ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 300 mg concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 300 mg mirikizumab in 15 mL solution (20 mg/mL).

After dilution (see section 6.6), the final concentration is approximately 1.2 mg/mL to approximately 6 mg/mL.

Mirikizumab is a humanised monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.

Excipients with known effect

Each 15 mL vial contains approximately 60 mg sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate)

The concentrate is a clear and colourless to slightly yellow solution with a pH of approximately 5.5 and an osmolarity of approximately 300 mOsm/L.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

This medicinal product is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of ulcerative colitis.
Omvoh 300 mg concentrate for solution for infusion should only be used for the induction dose.

Posology

The recommended mirikizumab dose regimen has 2 parts.

Induction dose
The induction dose is 300 mg by intravenous infusion for at least 30 minutes at weeks 0, 4 and 8.

Maintenance dose
The maintenance dose is 200 mg (i.e. two pre-filled syringes or two pre-filled pens) by subcutaneous injection every 4 weeks after completion of induction dosing.

For the posology of the subcutaneous dosing regimen, see section 4.2 of the Summary of Product Characteristics for Omvoh 100 mg solution for injection in pre-filled syringe and Omvoh 100 mg solution for injection in pre-filled pen.

Patients should be evaluated after the 12-week induction dosing and if there is adequate therapeutic response, transition to maintenance dosing. For patients who do not achieve adequate therapeutic benefit at week 12 of induction dosing, mirikizumab 300 mg by intravenous infusion may be continued at weeks 12, 16 and 20 (extended induction therapy). If therapeutic benefit is achieved with the additional intravenous therapy, patients may initiate mirikizumab subcutaneous maintenance dosing (200 mg) every 4 weeks, starting at week 24. Mirikizumab should be discontinued in patients who do not show evidence of therapeutic benefit to extended induction therapy by week 24.

Patients with loss of therapeutic response during maintenance treatment may receive 300 mg mirikizumab by intravenous infusion every 4 weeks, for a total of 3 doses (re-induction). If clinical benefit is achieved from this additional intravenous therapy, patients may resume mirikizumab subcutaneous dosing every 4 weeks. The efficacy and safety of repeated re-induction therapy have not been evaluated.

Elderly
No dose adjustment is required (see section 5.2). There is limited information in subjects aged ≥ 75 years.

Renal or hepatic impairment
Omvoh has not been studied in these patient populations. These conditions are generally not expected to have any significant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary (see section 5.2).

Paediatric population
The safety and efficacy of Omvoh in children and adolescents aged 2 to less than 18 years have not yet been established. No data are available.
There is no relevant use of Omvoh in children below 2 years for the indication of ulcerative colitis.

Method of administration

Omvoh 300 mg concentrate for solution for infusion is for intravenous use only. Each vial is for single use only.

For instructions on dilution of the medicinal product before administration, see section 6.6.

Administration of the diluted solution
- The intravenous administration set (infusion line) should be connected to the prepared intravenous bag and the line should be primed. The infusion should be administered for at least 30 minutes.
- At the end of the infusion, to ensure a full dose is administered, the infusion line should be flushed with sodium chloride 9 mg/mL (0.9 %) solution or 5 % glucose solution for injection. The flush should be administered at the same rate as used for Omvoh administration. The time required to flush Omvoh solution from the infusion line is in addition to the minimum 30 minutes infusion time.

4.3 Contraindications

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

Clinically important active infections (active tuberculosis).

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.

Hypersensitivity reactions

In clinical studies, hypersensitivity reactions have been reported. Most were mild or moderate, severe reactions were uncommon (see section 4.8). If a serious hypersensitivity reaction, including anaphylaxis, occurs, mirikizumab must be discontinued immediately and appropriate therapy must be initiated.

Infections

Mirikizumab may increase the risk of severe infection (see section 4.8). Treatment with mirikizumab should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated (see section 4.3). The risks and benefits of treatment should be considered prior to initiating use of mirikizumab in patients with a chronic infection or a history of recurrent infection. Patients should be instructed to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops, discontinuation of mirikizumab should be considered until the infection resolves.

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

Hepatic enzyme elevations

Cases of drug-induced liver injury (including one case meeting Hy's Law criteria) occurred in patients receiving mirikizumab in clinical trials. Liver enzymes and bilirubin should be evaluated at baseline and monthly during induction (including extended induction period, if applicable). Thereafter, liver enzymes and bilirubin should be monitored (every 1 - 4 months) according to standard practice for patient management and as clinically indicated. If increases in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) are observed and drug-induced liver injury is suspected, mirikizumab must be discontinued until this diagnosis is excluded.

Immunisations

Prior to initiating therapy with mirikizumab, completion of all appropriate immunisations should be considered according to current immunisation guidelines. Avoid use of live vaccines in patients treated with mirikizumab. No data are available on the response to live or non-live vaccines.

