 2, patients receiving benralizumab experienced statistically significant reductions in asthma symptoms (Total Asthma Score) compared to patients receiving placebo. Similar improvement in favour of benralizumab was observed for the ACQ-6 and Standardised Asthma Quality of Life Questionnaire for 12 Years and Older (AQLQ(S)+12) (Table 3).

Table 3. Treatment difference in mean change from baseline in total asthma symptom score, ACQ-6 and AQLQ(s)+12 at end of treatment - Patients on high-dose ICS and blood eosinophils ≥ 300 cells/μL

	Trial 1		Trial 2	
	Benralizumab (n ^a =267)	Placebo (n ^a =267)	Benralizumab (n ^a =239)	Placebo (n ^a =248)
Total asthma symptom score^b				
Mean baseline	2.68	2.74	2.76	2.71

	Trial 1		Trial 2	
	Benralizumab (n ^a =267)	Placebo (n ^a =267)	Benralizumab (n ^a =239)	Placebo (n ^a =248)
Improvement from baseline	-1.30	-1.04	-1.40	-1.16
Difference (95% CI)	-0.25 (-0.45, -0.06)		-0.23 (-0.43, -0.04)	
p-value	0.012		0.019	
ACQ-6				
Mean baseline	2.81	2.90	2.80	2.75
Improvement from baseline	-1.46	-1.17	-1.44	-1.19
Difference (95% CI)	-0.29 (-0.48, -0.10)		-0.25 (-0.44, -0.07)	
AQLQ(S)+12				
Mean baseline	3.93	3.87	3.87	3.93
Improvement from baseline	1.56	1.26	1.56	1.31
Difference (95% CI)	0.30 (0.10, 0.50)		0.24 (0.04, 0.45)	

^a. Number of patients (n) varies slightly due to the number of patients for whom data were available for each variable. Results shown based on last available data for each variable.

^b. Asthma symptom scale: total score from 0 (least) to 6 (most); day and night time asthma symptom scores from 0 (least) to 3 (most) symptoms. Individual day and night time scores were similar.

Subgroup analyses by prior exacerbation history

Subgroup analyses from Trials 1 and 2 identified patients with higher prior exacerbation history as a potential predictor of improved treatment response. When considered alone or in combination with baseline blood eosinophils count, these factors may further identify patients who may achieve greater response from benralizumab treatment (Table 4).

Table 4. Exacerbation rate and pulmonary function (FEV₁) at end of treatment by number of exacerbations in the previous year - Patients on high-dose ICS and blood eosinophils ≥ 300 cells/ μ L

	Trial 1		Trial 2	
	Benralizumab (N=267)	Placebo (N=267)	Benralizumab (N=239)	Placebo (N=248)
Baseline of 2 exacerbations				
n	164	149	144	151
Exacerbation rate	0.57	1.04	0.63	0.62
Difference	-0.47		0.01	
Rate ratio (95% CI)	0.55 (0.37, 0.80)		1.01 (0.70, 1.46)	
Pre-bronchodilator FEV ₁ mean change	0.343	0.230	0.266	0.236
Difference (95% CI)	0.113 (-0.002, 0.228)		0.029 (-0.079, 0.137)	
Baseline of 3 or more exacerbations				
n	103	118	95	97
Exacerbation rate	0.95	2.23	0.82	1.65
Difference	-1.28		-0.84	
Rate ratio (95% CI)	0.43 (0.29, 0.63)		0.49 (0.33, 0.74)	

	Trial 1		Trial 2	
	Benralizumab (N=267)	Placebo (N=267)	Benralizumab (N=239)	Placebo (N=248)
Pre-bronchodilator FEV ₁ mean change	0.486	0.251	0.440	0.174
Difference (95% CI)	0.235 (0.088, 0.382)		0.265 (0.115, 0.415)	

Oral corticosteroid dose reduction trials

ZONDA (Trial 3), a placebo-controlled study, and PONENTE (Trial 6), a single arm, open-label study, evaluated the effect of benralizumab on reducing the use of maintenance OCS.

In Trial 3, the primary endpoint was percent reduction from baseline of the final OCS dose during Weeks 24 to 28, while maintaining asthma control. Table 5 summarises the study results for Trial 3.

Table 5. Effect of benralizumab on OCS dose reduction, Trial 3

	Benralizumab (N=73)	Placebo (N=75)
Wilcoxon rank sum test (primary analysis method)		
Median % reduction in daily OCS dose from baseline (95% CI)	75 (60, 88)	25 (0, 33)
Wilcoxon rank sum test p-value	<0.001	
Proportional odds model (sensitivity analysis)		
Percent reduction in OCS from baseline at Week 28		
≥90% reduction	27 (37%)	9 (12%)
≥75% reduction	37 (51%)	15 (20%)
≥50% reduction	48 (66%)	28 (37%)
>0% reduction	58 (79%)	40 (53%)
No change or no decrease in OCS	15 (21%)	35 (47%)
Odds ratio (95% CI)	4.12 (2.22, 7.63)	
Reduction in the daily OCS dose to 0 mg/day*	22 (52%)	8 (19%)
Odds ratio (95% CI)	4.19 (1.58, 11.12)	
Reduction in the daily OCS dose to ≤5 mg/day	43 (59%)	25 (33%)
Odds ratio (95% CI)	2.74 (1.41, 5.31)	
Exacerbation rate	0.54	1.83
Rate ratio (95% CI)	0.30 (0.17, 0.53)	
Exacerbation rate requiring hospitalisation/emergency room visit	0.02	0.32
Rate ratio (95% CI)	0.07 (0.01, 0.63)	

* Only patients with an optimised baseline OCS dose of 12.5 mg or less were eligible to achieve a 100% reduction in OCS dose during the study.

Lung function, asthma symptom score, ACQ-6 and AQLQ(S)+12 were also assessed in Trial 3 and showed results similar to those in Trials 1 and 2.

Trial 6 enrolled 598 adult patients with severe asthma (blood eosinophil count ≥150 cells/μL at entry or ≥300 cells/μL in the past 12 months if study entry count was <150 cells/μL) who were oral corticosteroid-dependent. The primary endpoints were proportion of patients who eliminated OCS

while maintaining asthma control and proportion of patients who achieved a final OCS dose less than or equal to 5 mg while maintaining asthma control and taking into account adrenal function. The proportion of patients who eliminated maintenance OCS was 62.9%. The proportion of patients who achieved an OCS dose less than or equal to 5 mg (while maintaining asthma control and not limited by adrenal function) was 81.9%. Effects on OCS reduction were similar irrespective of blood eosinophil count at study entry (including patients with blood eosinophils <150 cells/ μ L) and maintained over an additional period of 24 to 32 weeks. The annualised exacerbation rate in Trial 6 was comparable to that reported in previous trials.

Long-term extension trials

The long-term efficacy and safety of benralizumab was evaluated in a phase 3, 56-week extension trial BORA (Trial 4). The trial enrolled 2 123 patients, 2 037 adults and 86 adolescent patients (aged 12 years and older) from Trials 1, 2 and 3. Trial 4 assessed the long-term effect of benralizumab on annual exacerbation rate, lung function, ACQ-6, AQLQ(S)+12 and maintenance of OCS reduction at the 2 dose regimens studied in the predecessor studies.

At the recommended dose regimen, the reduction in annual rate of exacerbations observed in the placebo-controlled predecessor Trials 1 and 2 (in patients with baseline blood eosinophil counts ≥ 300 cells/ μ L who were taking high-dose ICS) was maintained over the second year of treatment (Table 6). In patients who received benralizumab in predecessor Trials 1 and 2, 73% were exacerbation-free in the extension Trial 4.

Table 6. Exacerbations over an extended treatment period^a

	Placebo^b (N=338)	Benralizumab (N=318)		
	Trial 1 & 2	Trial 1 & 2	Trial 4	Trial 1, 2 & 4^c
Rate	1.23	0.65	0.48	0.56

^a. Patients that entered Trial 4 from predecessor Trials 1 and 2 with baseline blood eosinophil counts ≥ 300 cells/ μ L who were taking high-dose ICS.

^b. Placebo patients in Trials 1 and 2 are included up to the end of the predecessor trial (Week 48 in Trial 1, Week 56 in Trial 2).

^c. Total duration of treatment: 104 – 112 weeks.

Similar maintenance of effect was observed throughout Trial 4 in lung function, ACQ-6 and AQLQ(S)+12 (Table 7).