Sodium

This medicinal product contains 60 mg sodium per 300 mg dose, equivalent to 3 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

If prepared with sodium chloride 9 mg/mL (0.9 %) solution for injection the amount of sodium contributed by the sodium chloride diluent will range from 177 mg (for a 50 mL bag) to 885 mg (for a 250 mL bag), equivalent to 9-44 % of the WHO recommended maximum daily intake. This is in addition to the amount contributed by the medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
In ulcerative colitis studies, concomitant use of corticosteroids or oral immunomodulators did not influence the safety of mirikizumab.
Population pharmacokinetic data analyses indicated that the clearance of mirikizumab was not impacted by concomitant administration of 5-ASAs (5-aminosalicylic acid), corticosteroids or oral immunomodulators (azathioprine, mercaptopurine, thioguanine, and methotrexate) in patients with ulcerative colitis.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 10 weeks after treatment.

Pregnancy

There is a limited amount of data from the use of mirikizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Omvoh during pregnancy.

Breast-feeding

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

Fertility

The effect of mirikizumab on human fertility has not been evaluated (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions are upper respiratory tract infections (7.9 %, most frequently nasopharyngitis), headache (3.3 %), rash (1.1 %) and injection site reactions (8.7 %, maintenance period).

Tabulated list of adverse reactions

Adverse reactions from clinical studies (Table 1) are listed by MedDRA system organ class. The frequency category for each reaction is based on the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000).

Table 1: Adverse reactions

MedDRA System organ class	Frequency	Adverse reaction
Infections and infestations	Common	Upper respiratory tract infections[a]
	Uncommon	Herpes zoster
Immune system disorders	Uncommon	Infusion-related hypersensitivity reactions
Musculoskeletal and Connective Tissue Disorders	Common	Arthralgia
Nervous system disorders	Common	Headache
Skin and subcutaneous tissue disorders	Common	Rash[b]
General disorders and administration site conditions	Common	Injection site reactions[c]
	Uncommon	Infusion site reactions[d]
Investigations	Uncommon	Alanine aminotransferase increased
	Uncommon	Aspartate aminotransferase increased

[a] *Includes: acute sinusitis, nasopharyngitis, oropharyngeal discomfort, oropharyngeal pain, pharyngitis, rhinitis, sinusitis, tonsillitis, upper respiratory tract infection, and viral upper respiratory tract infection.*

[b] *Includes: rash, rash macular, rash maculo-papular, and rash papular and rash pruritic.*

[c] *Reported in the mirikizumab maintenance study where mirikizumab treatment is administered as subcutaneous injection.*

[d] *Reported in the mirikizumab induction study where mirikizumab treatment is administered as intravenous infusion.*

Description of selected adverse reactions

Infusion-related hypersensitivity reactions (LUCENT-1, weeks 1-12)
Infusion-related hypersensitivity reactions were reported in 0.4 % of mirikizumab-treated patients. All infusion-related hypersensitivity reactions were reported as non-serious.

Injection site reactions (LUCENT-2, weeks 12-52)
Injection site reactions were reported in 8.7 % mirikizumab-treated patients. The most frequent reactions were injection site pain, injection site reaction and injection site erythema. These symptoms were reported as non-serious, mild and transient in nature.

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) increased
In the first 12 weeks (LUCENT-1), ALT increased was reported in 0.4 % mirikizumab-treated patients. AST increased was reported by 0.5 % mirikizumab-treated patients. All adverse reactions were reported as mild to moderate in severity and non-serious.

Over all mirikizumab treatment periods in the ulcerative colitis clinical development program (including the placebo-controlled and open label induction and maintenance periods), there have been elevations of ALT to ≥ 3 x upper limit of normal (ULN) (2.0 %), ≥ 5 x ULN (0.7 %) and ≥ 10 x ULN (0.2 %) and AST to ≥ 3 x ULN (2.1 %), ≥ 5 x ULN (1.1 %) and ≥ 10 x ULN (0.1 %) in patients receiving mirikizumab (see section 4.4). These elevations have been noted with and without concomitant elevations in total bilirubin.

Immunogenicity
With 12 months of treatment, up to 23 % of mirikizumab-treated patients developed anti-drug antibodies, most of which were of low titer and tested positive for neutralising activity. Higher antibody titers in approximately 2 % of subjects treated with mirikizumab were associated with lower serum mirikizumab concentrations and reduced clinical response. No association was found between anti-mirikizumab antibodies and hypersensitivity or injection site reactions.

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

Mirikizumab doses up to 2 400 mg intravenously and up to 500 mg subcutaneously have been administered in clinical trials without dose-limiting toxicity. In the event of overdose, the patient must be monitored for signs or symptoms of adverse reactions and appropriate symptomatic treatment must be started immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC24

Mechanism of action

Mirikizumab is a humanised IgG4 monoclonal, anti-interleukin-23 (anti-IL-23) antibody that selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor.

IL-23, a regulatory cytokine, affects the differentiation, expansion, and survival of T cell subsets, (e.g., Th17 cells and Tc17 cells) and innate immune cell subsets, which represent sources of effector cytokines, including IL-17A, IL-17F and IL-22 that drive inflammatory disease. In humans, selective blockade of IL-23 was shown to normalise production of these cytokines.

Pharmacodynamic effects

Inflammatory biomarkers were measured in the phase 3 ulcerative colitis studies. Mirikizumab administered intravenously every 4 weeks during induction dosing significantly reduced levels of fecal calprotectin and C-reactive protein from baseline to week 12. Also, mirikizumab administered subcutaneously every 4 weeks during maintenance dosing sustained significantly reduced levels of fecal calprotectin and C-reactive protein through 40 weeks.

Clinical efficacy and safety

The efficacy and safety of mirikizumab was evaluated in adult patients with moderately to severely active ulcerative colitis in two randomised, double-blind, placebo-controlled, multicentre studies. Enrolled patients had a confirmed diagnosis of ulcerative colitis for at least 3 months and moderately to severely active disease, defined as a modified Mayo score of 4 to 9, including a Mayo endoscopy subscore ≥ 2. Patients had to have failed (defined as loss of response, inadequate response or intolerance) corticosteroids or immunomodulators (6-mercaptopurine, azathioprine) or at least one biologic (a TNFα antagonist and/or vedolizumab) or tofacitinib.

LUCENT-1 was an intravenous induction study with treatment of up to 12 weeks, followed by a 40 week subcutaneous randomised withdrawal maintenance study (LUCENT-2), representing at least 52 weeks of therapy. Mean age was 42.5 years. 7.8 % of patients were ≥ 65 of age and 1.0 % of patients ≥ 75 of age. 59.8 % were men; 40.2 % were women. 53.2 % had severely active disease with a modified Mayo score 7 to 9.

Efficacy results presented for LUCENT-1 and LUCENT-2 were based on central reading of endoscopies and histology.

LUCENT-1
LUCENT-1 included 1 162 patients in the primary efficacy population. Patients were randomised to receive a dose of 300 mg mirikizumab via intravenous infusion or placebo, at week 0, week 4 and week 8 with a 3:1 treatment allocation ratio. The primary endpoint for the induction study was the proportion of subjects in clinical remission [modified Mayo score (MMS) defined as: Stool frequency (SF) subscore = 0 or 1 with a ≥ 1-point decrease from baseline, and rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)] at week 12.

Patients in these studies may have received other concomitant therapies including aminosalicylates (74.3 %), immunomodulatory agents (24.1 % such as azathioprine, 6-mercaptopurine or methotrexate), and oral corticosteroids (39.9 %; prednisone daily dose up to 20 mg or equivalent) at a stable dose prior to and during the induction period. Per protocol oral corticosteroids were tapered after induction.

Of the primary efficacy population, 57.1 % were biologic-naive and tofacitinib-naive. 41.2 % of patients had failed a biologic or tofacitinib. 36.3 % of the patients had failed at least 1 prior anti-TNF therapy, 18.8 % had failed vedolizumab and 3.4 % of patients had failed tofacitinib. 20.1 % had failed more than one biologic or tofacitinib. An additional 1.7 % had previously received but had not failed a biologic or tofacitinib.

In LUCENT-1 a significantly greater proportion of patients were in clinical remission in the mirikizumab treated group compared to placebo at week 12 (Table 2). As early as week 2, mirikizumab-treated patients achieved a greater reduction in RB subscores and decreases in SF subscores.

Table 2: Summary of key efficacy outcomes in LUCENT-1 (week 12 unless indicated otherwise)

	Placebo N = 294		**Mirikizumab IV N = 868**		**Treatment difference and 99.875 % CI**
	N	**%**	**N**	**%**	
Clinical remission*[1]	39	13.3 %	210	24.2 %	11.1 % (3.2 %, 19.1 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	27/171	15.8 %	152/492	30.9 %	- - -

Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/118	8.5 %	55/361	15.2 %	- - -
Alternate clinical remission*[2]	43	14.6 %	222	25.6 %	11.1 % (3.0 %, 19.3 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	31/171	18.1 %	160/492	32.5 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/118	8.5 %	59/361	16.3 %	- - -
Clinical response*[3]	124	42.2 %	551	63.5 %	21.4 % (10.8 %, 32.0 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	86/171	50.3 %	345/492	70.1 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	35/118	29.7 %	197/361	54.6 %	- - -
Endoscopic improvement*[4]	62	21.1 %	315	36.3 %	15.4 % (6.3 %, 24.5 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	48/171	28.1 %	226/492	45.9 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	12/118	10.2 %	85/361	23.5 %	- - -
Symptomatic remission (week 4)*[5]	38	12.9 %	189	21.8 %	9.2 % (1.4 %, 16.9 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	26/171	15.2 %	120/492	24.4 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/118	8.5 %	67/361	18.6 %	- - -
Symptomatic remission*[5]	82	27.9 %	395	45.5 %	17.5 % (7.5 %, 27.6 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	57/171	33.3 %	248/492	50.4 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	22/118	18.6 %	139/361	38.5 %	- - -
Histo-endoscopic mucosal improvement*[6]	41	13.9 %	235	27.1 %	13.4 % (5.5 %, 21.4 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	32/171	18.7 %	176/492	35.8 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	8/118	6.8 %	56/361	15.5 %	- - -
	Placebo N = 294		**Mirikizumab IV N = 868**		**Treatment difference and 99.875 % CI**
	LS mean	**Standard error**	**LS mean**	**Standard error**	
Bowel urgency severity*[7]	-1.63	0.141	-2.59	0.083	-0.95 (-1.47, -0.44)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	-2.08	0.174	-2.72	0.101	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	-0.95	0.227	-2.46	0.126	- - -

Abbreviations: CI = confidence interval; IV = intravenous; LS = least square

*[1] *Clinical remission is based on the modified Mayo score (MMS) and is defined as: Stool frequency (SF) subscore = 0 or 1 with a ≥ 1-point decrease from baseline, and Rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)*

*[2] *Alternate clinical remission is based on the modified Mayo score (MMS) and is defined as: Stool frequency (SF) subscore = 0 or 1, and Rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)*

*[3] *Clinical response based on the MMS and is defined as: A decrease in the MMS of ≥ 2 points and ≥ 30 % decrease from baseline, and a decrease of ≥ 1 point in the RB subscore from baseline or a RB score of 0 or 1*

*[4] *Endoscopic improvement defined as: ES = 0 or 1 (excluding friability)*

*[5] *Symptomatic remission defined as: SF = 0, or SF = 1 with a ≥ 1-point decrease from baseline, and RB = 0*

*[6] *Histo-endoscopic mucosal improvement defined as achieving both: 1. Histologic improvement, defined using Geboes scoring system with neutrophil infiltration in < 5 % of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue. 2. Endoscopic improvement, defined as ES = 0 or 1 (excluding friability).*

*[7] *Change from baseline in the Urgency Numeric Rating Scale score*

a) *An additional 5 patients on placebo and 15 patients on mirikizumab where previously exposed to but did not fail a biologic or JAK-inhibitor.*
b) *Loss of response, inadequate response or intolerance.*
c) *p < 0.001*
d) *Mirikizumab results in the subgroup of patients who failed more than one biologic or JAK-inhibitor were consistent with results in the overall population.*

LUCENT-2

LUCENT-2 evaluated 544 patients out of the 551 patients who achieved clinical response with mirikizumab in LUCENT-1 at week 12 (see Table 2). Patients were re-randomised in a 2:1 treatment allocation ratio to receive a subcutaneous maintenance regimen of 200 mg mirikizumab or placebo every 4 weeks for 40 weeks (which is 52 weeks from initiation of the induction dose). The primary endpoint for the maintenance study was the proportion of subjects in clinical remission (same definition as in LUCENT-1) at week 40. Corticosteroid tapering was required upon entrance into LUCENT-2 for patients who were receiving corticosteroids during LUCENT-1. Significantly greater proportions of patients were in clinical remission in the mirikizumab-treated group compared to the placebo group at week 40 (see Table 3).

Table 3: Summary of key efficacy measures in LUCENT-2 (week 40; 52 weeks from initiation of the induction dose)

	Placebo N = 179		**Mirikizumab SC N = 365**		**Treatment difference and 95 % CI**
	N	**%**	**N**	**%**	
Clinical remission*[1]	45	25.1 %	182	49.9 %	23.2 % (15.2 %, 31.2 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	35/114	30.7 %	118/229	51.5 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/64	15.6 %	59/128	46.1 %	- - -
Alternate clinical remission*[2]	47	26.3 %	189	51.8 %	24.1 % (16.0 %, 32.2 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	37/114	32.5 %	124/229	54.1 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/64	15.6 %	60/128	46.9 %	- - -
Maintenance of clinical remission through week 40*[3]	24/65	36.9 %	91/143	63.6 %	24.8 % (10.4 %, 39.2 %)[c]