Table 7. Change from baseline for lung function, ACQ-6, and AQLQ(S)+12^a

	Trial 1 & 2 Baseline^b	Trial 1 & 2 EOT^c	Trial 4 EOT^d
Pre-bronchodilator FEV₁ (L)			
n	318	305	290
Mean baseline (SD)	1.741 (0.621)	--	--
Change from baseline (SD) ^e	--	0.343 (0.507)	0.404 (0.555)
ACQ-6			
n	318	315	296
Mean baseline (SD)	2.74 (0.90)	--	--
Change from baseline (SD) ^e	--	-1.44 (1.13)	-1.47 (1.05)
AQLQ(S)+12			
n	307	306	287
Mean baseline (SD)	3.90 (0.99)	--	--
Change from baseline (SD) ^e	--	1.58 (1.23)	1.61 (1.21)

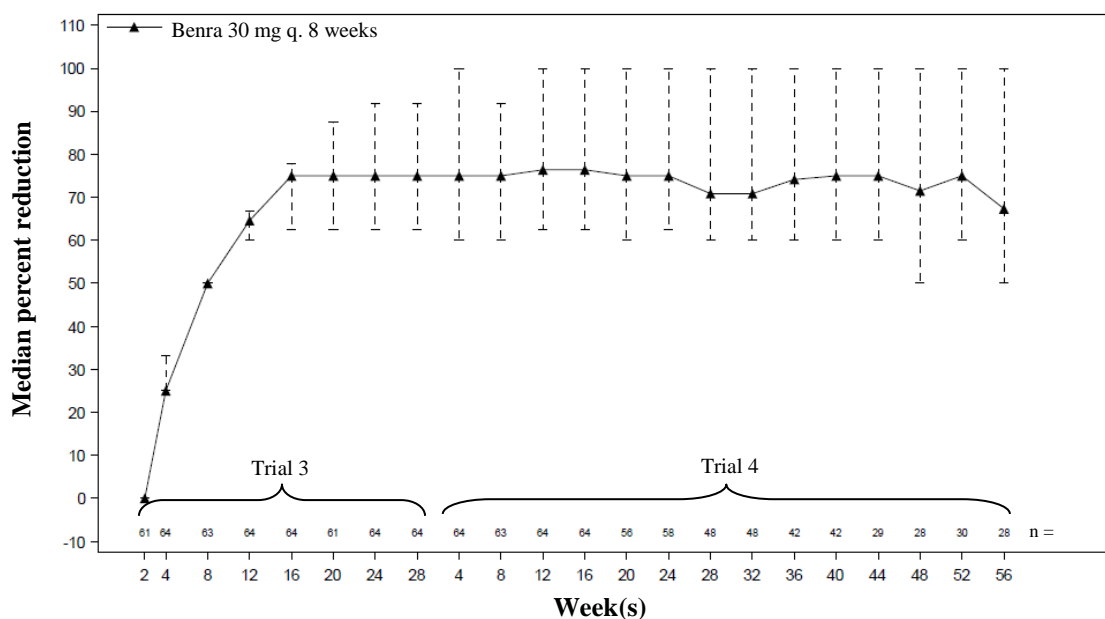
n=number of patients with data at timepoint. SD=standard deviation.

- a. Baseline blood eosinophil counts ≥ 300 cells/ μ L and taking high-dose ICS: benralizumab administered at the recommended dose regimen.
- b. Integrated analysis of Trial 1 and 2 baseline includes adults and adolescents.
- c. Integrated analysis at End of Treatment (EOT) of Trial 1 (Week 48) and Trial 2 (Week 56).
- d. EOT for Trial 4 was Week 48 (the last timepoint for adults and adolescent data).
- e. Baseline is prior to benralizumab treatment in Trial 1 and 2.

Efficacy in Trial 4 was also evaluated in patients with baseline blood eosinophil counts < 300 cells/ μ L and was consistent with Trials 1 and 2.

Maintenance of the reduction in daily OCS dose was also observed over the extension trial in patients enrolled from Trial 3 (Figure 1).

Figure 1. Median percent reductions in daily OCS over time (Trial 3 and 4)^a



- a. Predecessor Trial 3 patients who continued benralizumab treatment into Trial 4. Patients were permitted to enter a second extension trial after a minimum of 8 weeks in Trial 4 without completing the 56-week extension period.

In Trial 5, a second long-term safety extension study (see section 4.8), the annualised exacerbation rate (0.47) in patients receiving the approved dose regimen was comparable to that reported in the predecessor Trials 1, 2 (0.65) and 4 (0.48).

Eosinophilic granulomatosis with polyangiitis (EGPA)

The efficacy of benralizumab was evaluated in a randomised, double-blind, active-controlled, non-inferiority clinical trial of 52-weeks treatment duration, in patients aged 18 years and older with EGPA. A total of 140 patients were randomised to receive either 30 mg of benralizumab or 300 mg of mepolizumab administered subcutaneously every 4 weeks. Patients enrolled had a history of relapsing or refractory disease and were on stable OCS therapy (OCS; ≥ 7.5 to ≤ 50 mg/day prednisolone/prednisone), with or without stable immunosuppressant therapy (excluding cyclophosphamide). The median baseline OCS daily dose was 10 mg and 36% were receiving immunosuppressive therapy. The OCS dose was tapered at the discretion of the investigator. Patients with active organ threatening or life-threatening EGPA were excluded from the trial.

Remission

The primary endpoint was the proportion of subjects in remission, defined as Birmingham Vasculitis Activity Score (BVAS)=0 (no active vasculitis) plus prednisolone/prednisone dose ≤ 4 mg/day, at both Week 36 and Week 48. As shown in Table 8, benralizumab demonstrated non-inferiority to mepolizumab for the primary endpoint. Results for accrued duration of remission and the components of remission are also shown in Table 8.

Table 8. Remission and components of remission in EGPA

	Remission (OCS≤4 mg/day + BVAS=0)		OCS≤4 mg/day		BVAS=0	
	Benra ^a N=70	Mepo ^b N=70	Benra ^a N=70	Mepo ^b N=70	Benra ^a N=70	Mepo ^b N=70
Patients in remission at both Weeks 36 and 48						
Patients, n (%) ^c	40 (58)	40 (57)	42 (61)	41 (58)	58 (83)	59 (84)
Differences in remission rate (%) ^c (95% CI) (p-value)	1.21 (-14.12, 16.53) (0.88) ^d		2.64 (-12.67, 17.95) (0.74) ^{d e}		-1.17 (-13.27, 10.94) (0.85) ^{d e}	
Accrued duration over 52 weeks, n (%)						
0 weeks ^f	9 (13)	15 (21)	9 (13)	12 (17)	0	0
>0 to <12 weeks	13 (19)	10 (14)	11 (16)	12 (17)	0	2 (3)
12 to <24 weeks	8 (11)	8 (11)	9 (13)	8 (11)	2 (3)	2 (3)
24 to <36 weeks	20 (29)	19 (27)	19 (27)	18 (26)	6 (9)	7 (10)
≥36 weeks	20 (29)	18 (26)	22 (31)	20 (29)	62 (89)	59 (84)

N=number of patients in analysis.

a. Benralizumab (Benra) 30 mg administered every 4 weeks.

b. Mepolizumab (Mepo) 300 mg administered every 4 weeks.

c. Model adjusted percentages.

d. Used for superiority testing.

e. Not formally tested in a pre-specified multiplicity testing procedure.

f. Did not achieve remission at any point.

The proportion of patients achieving remission within the first 24 weeks of treatment and remaining in remission through Week 52 was 42% for benralizumab and 37% for mepolizumab (difference in responder rate 5.54%, 95% CI: -9.30, 20.37, nominal p-value 0.46).

Using an alternative remission definition of BVAS=0 plus prednisolone/prednisone ≤ 7.5 mg/day, a consistent efficacy between groups for these endpoints was observed.

Patients achieved the primary remission endpoint across the prespecified demographic and baseline characteristic subgroups.

Relapse

The hazard ratio for time to first relapse (vasculitis, asthma, or sino-nasal) was 0.98 (95% CI: 0.53, 1.82, nominal p-value 0.95). Relapse was observed in 30% of patients on benralizumab and 30% of patients on mepolizumab. The annualised relapse rate was 0.50 for patients receiving benralizumab versus 0.49 for patients receiving mepolizumab (rate ratio 1.03, 95% CI: 0.56, 1.90, nominal p-value 0.93). The types of relapse were consistent for patients receiving benralizumab or mepolizumab.

Oral corticosteroids

The average daily OCS dose during Weeks 48 to 52 is presented in Table 9. A 100% reduction in the OCS dose was observed in 41% of patients receiving benralizumab compared to 26% of those receiving mepolizumab (difference 15.69%, 95% CI: 0.67, 30.71, nominal p-value 0.04).

Table 9. Average daily oral corticosteroid dose during weeks 48 to 52 in EGPA

	Number (%) of Patients	
	Benralizumab ^a (N=70)	Mepolizumab ^b (N=70)
0 mg	29 (41)	19 (27)
>0 to ≤ 4.0 mg	19 (27)	30 (43)
>4.0 to ≤ 7.5 mg	15 (21)	13 (19)
>7.5 mg	7 (10)	8 (11)

N=number of patients in analysis.

a. Benralizumab 30 mg administered every 4 weeks.

b. Mepolizumab 300 mg administered every 4 weeks.