Patients who were biologic and JAK-inhibitor naïve [a]	22/47	46.8 %	65/104	62.5 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	2/18	11.1 %	24/36	66.7 %	- - -
Corticosteroid-free remission*[4]	39	21.8 %	164	44.9 %	21.3 % (13.5 %, 29.1 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	30/114	26.3 %	107/229	46.7 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	9/64	14.1 %	52/128	40.6 %	- - -
Endoscopic improvement*[5]	52	29.1 %	214	58.6 %	28.5 % (20.2 %, 36.8 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	39/114	34.2 %	143/229	62.4 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	13/64	20.3 %	65/128	50.8 %	- - -
Histo-endoscopic mucosal remission*[6]	39	21.8 %	158	43.3 %	19.9 % (12.1 %, 27.6 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	30/114	26.3 %	108/229	47.2 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	9/64	14.1 %	46/128	35.9 %	- - -
Bowel urgency remission*[7]	43/172	25.0 %	144/336	42.9 %	18.1 % (9.8 %, 26.4 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	31/108	28.7 %	96/206	46.6 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	12/63	19.0 %	43/122	35.2 %	- - -
	Placebo N = 179		**Mirikizumab SC N = 365**		**Treatment difference and 95 % CI**
	LS mean	**Standard error**	**LS mean**	**Standard error**	
Bowel urgency severity*[8]	-2.74	0.202	-3.80	0.139	-1.06 (-1.51, -0.61)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	-2.69	0.233	-3.82	0.153	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	-2.66	0.346	-3.60	0.228	- - -

Abbreviations: CI = confidence interval; SC = subcutaneous; LS = least square

**[1, 2]* *See footnotes on Table 2*

**[3]* *The proportion of patients who were in clinical remission at week 40 among patients in clinical remission at week 12, with clinical remission defined as: Stool frequency (SF) subscore = 0 or SF = 1 with a ≥ 1-point decrease from induction baseline, and Rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)*

**[4]* *Corticosteroid-free remission without surgery, defined as: Clinical remission at week 40, and Symptomatic remission at week 28, and no corticosteroid use for ≥ 12 weeks prior to week 40*

**[5]* *Endoscopic improvement defined as: ES = 0 or 1 (excluding friability)*

**[6]* *Histo-endoscopic mucosal remission, defined as achieving both: 1. Histologic remission, defined as Geboes subscores of 0 for grades: 2b (lamina propria neutrophils), and 3 (neutrophils in epithelium), and 4 (crypt destruction), and 5 (erosion or ulceration) and 2. Mayo endoscopic score 0 or 1 (excluding friability)*

**[7]* *Numeric Rating Scale (NRS) 0 or 1 in patients with urgency NRS ≥ 3 at baseline in LUCENT-1*

*[8] *Change from baseline in the Urgency NRS score*

a) An additional 1 patient on placebo and 8 patients on mirikizumab where previously exposed to but did not fail a biologic or JAK-inhibitor.
b) Loss of response, inadequate response or intolerance.
c) p < 0.001
d) Mirikizumab results in the subgroup of patients who failed more than one biologic or JAK-inhibitor were consistent with results in the overall population.

The efficacy and safety profile of mirikizumab was consistent across subgroups, i.e. age, gender, body weight, disease activity severity at baseline and region. The effect size may vary.

At week 40, a greater proportion of patients were in clinical response (defined as decrease in the MMS of ≥ 2 points and ≥ 30 % decrease from baseline, and a decrease of ≥ 1 point in the RB subscore from baseline or a RB score of 0 or 1) in the mirikizumab responder group re-randomised to mirikizumab (80 %) compared to the mirikizumab responder group re-randomised to placebo (49 %).

Week 24 responders to mirikizumab extended induction (LUCENT-2)
For the mirikizumab patients who were not in response at week 12 of LUCENT-1 and received open-label additional 3 doses of 300 mg mirikizumab IV every 4 weeks (Q4W) 53.7 % achieved clinical response at week 12 of LUCENT-2 and 52.9 % mirikizumab patients continued to maintenance receiving 200 mg mirikizumab Q4W SC, and among these patients 72.2 % achieved clinical response and 36.1 % achieved clinical remission at week 40.

Recapture of efficacy after loss of response to mirikizumab maintenance (LUCENT-2)
19 patients who experienced a first loss of response (5.2 %) between week 12 and 28 of LUCENT-2 received open-label mirikizumab rescue dosing with 300 mg mirikizumab Q4W IV for 3 doses and 12 of these patients (63.2 %) achieved symptomatic response and 7 patients (36.8 %) achieved symptomatic remission after 12 weeks.

Endoscopic normalisation at week 40
Normalisation of endoscopic appearance of the mucosa was defined as a Mayo endoscopic subscore of 0. At week 40 of LUCENT-2, endoscopic normalisation was achieved in 81/365 (22.2 %) of patients treated with mirikizumab and in 24/179 (13.4 %) of patients in placebo group.