Asthma Control Questionnaire-6 (ACQ-6)

The ACQ-6 mean change from baseline was -0.57 for benralizumab versus -0.61 for mepolizumab (difference 0.05, 95% CI: -0.18, 0.27, nominal p-value 0.67).

Immunogenicity

Overall, treatment-emergent anti-drug antibody (ADA) response developed in 107 out of 809 (13%) patients with asthma treated with benralizumab at the recommended dose regimen during the 48 to 56 week treatment period of the phase 3 placebo-controlled exacerbation trials. Most antibodies were neutralising and persistent. Anti-benralizumab antibodies were associated with increased clearance of benralizumab and increased blood eosinophil levels in patients with high ADA titres compared to antibody negative patients; in rare cases, blood eosinophil levels returned to pre-treatment levels. Based on current patient follow-up, no evidence of an association of ADA with efficacy or safety was observed.

Following a second year of treatment of these patients with asthma from the phase 3 placebo-controlled trials, an additional 18 out of 510 (4%) had newly developed treatment-emergent antibodies. Overall, in patients who were ADA positive in the predecessor trials, titres remained stable or declined in the second year of treatment. No evidence of an association of ADA with efficacy or safety was observed.

In patients with EGPA, treatment-emergent ADA response developed in 6 out of 67 (9%) patients treated with benralizumab during the Phase 3 active-controlled 52-week treatment period. Neutralising antibody activity was detected in one of the ADA positive patients.

Paediatric population

Asthma

There were 108 adolescents aged 12 to 17 with asthma enrolled in the phase 3 trials (Trial 1: n=53, Trial 2: n=55). Of these, 46 received placebo, 40 received benralizumab every 4 weeks for 3 doses, followed by every 8 weeks thereafter, and 22 received benralizumab every 4 weeks. In these trials, the asthma exacerbation rate in adolescent patients treated with benralizumab administered at the recommended dose regimen was 0.70 (n=40, 95% CI: 0.42, 1.18) compared to 0.41 for placebo (n=46, 95% CI: 0.23, 0.73) [rate ratio 1.70, 95% CI: 0.78, 3.69].

Adolescent patients aged 12 to 17 (n=86) from Trials 1 and 2 continued treatment with benralizumab in Trial 4 for up to 108 weeks. Efficacy and safety were consistent with the predecessor trials.

In an open-label, uncontrolled pharmacokinetic and pharmacodynamic study of 48 weeks duration in a limited number of patients 6 to 11 years (n=28) with uncontrolled severe asthma, the magnitude of blood eosinophil depletion was similar to adults and adolescents.

No conclusion can be drawn regarding asthma efficacy in the paediatric population (see section 4.2).

The European Medicines Agency has deferred the obligation to submit the results of studies with benralizumab in one or more subsets of the paediatric population in asthma (see section 4.2 for information on paediatric use).

Eosinophilic granulomatosis with polyangiitis (EGPA)

The European Medicines Agency has deferred the obligation to submit the results of studies with benralizumab in one or more subsets of the paediatric population in EGPA (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

The pharmacokinetic properties of benralizumab below are based on the population pharmacokinetics analyses from the asthma trials. The pharmacokinetics of benralizumab were dose-proportional in patients with asthma following subcutaneous administration over a dose range of 2 to 200 mg.

Absorption

Following subcutaneous administration to patients with asthma, the absorption half-life was 3.5 days. Based on population pharmacokinetic analysis, the estimated absolute bioavailability was approximately 59% and there was no clinically relevant difference in relative bioavailability in the administration to the abdomen, thigh, or upper arm.

Distribution

Based on population pharmacokinetic analysis, central and peripheral volume of distribution of benralizumab was 3.1 L and 2.5 L, respectively, for a 70 kg individual.

Biotransformation

Benralizumab is a humanised IgG1 monoclonal antibody that is degraded by proteolytic enzymes widely distributed in the body and not restricted to hepatic tissue.

Elimination

From population pharmacokinetic analysis, benralizumab exhibited linear pharmacokinetics and no evidence of target receptor-mediated clearance pathway. The estimated systemic clearance (CL) for benralizumab was at 0.29 L/d. In patients with EGPA, the model estimated systemic clearance was 0.22 L/d. Following subcutaneous administration, the elimination half-life was approximately 15.5 days.

Special populations

Elderly (≥ 65 years old)

Based on population pharmacokinetic analysis, age did not affect benralizumab clearance. However, no data are available in patients over 75 years of age.

Paediatric population

Based on population pharmacokinetic analysis and clinical study data, the pharmacokinetics of benralizumab in children and adolescents aged 6 to 17 years with asthma were consistent with adults after accounting for bodyweight as applicable (see section 4.2).

Gender, race

A population pharmacokinetics analysis, indicated that there was no significant effect of gender and race on benralizumab clearance.

Renal impairment

No formal clinical studies have been conducted to investigate the effect of renal impairment on benralizumab. Based on population pharmacokinetic analysis, benralizumab clearance was comparable in subjects with creatinine clearance values between 30 and 80 mL/min and patients with normal renal function. There are limited data available in subjects with creatinine clearance values less than 30 mL/min; however, benralizumab is not cleared renally.

Hepatic impairment

No formal clinical studies have been conducted to investigate the effect of hepatic impairment on benralizumab. IgG monoclonal antibodies are not primarily cleared via hepatic pathway; change in hepatic function is not expected to influence benralizumab clearance. Based on population pharmacokinetic analysis, baseline hepatic function biomarkers (ALT, AST, and bilirubin) had no clinically relevant effect on benralizumab clearance.

Interaction

Based on the population pharmacokinetic analysis, commonly co-administered medicinal products (montelukast, paracetamol, proton pump inhibitors, macrolides and theophylline/aminophylline) had no effect on benralizumab clearance in patients with asthma.

5.3 Preclinical safety data

As benralizumab is a monoclonal antibody, no genotoxicity or carcinogenicity studies have been conducted.

Animal toxicology and/or pharmacology

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology or repeated dose toxicity studies in monkeys. Intravenous and subcutaneous administration to cynomolgus monkeys was associated with reductions in peripheral blood and bone marrow eosinophil counts, with no toxicological findings.

Pregnancy

In a prenatal and postnatal development study in pregnant cynomolgus monkeys, there were no benralizumab-related maternal, embryo-foetal, or postnatal effects observed.

Fertility

No dedicated animal studies have been conducted. No benralizumab-related impairment was observed in reproductive parameters of male and female cynomolgus monkeys. Examination of surrogate fertility parameters (including organ weights and histopathology of reproductive tissues) in animals treated with benralizumab suggested no impairment of fertility. However, in the offspring of monkeys dosed while pregnant, there was a reduction in eosinophils.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Histidine
Histidine hydrochloride monohydrate
Trehalose dihydrate
Polysorbate 20 (E 432)
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

3 years

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C).

Fasenra may be kept at room temperature up to 25°C for a maximum of 14 days. After removal from the refrigerator, Fasenra must be used within 14 days or discarded.

Store in the original package in order to protect from light.

Do not freeze. Do not shake. Do not expose to heat.

6.5 Nature and contents of container

Pre-filled syringe

One mL solution in a single-use pre-filled syringe made from type I glass with a staked 29-gauge ½-inch (12.7 mm) stainless steel needle, rigid needle shield, and Fluorotec-coated plunger stopper in a passive safety device.

Pack containing 1 pre-filled syringe.

Pre-filled pen

One mL solution in a sterile, single use pre-filled pen made from type I glass with staked 29-gauge ½-inch (12.7 mm) stainless steel needle, rigid needle shield, and Fluorotec-coated stopper in a pre-filled pen.

Pack containing 1 pre-filled pen.

Not all presentations may be marketed.

6.6 Special precautions for disposal and other handling

Prior to administration, allow the pre-filled syringe or pre-filled pen to reach room temperature 20°C to 25°C by leaving the carton out of the refrigerator for around 30 minutes.

Visually inspect Fasenra for particulate matter and discolouration prior to administration. Fasenra is clear to opalescent, colourless to yellow, and may contain translucent or white to off-white particles. Do not use Fasenra if liquid is cloudy, discoloured, or if it contains large particles or foreign particulate matter.

Additional information and instructions for the preparation and administration of Fasenra using the pre-filled syringe or pre-filled pen are given in the package leaflet and 'Instructions for Use'.

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

7. MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1252/001 1 pre-filled syringe
EU/1/17/1252/002 1 pre-filled pen

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 January 2018
Date of latest renewal: 15 September 2022

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 OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS 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 OF THE BIOLOGICAL ACTIVE SUBSTANCE AND
MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer of the biological active substance

AstraZeneca Pharmaceuticals LP Frederick Manufacturing Center (FMC)
633 Research Court
Frederick, Maryland
21703
United States

Name and address of the manufacturers responsible for batch release

AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

MedImmune UK Ltd
6 Renaissance Way
Liverpool, L24 9JW
United Kingdom

AstraZeneca Nijmegen B.V., Nijmegen
Lagelandseweg 78
Nijmegen, 6545CG
Netherlands

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.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

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- PRE-FILLED SYRINGE****1. NAME OF THE MEDICINAL PRODUCT**

Fasenra 30 mg solution for injection in pre-filled syringe
benralizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 30 mg benralizumab in 1 mL.

3. LIST OF EXCIPIENTS

Excipients: histidine, histidine hydrochloride monohydrate, trehalose dihydrate, polysorbate 20, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the instructions for use and the package leaflet before use.

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

Discard date:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze, shake or expose to heat.

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

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1252/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

fasenra 30 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
--

BLISTERED PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Fasenra 30 mg solution for injection in pre-filled syringe
benralizumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER
--

AstraZeneca

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Subcutaneous use
Store in a refrigerator.
Do not freeze, shake or expose to heat.
Keep the pre-filled syringe in the outer carton in order to protect from light.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS PRE-FILLED SYRINGE LABEL
--

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

Fasenra 30 mg injection
benralizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT
--

1 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**OUTER CARTON- PRE-FILLED PEN****1. NAME OF THE MEDICINAL PRODUCT**

Fasenra 30 mg solution for injection in pre-filled pen
benralizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 30 mg benralizumab in 1 mL.

3. LIST OF EXCIPIENTS

Excipients: histidine, histidine hydrochloride monohydrate, trehalose dihydrate, polysorbate 20, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled pen

Each pack contains 1 Fasenra Pen

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use

Read the instructions for use and the package leaflet before use.

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

Discard date:

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze, shake or expose to heat.

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

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)
--

EU/1/17/1252/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY
--

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

fasenra 30 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 PRE-FILLED PEN LABEL
--

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

Fasenra 30 mg injection
benralizumab
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT
--

1 mL

6. OTHER

AstraZeneca

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Fasenra 30 mg solution for injection in pre-filled syringe benralizumab

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 Fasenra is and what it is used for
2. What you need to know before you use Fasenra
3. How to use Fasenra
4. Possible side effects
5. How to store Fasenra
6. Contents of the pack and other information

1. What Fasenra is and what it is used for

What Fasenra is

Fasenra contains the active substance benralizumab, which is a monoclonal antibody, a type of protein that recognises and attaches to a specific target substance in the body. The target of benralizumab is a protein called interleukin-5 receptor, which is found particularly on a type of white blood cell called an eosinophil.

What Fasenra is used for

Asthma

Fasenra is used to treat **severe eosinophilic asthma** in adults. Eosinophilic asthma is a type of asthma where patients have too many eosinophils in the blood or lungs.

Fasenra is used together with other medicines to treat asthma (high doses of ‘corticosteroid inhalers’ plus other asthma medicines) when the condition is not well controlled by those other medicines alone.

Eosinophilic granulomatosis with polyangiitis (EGPA)

Fasenra is used to treat EGPA in adults. EGPA is a condition where people have too many eosinophils in the blood and tissues and also have a form of vasculitis. This means there is inflammation of the blood vessels. This condition most commonly affects the lungs and sinuses but often affects other organs such as the skin, heart and kidneys.

How Fasenra works

Eosinophils are white blood cells involved in asthma and EGPA inflammation. By attaching to the eosinophils, Fasenra helps to reduce their numbers and inflammation.

What are the benefits of using Fasenra

Asthma

Fasenra may reduce the number of asthma attacks you are experiencing, help you breathe better and decrease your asthma symptoms. If you are taking medicines called ‘oral corticosteroids’, using Fasenra may also allow you to reduce the daily dose or stop the oral corticosteroids you need to control your asthma.

EGPA

Fasenra can reduce symptoms and prevent flare-ups of EGPA. This medicine may also allow you to reduce the daily dose of oral corticosteroids you need to control your symptoms.

2. What you need to know before you use Fasenra

Do not use Fasenra:

- If you are **allergic** to benralizumab or any of the other ingredients of this medicine (listed in section 6). **Check with your doctor, nurse or pharmacist** if you think this applies to you.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before you are given Fasenra:

- if you have a **parasitic infection** or if you live in an area where parasitic infections are common or you are travelling to such a region. This medicine may weaken your ability to fight certain types of parasitic infections.
- if you have had an **allergic reaction to an injection or medicine in the past** (see section 4 for symptoms of an allergic reaction).

Also, talk to your doctor, nurse or pharmacist when you are given Fasenra:

- if your **asthma remains uncontrolled or worsens** during treatment with this medicine.
- if you have any symptoms of an **allergic reaction** (see section 4). Allergic reactions have occurred in patients receiving this medicine.

Fasenra is **not a rescue medicine**. Do not use it to treat a sudden asthma attack.

Look out for signs of serious allergic reactions

Fasenra can potentially cause serious allergic reactions. You must look out for signs of these reactions (such as hives, rash, breathing problems, fainting, dizziness, feeling lightheaded and/or swelling of your face, tongue or mouth) while you are taking Fasenra.

It is important that you talk to your doctor about how to recognise early symptoms of serious allergic reactions and how to manage these reactions if they occur.

In order to improve the traceability of biological medicinal products, record the name and the lot number, included on the outer carton and the label of the pre-filled syringe, every time you get a new package of Fasenra and provide this information when reporting any side effects.

Other medicines for asthma or EGPA

Do not suddenly stop taking or change the dose of your other medicines for your condition once you have started Fasenra.

If your response to the treatment allows it, your doctor may try to reduce the dose of some of these medicines, especially ones called ‘corticosteroids’. This should be done gradually and under the direct supervision of your doctor.

Tell your doctor if you are taking, have recently taken or might take any other medicines before using Fasenra.

Children and adolescents

Do not give this medicine to children below the age of 18 because the safety and benefits of this medicine are not known in this population.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, **ask your doctor for advice** before using this medicine.

Do not use Fasenra if you are pregnant unless your doctor tells you otherwise. It is not known whether Fasenra could harm your unborn baby.

It is not known whether the ingredients of Fasenra can pass into breast milk. **If you are breast-feeding or plan to breast-feed, talk to your doctor.**

Driving and using machines

It is unlikely that Fasenra will affect your ability to drive and use machines.

Fasenra contains Polysorbate 20

This medicine contains 0.06 mg of polysorbate 20 (plant-derived) in each 30 mg pre-filled syringe. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Fasenra

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

Asthma

The recommended dose is an injection of 30 mg. The first 3 injections are every 4 weeks. After this, injections are 30 mg every 8 weeks.

EGPA

The recommended dose is an injection of 30 mg every 4 weeks.

Fasenra is given as an injection just under the skin (subcutaneously). You and your doctor or nurse should decide if you should inject Fasenra yourself. You should not inject Fasenra yourself if you have not received Fasenra previously and if you had previous allergic reaction with Fasenra.

You or your caregiver should receive training on the right way to inject Fasenra. Read the 'Instructions for Use' for the pre-filled syringe carefully before using Fasenra.

If you forget to use Fasenra

If you have forgotten to inject a dose of Fasenra, talk to your doctor, pharmacist or nurse as soon as possible.

Stopping treatment with Fasenra

Do not stop treatment with Fasenra unless your doctor advises you to. Interrupting or stopping the treatment with Fasenra may cause your asthma symptoms and attacks to come back.

If your asthma symptoms get worse while receiving injections of Fasenra, **call your doctor.**

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 allergic reactions

Seek medical attention immediately if you think you may be having an allergic reaction. Such reactions may happen within hours or days after the injection.

Not known (the frequency cannot be estimated from the available data):

- anaphylaxis
symptoms usually include:
 - swelling of your face, tongue, or mouth
 - breathing problems
 - fainting, dizziness, feeling lightheaded (due to a drop in blood pressure)

Common (these may affect **up to 1 in 10 people**):

- hypersensitivity reactions (hives, rash)

Other side effects

Common (these may affect **up to 1 in 10 people**)

- headache
- pharyngitis (sore throat)
- fever (high temperature)
- injection site reaction (for example pain, redness, itching, swelling near where the injection was given)

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 Fasenra

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

Fasenra is for single use only.

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

The expiry date refers to the last day of that month.

Store in the original package in order to protect from light.

Store in a refrigerator (2°C to 8°C).

The syringe may be kept at room temperature up to 25°C for a maximum of 14 days. After removal from the refrigerator, Fasenra must be used within 14 days or discarded, and the discard date should be written on the carton.

Do not shake, freeze or expose to heat.

Do not throw away any medicines via wastewater. 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 Fasenra contains

The active substance is benralizumab. One pre-filled syringe of 1 mL solution contains 30 mg benralizumab.

The other ingredients are histidine, histidine hydrochloride monohydrate, trehalose dihydrate, polysorbate 20 (E 432) and water for injections.

What Fasenra looks like and contents of the pack

Fasenra is a solution in a clear glass syringe. Its colour may vary from colourless to yellow. It may contain particles.