Histologic outcomes
At week 12 greater proportions of patients in the mirikizumab group achieved histologic improvement (39.2 %) compared with patients in the placebo group (20.7 %). At week 40 histologic remission was observed with more patients in the mirikizumab group (48.5 %) as compared to placebo (24.6 %).

Stable maintenance of symptomatic remission
Stable maintenance of symptomatic remission was defined as the proportion of patients in symptomatic remission for at least 7 out of 9 visits from week 4 to week 36 and in symptomatic remission at week 40 among patients in symptomatic remission and clinical response at week 12 of LUCENT-1. At week 40 of LUCENT-2, the proportion of patients achieving stable maintenance of symptomatic remission was greater in patients treated with mirikizumab (69.7 %) versus placebo (38.4 %).

Health-related quality of life
At week 12 of LUCENT-1, patients receiving mirikizumab showed significantly greater clinically relevant improvements on the Inflammatory Bowel Disease Questionnaire (IBDQ) total score ($p \leq 0.001$) when compared to placebo. IBDQ response was defined as at least a 16-point improvement from baseline in IBDQ score and IBDQ remission was defined as a score of at least 170. At week 12 of LUCENT-1, 57.5 % of mirikizumab-treated patients achieved IBDQ

remission versus 39.8 % with placebo ($p < 0.001$) and 72.7 % of mirikizumab-treated patients achieved IBDQ response versus 55.8 % in placebo. In LUCENT-2 at week 40, 72.3 % of mirikizumab-treated patients achieved maintenance of IBDQ remission versus 43.0 % placebo treated patients and 79.2 % mirikizumab treated patients achieved IBDQ response versus 49.2 % of placebo treated patients.

Patient reported outcomes
Decreases in bowel urgency severity were observed as early as week 2 in patients treated with mirikizumab in LUCENT-1. Patients receiving mirikizumab achieved significant bowel urgency remission compared with patients in the placebo group at week 12 in LUCENT-1 (22.1 % vs 12.3 %), and week 40 in LUCENT-2 (42.9 % vs 25 %). Patients receiving mirikizumab showed significant improvements in fatigue as early as week 2 of LUCENT-1 and the improvements were maintained at week 40 of LUCENT-2. As early as week 4 there was also a significantly greater reduction in abdominal pain.

Hospitalisations and ulcerative colitis related surgeries
Through week 12 of LUCENT-1, the proportion of patients with UC-related hospitalisations were 0.3 % (3/868) in the mirikizumab and 3.4 % (10/294) in the placebo group. UC-related surgeries were reported in 0.3 % (3/868) patients receiving mirikizumab and 0.7 % (2/294) patients in the placebo group. There were no UC-related hospitalisations and no UC-related surgeries in LUCENT-2 in the mirikizumab arm.

Paediatric population

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

5.2 Pharmacokinetic properties

There was no apparent accumulation in serum mirikizumab concentration over time when given subcutaneously every 4 weeks.

Mean (coefficient variation [CV %]) C_{max} and area under the curve (AUC) after induction dosing (300 mg every 4 weeks administered by intravenous infusion) in patients with ulcerative colitis were 99.7 (22.7) µg/mL and 538 (34.4) µg*day/mL, respectively. The mean (CV %) C_{max} and AUC after maintenance dosing (200 mg every 4 weeks by subcutaneous injection) were 10.1 (52.1) µg/mL and 160 (57.6) µg*day/mL, respectively.

Absorption

Following subcutaneous dosing of mirikizumab, peak serum concentrations were achieved 2-3 days post dose with an estimated absolute bioavailability of 44 %.
Injection site location did not significantly influence absorption of mirikizumab.

Distribution

The mean total volume of distribution was 4.83 L.

Biotransformation

Mirikizumab is a humanised IgG4 monoclonal antibody and is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgGs.

Elimination

In the population PK analysis, mean apparent clearance was 0.0229 L/hr and the mean elimination half-life is approximately 9.3 days in patients with ulcerative colitis. Clearance is independent of dose.

Dose proportionality

Mirikizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure over a dose range of 5 to 2 400 mg given as an intravenous infusion or over a dose range of 120 to 400 mg given as a subcutaneous injection in patients with ulcerative colitis or in healthy volunteers.

Special populations

Population pharmacokinetic analysis showed that age, sex, weight, or race/ethnicity did not have a clinically meaningful effect on the pharmacokinetics of mirikizumab (see also section 4.8, "immunogenicity"). Among the 1 362 subjects with ulcerative colitis exposed to mirikizumab in Phase 2 and Phase 3 studies, 99 (7.3 %) patients were 65 years or older and 11 (0.8 %) patients were 75 years or older.

Renal or hepatic impairment
Specific clinical pharmacology studies to evaluate the effects of renal impairment and hepatic impairment on the pharmacokinetics of mirikizumab have not been conducted. Population pharmacokinetic analysis showed that creatinine clearance (range of 36.2 to 291 mL/min) or total bilirubin (range of 1.5 to 29 µmol/L) did not affect mirikizumab pharmacokinetics.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction and development.