Fasenra is available in a pack containing 1 pre-filled syringe.

Marketing Authorisation Holder

AstraZeneca AB
SE-151 85 Södertälje
Sweden

Manufacturer

AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

MedImmune UK Ltd
6 Renaissance Way
Liverpool, L24 9JW
United Kingdom

AstraZeneca Nijmegen B.V., Nijmegen
Lagelandseweg 78
Nijmegen, 6545CG
Netherlands

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

België/Belgique/Belgien

AstraZeneca S.A./N.V.
Tel: +32 2 370 48 11

Lietuva

UAB AstraZeneca Lietuva
Tel: +370 5 2660550

България

АстраЗенека България ЕООД
Тел.: +359 24455000

Luxembourg/Luxemburg

AstraZeneca S.A./N.V.
Tél/Tel: +32 2 370 48 11

Česká republika

AstraZeneca Czech Republic s.r.o.
Tel: +420 222 807 111

Magyarország

AstraZeneca Kft.
Tel.: +36 1 883 6500

Danmark

AstraZeneca A/S
Tlf.: +45 43 66 64 62

Malta

Associated Drug Co. Ltd
Tel: +356 2277 8000

Deutschland

AstraZeneca GmbH
Tel: +49 40 809034100

Nederland

AstraZeneca BV
Tel: +31 85 808 9900

Eesti

AstraZeneca
Tel: +372 6549 600

Norge

AstraZeneca AS
Tlf: +47 21 00 64 00

Ελλάδα

AstraZeneca A.E.
Τηλ: +30 210 6871500

Österreich

AstraZeneca Österreich GmbH
Tel: +43 1 711 31 0

España

AstraZeneca Farmacéutica Spain, S.A.
Tel: +34 91 301 91 00

France

AstraZeneca
Tél: +33 1 41 29 40 00

Hrvatska

AstraZeneca d.o.o.
Tel: +385 1 4628 000

Ireland

AstraZeneca Pharmaceuticals (Ireland) DAC
Tel: +353 1609 7100

Ísland

Vistor hf.
Sími: +354 535 7000

Italia

AstraZeneca S.p.A.
Tel: +39 02 00704500

Κύπρος

Αλέκτωρ Φαρμακευτική Λτδ
Τηλ: +357 22490305

Latvija

SIA AstraZeneca Latvija
Tel: +371 67377100

Polska

AstraZeneca Pharma Poland Sp. z o.o.
Tel.: +48 22 245 73 00

Portugal

AstraZeneca Produtos Farmacêuticos, Lda.
Tel: +351 21 434 61 00

România

AstraZeneca Pharma SRL
Tel: +40 21 317 60 41

Slovenija

AstraZeneca UK Limited
Tel: +386 1 51 35 600

Slovenská republika

AstraZeneca AB, o.z.
Tel: +421 2 5737 7777

Suomi/Finland

AstraZeneca Oy
Puh/Tel: +358 10 23 010

Sverige

AstraZeneca AB
Tel: +46 8 553 26 000

United Kingdom (Northern Ireland)

AstraZeneca UK Ltd
Tel: +44 1582 836 836

This leaflet was last revised in

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

<----->

Instructions for use

Fasenra 30 mg solution for injection in pre-filled syringe
benralizumab

For subcutaneous injection

Single-use pre-filled syringe

Before using your Fasenra pre-filled syringe, your healthcare provider should show you or your caregiver how to use it correctly.

Read this 'Instructions for Use' before you start using your Fasenra pre-filled syringe and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

If you or your caregiver have any questions, talk to your healthcare provider.

Important information

Store Fasenra in a refrigerator between 2 °C to 8 °C in its carton until you are ready to use it.

Fasenra may be kept at room temperature up to 25°C for a maximum of 14 days. After removal from the refrigerator, Fasenra must be used within 14 days or discarded.

Do not use your Fasenra pre-filled syringe if:

- it has been frozen
- it has been dropped or damaged
- the security seal on the carton has been broken
- the expiry date (EXP) has passed

Do not:

- shake your pre-filled syringe
- share or re-use your pre-filled syringe

If any of the above happens, throw away the syringe in a puncture-resistant sharps container and use a new pre-filled syringe.

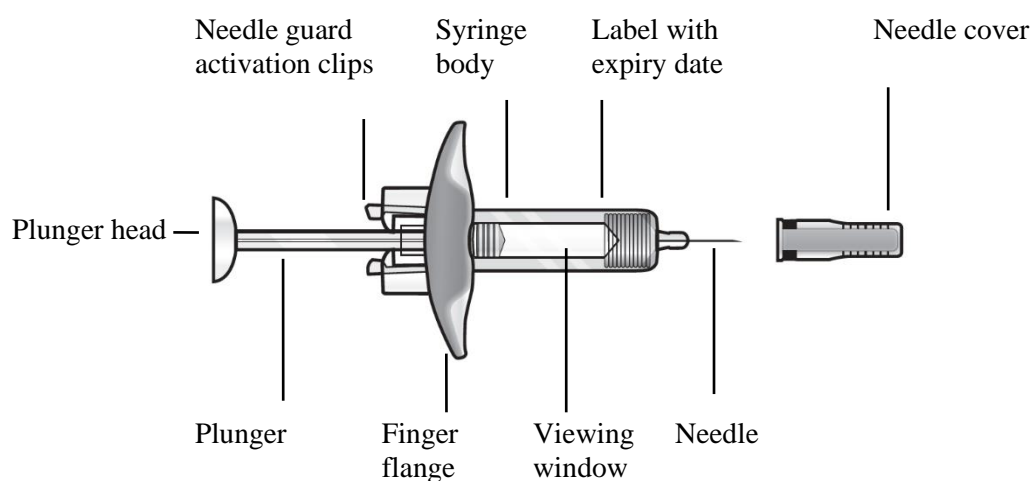
Each Fasenra pre-filled syringe contains 1 dose of Fasenra that is for one-time use only.

Keep Fasenra and all medicines out of the sight and reach of children.

Your Fasenra pre-filled syringe

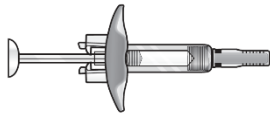
Do not remove the needle cover until you have reached Step 6 of these instructions and are ready to inject Fasenra.

Do not touch the needle guard activation clips to keep from activating the safety device (needle guard) too soon.



Step 1 - Gather supplies

- 1 Fasenra pre-filled syringe from the refrigerator
- 1 alcohol wipe
- 1 cotton ball or gauze
- 1 puncture-resistant sharps container.
(See Step 9 - Dispose of the used pre-filled syringe)



Pre-filled syringe



Alcohol wipe



Cotton ball or gauze



Sharps container

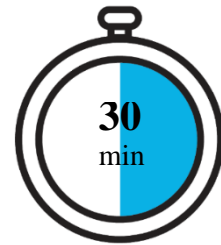
Step 2 - Prepare to use your pre-filled syringe

Check the expiry (EXP) date. Do not use if the expiry date has passed.

Prior to administration, allow the pre-filled syringe to reach room temperature 20 °C to 25 °C by leaving the carton out of the refrigerator for about 30 minutes.

Do not warm the pre-filled syringe in any other way. For example, do not warm it in a microwave or hot water, or put it near other heat sources.

Use Fasenra within 14 days of removing from the refrigerator.



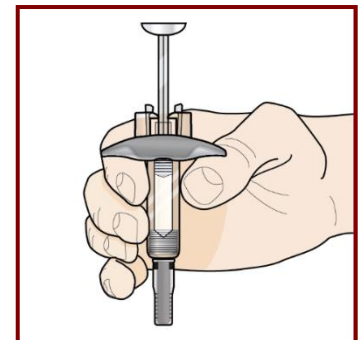
Step 3 - Check the liquid

Grasp the syringe body (not the plunger) to remove the pre-filled syringe.

Look at the liquid through the viewing window. The liquid should be clear and colourless to yellow. It may contain small white particles.

Do not inject Fasenra if the liquid is cloudy, discoloured, or contains large particles.

You may see a small air bubble in the liquid. This is normal. You do not need to do anything about it.



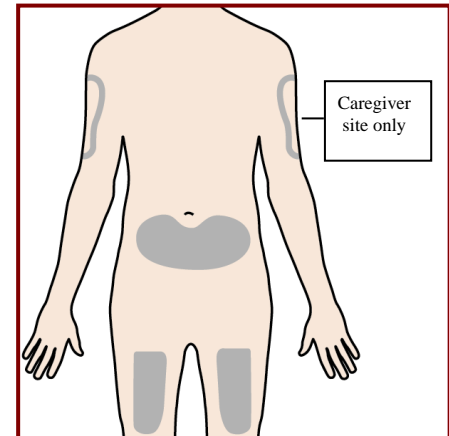
Step 4 - Choose the injection site

The recommended injection site is the front of your thigh. You may also use the lower part of your abdomen.

Do not inject:

- into the 5 cm area around your belly-button
- where the skin is tender, bruised, scaly or hard
- into scars or damaged skin
- through clothing

A caregiver may inject you in the upper-arm, thigh, or abdomen. **Do not** try to inject yourself in the arm. For each injection, choose a different site that is at least 3 cm away from where you last injected.

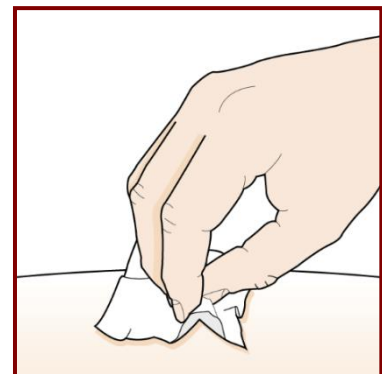


Step 5 - Clean the injection site

Wash your hands well with soap and water. Clean the injection site with an alcohol wipe in a circular motion. Let it air dry.

Do not touch the cleaned area before injecting.

Do not fan or blow on the cleaned area.



Step 6 - Pull off the needle cover

Hold the syringe body with 1 hand, and carefully pull the needle cover straight off with your other hand.

Do not hold the plunger or plunger head while removing the needle cover.

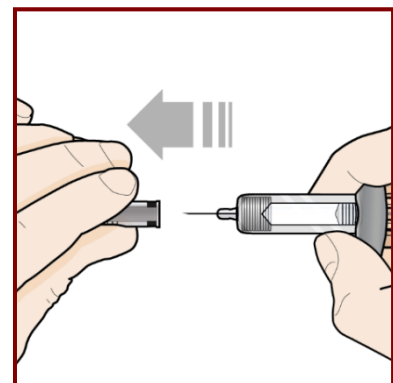
Put the needle cover aside to throw away later.

You may see a drop of liquid at the end of the needle. This is normal.

Do not use the syringe if it is dropped without the needle cover in place or if the needle is damaged or dirty.

Do not touch the needle, or let it touch any surface.

Go straight on to the next steps, without delay.



Step 7 - Inject Fasenra

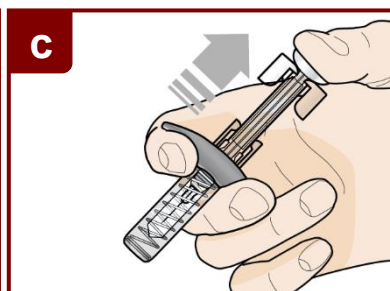
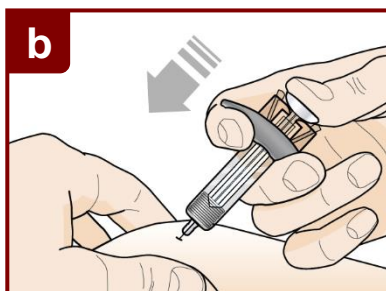
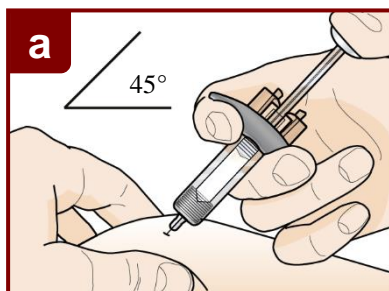
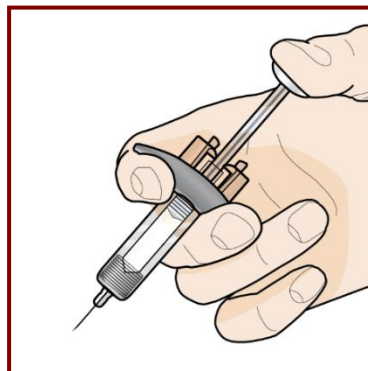
Hold the pre-filled syringe in 1 hand as shown.

Use your other hand to gently pinch and hold the area of skin where you want to inject. This creates a firmer surface.

Do not press down on the plunger until the needle is completely inserted into the skin.

Do not pull back on the plunger at any time.

Inject Fasenra by following the steps in figures a, b and c.



Use a quick, dart-like motion to insert the needle into the pinched skin.

Insert the needle at an angle of 45 degrees.

Use your thumb to push down on the plunger head.

Keep pushing until it is down as far as it will go. This is to make sure you inject all of the medication.

Keep your thumb pressed down on the plunger head as you take the needle out of the skin.

Slowly ease up on the plunger until the needle guard covers the needle.

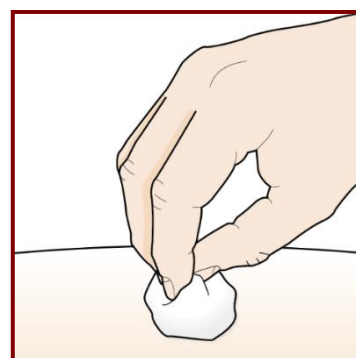
Step 8 - Check the injection site

There may be a small amount of blood or liquid where you injected. This is normal.

Gently hold pressure over your skin with a cotton ball or gauze until the bleeding stops.

Do not rub the injection site.

If needed, cover the injection site with a small bandage.



Step 9 - Dispose of the used pre-filled syringe

- Each pre-filled syringe contains a single dose of Fasenra and **cannot be re-used**.
- Put your used pre-filled syringe in a puncture-resistant **sharps container** right away after use.

Do not throw away the pre-filled syringe in your household waste.

Do not re-cap the pre-filled syringe.

Throw away the cap and other used supplies in your household waste.



Disposal guidelines

Dispose of the full container as instructed by your healthcare provider or pharmacist.

Do not recycle your used sharps container.

Package leaflet: Information for the patient

Fasenra 30 mg solution for injection in pre-filled pen benralizumab

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 Fasenra is and what it is used for
2. What you need to know before you use Fasenra
3. How to use Fasenra Pen
4. Possible side effects
5. How to store Fasenra Pen
6. Contents of the pack and other information

1. What Fasenra is and what it is used for

What Fasenra is

Fasenra contains the active substance benralizumab, which is a monoclonal antibody, a type of protein that recognises and attaches to a specific target substance in the body. The target of benralizumab is a protein called interleukin-5 receptor, which is found particularly on a type of white blood cell called an eosinophil.

What Fasenra is used for

Asthma

Fasenra is used to treat **severe eosinophilic asthma** in adults. Eosinophilic asthma is a type of asthma where patients have too many eosinophils in the blood or lungs.

Fasenra is used together with other medicines to treat asthma (high doses of ‘corticosteroid inhalers’ plus other asthma medicines) when the condition is not well controlled by those other medicines alone.

Eosinophilic granulomatosis with polyangiitis (EGPA)

Fasenra is used to treat EGPA in adults. EGPA is a condition where people have too many eosinophils in the blood and tissues and also have a form of vasculitis. This means there is inflammation of the blood vessels. This condition most commonly affects the lungs and sinuses but often affects other organs such as the skin, heart and kidneys.

How Fasenra works

Eosinophils are white blood cells involved in asthma and EGPA inflammation. By attaching to the eosinophils, Fasenra helps to reduce their numbers and inflammation.

What are the benefits of using Fasenra

Asthma

Fasenra may reduce the number of asthma attacks you are experiencing, help you breathe better and decrease your asthma symptoms. If you are taking medicines called ‘oral corticosteroids’, using Fasenra may also allow you to reduce the daily dose or stop the oral corticosteroids you need to control your asthma.

EGPA

Fasenra can reduce symptoms and prevent flare-ups of EGPA. This medicine may also allow you to reduce the daily dose of oral corticosteroids you need to control your symptoms.

2. What you need to know before you use Fasenra

Do not use Fasenra:

- If you are **allergic** to benralizumab or any of the other ingredients of this medicine (listed in section 6). **Check with your doctor, nurse or pharmacist** if you think this applies to you.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before you are given Fasenra:

- if you have a **parasitic infection** or if you live in an area where parasitic infections are common or you are travelling to such a region. This medicine may weaken your ability to fight certain types of parasitic infections.
- if you have had an **allergic reaction to an injection or medicine in the past** (see section 4 for symptoms of an allergic reaction).

Also, talk to your doctor, nurse or pharmacist when you are given Fasenra:

- if your **asthma remains uncontrolled or worsens** during treatment with this medicine.
- if you have any symptoms of an **allergic reaction** (see section 4). Allergic reactions have occurred in patients receiving this medicine.

Fasenra is **not a rescue medicine**. Do not use it to treat a sudden asthma attack.

Look out for signs of serious allergic reactions

Fasenra can potentially cause serious allergic reactions. You must look out for signs of these reactions (such as hives, rash, breathing problems, fainting, dizziness, feeling lightheaded and/or swelling of your face, tongue or mouth) while you are taking Fasenra.

It is important that you talk to your doctor about how to recognise early symptoms of serious allergic reactions and how to manage these reactions if they occur.

In order to improve the traceability of biological medicinal products, record the name and the lot number, included on the outer carton and the label of the pre-filled pen, every time you get a new package of Fasenra and provide this information when reporting any side effects.