Carcinogenesis / mutagenesis

Non-clinical studies have not been conducted to evaluate the carcinogenic or mutagenic potential of mirikizumab.

Impairment of fertility

No reproductive organ weight or histopathology effects were observed in sexually mature cynomolgus monkeys that received mirikizumab once weekly for 26 weeks, at a dose of 100 mg/kg (at least 30 times the human maintenance dose).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate dihydrate
Citric acid, anhydrous
Sodium chloride
Polysorbate 80
Water for injections

6.2 Incompatibilities

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

Omvoh should not be administered concomitantly in the same intravenous line with other medicinal products.

6.3 Shelf life

2 years.

After dilution

Chemical and physical in-use stability has been demonstrated for diluted infusion solution prepared with sodium chloride 9 mg/mL (0.9 %) solution for 96 hours at 2 °C to 8 °C of which not more than 10 hours are permitted at non-refrigerated temperatures not to exceed 25 ºC, starting from the time of vial puncture.
Chemical and physical in-use stability has been demonstrated for diluted infusion solution prepared with 5 % glucose for 48 hours at 2 °C to 8 °C of which not more than 5 hours are permitted at non-refrigerated temperatures not to exceed 25 °C, starting from the time of vial puncture.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Keep the diluted solution away from direct heat or light.
Do not freeze the diluted solution.

6.4 Special precautions for storage

Unopened vial

Store in a refrigerator (2 ºC – 8 ºC).
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

15 mL concentrate in a type I clear glass vial with a chlorobutyl rubber stopper, an aluminium seal and polypropylene flip top.

Pack size of 1 vial.

6.6 Special precautions for disposal and other handling

Do not use Omvoh that has been frozen.

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

Dilution prior to intravenous infusion

1. Each vial is for single use only.
2. Prepare the infusion solution using aseptic technique to ensure the sterility of the prepared solution.
3. Inspect the content of the vial. The concentrate should be clear, colourless to slightly yellow and free of visible particles. Otherwise, it should be discarded.
4. Withdraw 15 mL of the mirikizumab vial (300 mg) using an appropriately sized needle (18 to 21 gauge is recommended) and transfer to the infusion bag. The concentrate should be diluted only in infusion bags (bag size ranging from 50 - 250 mL) containing either sodium chloride 9 mg/mL (0.9 %) solution for injection or 5 % glucose solution for injection. The final concentration after dilution is approximately 1.2 mg/mL to approximately 6 mg/mL.
5. Gently invert the infusion bag to mix. Do not shake the prepared bag.

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83
3528 BJ Utrecht
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 May 2023

10. DATE OF REVISION OF THE TEXT

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

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 100 mg solution for injection in pre-filled syringe
Omvoh 100 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Omvoh 100 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 100 mg mirikizumab in 1 mL solution.

Omvoh 100 mg solution for injection in pre-filled pen

Each pre-filled pen contains 100 mg mirikizumab in 1 mL solution.

Mirikizumab 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)

The solution is a clear and colourless to slightly yellow solution with a pH of approximately 5.5 and an osmolarity of approximately 300 mOsm/L.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

This medicinal product is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of ulcerative colitis.
Omvoh 100 mg solution for injection should only be used for the subcutaneous maintenance doses.

Posology

The recommended mirikizumab dose regimen has 2 parts.

Induction dose
The induction dose is 300 mg by intravenous infusion for at least 30 minutes at weeks 0, 4 and 8. (See Summary of Product Characteristics for Omvoh 300 mg concentrate for solution for infusion, section 4.2.)

Maintenance dose
The maintenance dose is 200 mg (i.e. two pre-filled syringes or two pre-filled pens) by subcutaneous injection every 4 weeks after completion of induction dosing.

Patients should be evaluated after the 12-week induction dosing and if there is adequate therapeutic response, transition to maintenance dosing. For patients who do not achieve adequate therapeutic benefit at week 12 of induction dosing, mirikizumab 300 mg by intravenous infusion may be continued at weeks 12, 16 and 20 (extended induction therapy). If therapeutic benefit is achieved with the additional intravenous therapy, patients may initiate mirikizumab subcutaneous maintenance dosing (200 mg) every 4 weeks, starting at week 24. Mirikizumab should be discontinued in patients who do not show evidence of therapeutic benefit to extended induction therapy by week 24.

Patients with loss of therapeutic response during maintenance treatment may receive 300 mg mirikizumab by intravenous infusion every 4 weeks, for a total of 3 doses (re-induction). If clinical benefit is achieved from this additional intravenous therapy, patients may resume mirikizumab subcutaneous dosing every 4 weeks. The efficacy and safety of repeated re-induction therapy have not been evaluated.