Other medicines for asthma or EGPA

Do not suddenly stop taking or change the dose of your other medicines for your condition once you have started Fasenra.

If your response to the treatment allows it, your doctor may try to reduce the dose of some of these medicines, especially ones called ‘corticosteroids’. This should be done gradually and under the direct supervision of your doctor.

Tell your doctor if you are taking, have recently taken or might take any other medicines before using Fasenra.

Children and adolescents

Do not give this medicine to children below the age of 18 because the safety and benefits of this medicine are not known in this population.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, **ask your doctor for advice** before using this medicine.

Do not use Fasenra if you are pregnant unless your doctor tells you otherwise. It is not known whether Fasenra could harm your unborn baby.

It is not known whether the ingredients of Fasenra can pass into breast milk. **If you are breast-feeding or plan to breast-feed, talk to your doctor.**

Driving and using machines

It is unlikely that Fasenra will affect your ability to drive and use machines.

Fasenra contains Polysorbate 20

This medicine contains 0.06 mg of polysorbate 20 (plant-derived) in each 30 mg pre-filled pen. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Fasenra Pen

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

Asthma

The recommended dose is an injection of 30 mg. The first 3 injections are every 4 weeks. After this, injections are 30 mg every 8 weeks.

EGPA

The recommended dose is an injection of 30 mg every 4 weeks.

Fasenra is given as an injection just under the skin (subcutaneously). You and your doctor or nurse should decide if you should inject Fasenra yourself. You should not inject Fasenra yourself if you have not received Fasenra previously and if you had previous allergic reaction with Fasenra.

You or your caregiver should receive training on the right way to inject Fasenra. Read the 'Instructions for Use' for the Fasenra Pen carefully before using Fasenra.

If you forget to use Fasenra

If you have forgotten to inject a dose of Fasenra, talk to your doctor, pharmacist or nurse as soon as possible.

Stopping treatment with Fasenra

Do not stop treatment with Fasenra unless your doctor advises you to. Interrupting or stopping the treatment with Fasenra may cause your asthma symptoms and attacks to come back.

If your asthma symptoms get worse while receiving injections of Fasenra, **call your doctor.**

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 allergic reactions

Seek medical attention immediately if you think you may be having an allergic reaction. Such reactions may happen within hours or days after the injection.

Not known (the frequency cannot be estimated from the available data):

- anaphylaxis
symptoms usually include:
 - swelling of your face, tongue, or mouth
 - breathing problems
 - fainting, dizziness, feeling lightheaded (due to a drop in blood pressure)

Common (these may affect **up to 1 in 10 people**):

- hypersensitivity reactions (hives, rash)

Other side effects

Common (these may affect **up to 1 in 10 people**)

- headache
- pharyngitis (sore throat)
- fever (high temperature)
- injection site reaction (for example pain, redness, itching, swelling near where the injection was given)

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 Fasentra Pen

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

Fasentra Pen is for single-use only.

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

The expiry date refers to the last day of that month.

Store in the original package in order to protect from light.

Store in a refrigerator (2°C to 8°C).

The Fasentra Pen may be kept at room temperature up to 25°C for a maximum of 14 days. After removal from the refrigerator, Fasentra must be used within 14 days or discarded, and the discard date should be written on the carton.

Do not shake, freeze or expose to heat.

Do not throw away any medicines via wastewater. 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 Fasentra Pen contains

The active substance is benralizumab. One pre-filled pen of 1 mL solution contains 30 mg benralizumab.

The other ingredients are histidine, histidine hydrochloride monohydrate, trehalose dihydrate, polysorbate 20 (E 432) and water for injections.

What Fasentra looks like and contents of the pack

Fasentra is a solution which is colourless to yellow. It may contain particles.

Fasentra is available in a pack containing 1 pre-filled pen.

Marketing Authorisation Holder

AstraZeneca AB
SE-151 85 Södertälje
Sweden

Manufacturer

AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

MedImmune UK Ltd
6 Renaissance Way
Liverpool, L24 9JW
United Kingdom

AstraZeneca Nijmegen B.V., Nijmegen
Lagelandseweg 78
Nijmegen, 6545CG
Netherlands

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

België/Belgique/Belgien

AstraZeneca S.A./N.V.
Tel: +32 2 370 48 11

Lietuva

UAB AstraZeneca Lietuva
Tel: +370 5 2660550

България

АстраЗенека България ЕООД
Тел.: +359 24455000

Luxembourg/Luxemburg

AstraZeneca S.A./N.V.
Tél/Tel: +32 2 370 48 11

Česká republika

AstraZeneca Czech Republic s.r.o.
Tel: +420 222 807 111

Magyarország

AstraZeneca Kft.
Tel.: +36 1 883 6500

Danmark

AstraZeneca A/S
Tlf.: +45 43 66 64 62

Malta

Associated Drug Co. Ltd
Tel: +356 2277 8000

Deutschland

AstraZeneca GmbH
Tel: +49 40 809034100

Nederland

AstraZeneca BV
Tel: +31 85 808 9900

Eesti

AstraZeneca
Tel: +372 6549 600

Norge

AstraZeneca AS
Tlf: +47 21 00 64 00

Ελλάδα

AstraZeneca A.E.
Τηλ: +30 210 6871500

Österreich

AstraZeneca Österreich GmbH
Tel: +43 1 711 31 0

España

Polska

AstraZeneca Farmacéutica Spain, S.A.
Tel: +34 91 301 91 00

France

AstraZeneca
Tél: +33 1 41 29 40 00

Hrvatska

AstraZeneca d.o.o.
Tel: +385 1 4628 000

Ireland

AstraZeneca Pharmaceuticals (Ireland) DAC
Tel: +353 1609 7100

Ísland

Vistor hf.
Sími: +354 535 7000

Italia

AstraZeneca S.p.A.
Tel: +39 02 00704500

Κύπρος

Αλέκτωρ Φαρμακευτική Λτδ
Τηλ: +357 22490305

Latvija

SIA AstraZeneca Latvija
Tel: +371 67377100

AstraZeneca Pharma Poland Sp. z o.o.
Tel.: +48 22 245 73 00

Portugal

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Tel: +351 21 434 61 00

România

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Tel: +40 21 317 60 41

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AstraZeneca AB, o.z.
Tel: +421 2 5737 7777

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Puh/Tel: +358 10 23 010

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AstraZeneca AB
Tel: +46 8 553 26 000

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AstraZeneca UK Ltd
Tel: +44 1582 836 836

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<https://www.ema.europa.eu>.

<----->

Instructions for Use

Fasenra 30 mg solution for injection in pre-filled pen

benralizumab

For subcutaneous injection

Single-use pre-filled pen

Before using your Fasenra Pen, your healthcare provider should show you or your caregiver how to use it correctly.

Read this ‘Instructions for Use’ before you start using your Fasenra Pen and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

If you or your caregiver have any questions, talk to your healthcare provider.

Important information

Store Fasenra in a refrigerator between 2 °C to 8 °C in its carton until you are ready to use it.

Fasenra may be kept at room temperature up to 25°C for a maximum of 14 days. After removal from the refrigerator, Fasenra must be used within 14 days or discarded.

Do not use your Fasenra Pen if:

- it has been frozen
- it has been dropped or damaged
- the security seal on the carton has been broken
- the expiry date (EXP) has passed

Do not:

- shake your Fasenra Pen
- share or re-use your Fasenra Pen

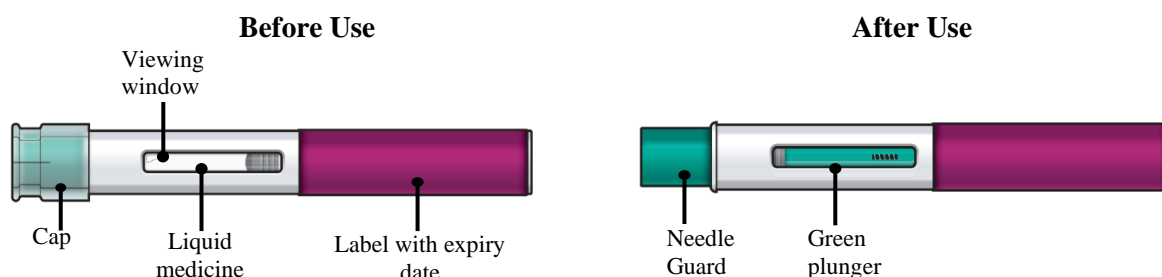
If any of the above happens, throw away the Fasenra Pen in a puncture-resistant sharps container and use a new Fasenra Pen.

Each Fasenra Pen contains 1 dose of Fasenra that is for one-time use only.

Keep Fasenra and all medicines out of the sight and reach of children.

Your Fasenra Pen

Do not remove the cap until you have reached Step 6 of these instructions and are ready to inject Fasenra.



Step 1 - Gather supplies

- 1 Fasenra Pen from the refrigerator
- 1 alcohol wipe
- 1 cotton ball or gauze
- 1 puncture-resistant sharps container.
(See Step 10 – Dispose of the used Fasenra Pen safely)



Fasenra Pen



Alcohol wipe



Cotton ball or gauze



Sharps container

Step 2 - Prepare to use your Fasenra Pen

Check the expiry date (EXP). Do not use if the expiry date has passed.
Prior to administration, allow the pre-filled pen to reach room temperature 20 °C to 25 °C by leaving the carton out of the refrigerator for about 30 minutes.

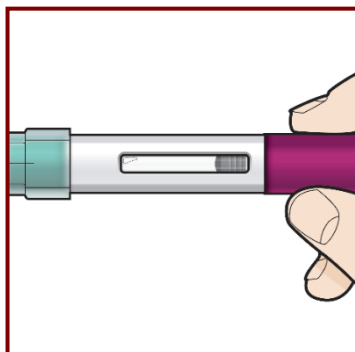
Do not warm the Fasenra Pen in any other way. For example, do not warm it in a microwave or hot water, or put it near other heat sources.

Use Fasenra within 14 days of removing from the refrigerator.

Do not remove the cap until you have reached Step 6.



Step 3 - Check the liquid

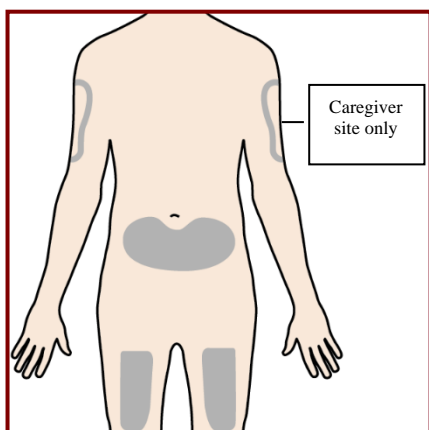


Look at the liquid in the Fasenra Pen through the viewing window. The liquid should be clear and colourless to yellow. It may contain small white particles.

Do not inject Fasenra if the liquid is cloudy, discoloured, or contains large particles.

You may see a small air bubble in the liquid. This is normal. You do not need to do anything about it.

Step 4 - Choose the injection site



The recommended injection site is the front of your thigh. You may also use the lower part of your abdomen.

Do not inject:

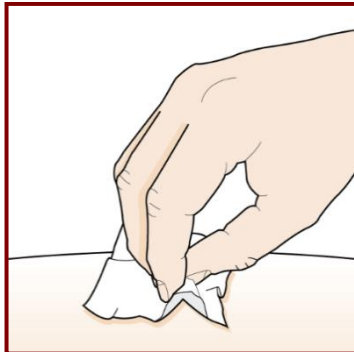
- into the 5 cm area around your belly-button
- where the skin is tender, bruised, scaly or hard
- into scars or damaged skin
- through clothing

A caregiver may inject you in the upper-arm, thigh, or abdomen.

Do not try to inject yourself in the arm.

For each injection, choose a different site that is at least 3 cm away from where you last injected.

Step 5 - Clean the injection site

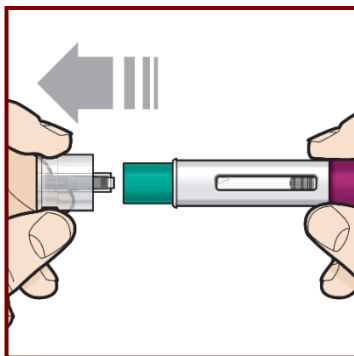


Wash your hands well with soap and water.
Clean the injection site with an alcohol wipe in a circular motion. Let it air dry.

Do not touch the cleaned area before injecting.

Do not fan or blow on the cleaned area.

Step 6 - Pull off the cap



Hold the Fasenra Pen with 1 hand. Carefully pull the cap straight off with your other hand.

Put the cap aside to throw away later.

The green needle guard is now exposed. It is there to prevent you from touching the needle.

Do not try to touch the needle or push on the needle guard with your finger.

Do not try to put the cap back on the Fasenra Pen. You could cause the injection to happen too soon or damage the needle.

Complete the following steps right away after removing the cap.

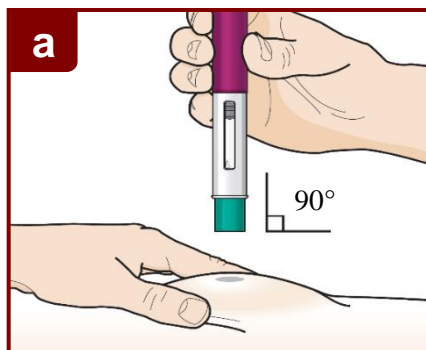
Step 7 - Inject Fasenra

Follow your healthcare provider's instructions on how to inject. You can either gently pinch at the injection site or give the injection without pinching the skin.

Inject Fasenra by following the steps in figures **a**, **b**, **c** and **d**.

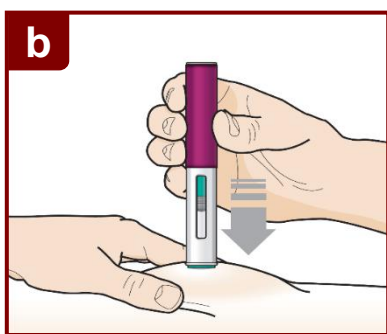
Hold the Fasenra Pen in place for the entire injection.

Do not change the position of the Fasenra Pen after the injection has started.

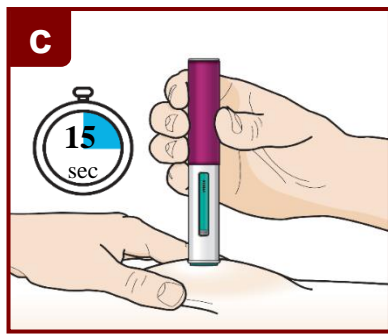


Position the Fasenra Pen at the injection site.

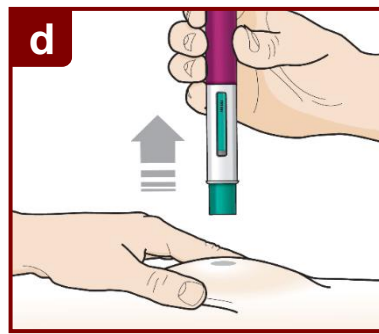
Place the needle guard of the Fasenra Pen flat against your skin (90-degree angle). Make sure you can see the viewing window.



Press down firmly.
You will hear a click. A ‘click’ tells you the injection has started. The green plunger will move down in the viewing window during the injection.

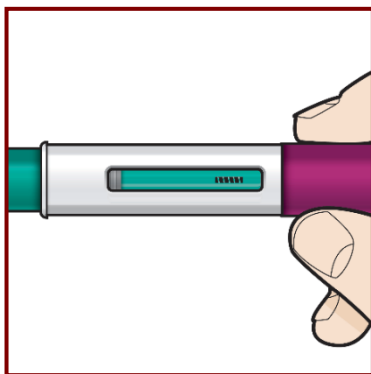


Hold down firmly for 15 seconds.
You will hear a second ‘click’. The second click tells you the injection has finished. The green plunger will fill the viewing window.



Lift the Fasenra Pen straight up.
The needle guard will slide down and lock into place over the needle.

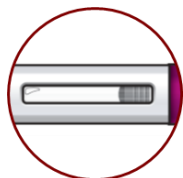
Step 8 - Check the viewing window



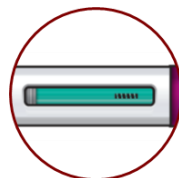
Check the viewing window to make sure all the liquid has been injected.

If the green plunger does not fill the viewing window, you may not have received the full dose. If this happens or if you have any other concerns, call your healthcare provider.

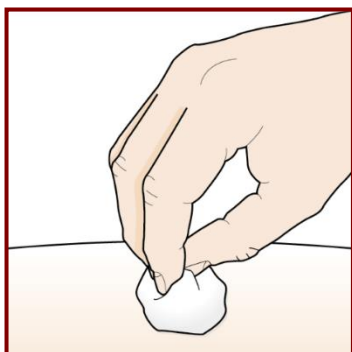
Before
Injection



After
Injection



Step 9 - Check the injection site



There may be a small amount of blood or liquid where you injected. This is normal.

Gently hold pressure over your skin with a cotton ball or gauze until the bleeding stops.

Do not rub the injection site.

If needed, cover the injection site with a small bandage.

Step 10 - Dispose of the used Fasenra Pen safely



- Each Fasenra Pen contains a single dose of Fasenra and **cannot be re-used**.
- Put your used Fasenra Pen in a puncture-resistant **sharps container** right away after use.

Do not throw away the Fasenra Pen in your household waste. Throw away the cap and other used supplies in your household waste.

Disposal guidelines

Dispose of the full container as instructed by your healthcare provider or pharmacist.

Do not recycle your used sharps container.