In case of a missed dose, instruct patients to inject as soon as possible. Thereafter, resume dosing every 4 weeks.

Elderly
No dose adjustment is required (see section 5.2). There is limited information in subjects aged ≥ 75 years.

Renal or hepatic impairment
Omvoh has not been studied in these patient populations. These conditions are generally not expected to have any significant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary (see section 5.2).

Paediatric population
The safety and efficacy of Omvoh in children and adolescents aged 2 to less than 18 years have not yet been established. No data are available.
There is no relevant use of Omvoh in children below 2 years for the indication of ulcerative colitis.

Method of administration

For subcutaneous injection only.

Sites for injection include the abdomen, thigh, and back of the upper arm. After training in subcutaneous injection technique, a patient may self-inject with mirikizumab.
Patients should be instructed to inject in a different location every time. For example, if the first injection was in the abdomen, the second injection—to complete a full dose—could be in another area of the abdomen.

4.3 Contraindications

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

Clinically important active infections (active tuberculosis).

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.

Hypersensitivity reactions

In clinical studies, hypersensitivity reactions have been reported. Most were mild or moderate, severe reactions were uncommon (see section 4.8). If a serious hypersensitivity reaction, including anaphylaxis, occurs, mirikizumab must be discontinued immediately and appropriate therapy must be initiated.

Infections

Mirikizumab may increase the risk of severe infection (see section 4.8). Treatment with mirikizumab should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated (see section 4.3). The risks and benefits of treatment should be considered prior to initiating use of mirikizumab in patients with a chronic infection or a history of recurrent infection. Patients should be instructed to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops, discontinuation of mirikizumab should be considered until the infection resolves.

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

Hepatic enzyme elevations

Cases of drug-induced liver injury (including one case meeting Hy's Law criteria) occurred in patients receiving mirikizumab in clinical trials. Liver enzymes and bilirubin should be evaluated at baseline and monthly during induction (including extended induction period, if applicable). Thereafter, liver enzymes and bilirubin should be monitored (every 1 - 4 months) according to standard practice for patient management and as clinically indicated. If increases in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) are observed and drug-induced liver injury is suspected, mirikizumab must be discontinued until this diagnosis is excluded.

Immunisations

Prior to initiating therapy with mirikizumab, completion of all appropriate immunisations should be considered according to current immunisation guidelines. Avoid use of live vaccines in patients treated with mirikizumab. No data are available on the response to live or non-live vaccines.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per 200 mg dose, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
In ulcerative colitis studies, concomitant use of corticosteroids or oral immunomodulators did not influence the safety of mirikizumab.
Population pharmacokinetic data analyses indicated that the clearance of mirikizumab was not impacted by concomitant administration of 5-ASAs (5-aminosalicylic acid), corticosteroids or oral immunomodulators (azathioprine, mercaptopurine, thioguanine, and methotrexate) in patients with ulcerative colitis.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 10 weeks after treatment.

Pregnancy

There is a limited amount of data from the use of mirikizumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Omvoh during pregnancy.

Breast-feeding

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

Fertility

The effect of mirikizumab on human fertility has not been evaluated (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse reactions are upper respiratory tract infections (7.9 %, most frequently nasopharyngitis), headache (3.3 %), rash (1.1 %) and injection site reactions (8.7 %, maintenance period).

Tabulated list of adverse reactions

Adverse reactions from clinical studies (Table 1) are listed by MedDRA system organ class. The frequency category for each reaction is based on the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000).

Table 1: Adverse reactions

MedDRA System organ class	Frequency	Adverse reaction
Infections and infestations	Common	Upper respiratory tract infections[a]
	Uncommon	Herpes zoster
Immune system disorders	Uncommon	Infusion-related hypersensitivity reactions
Musculoskeletal and Connective Tissue Disorders	Common	Arthralgia
Nervous system disorders	Common	Headache
Skin and subcutaneous tissue disorders	Common	Rash[b]
General disorders and administration site conditions	Common	Injection site reactions[c]
	Uncommon	Infusion site reactions[d]
Investigations	Uncommon	Alanine aminotransferase increased
	Uncommon	Aspartate aminotransferase increased

[a] *Includes: acute sinusitis, nasopharyngitis, oropharyngeal discomfort, oropharyngeal pain, pharyngitis, rhinitis, sinusitis, tonsillitis, upper respiratory tract infection, and viral upper respiratory tract infection.*

[b] *Includes: rash, rash macular, rash maculo-papular, and rash papular and rash pruritic.*

[c] *Reported in the mirikizumab maintenance study where mirikizumab treatment is administered as subcutaneous injection.*

[d] *Reported in the mirikizumab induction study where mirikizumab treatment is administered as intravenous infusion*.

Description of selected adverse reactions

Infusion-related hypersensitivity reactions (LUCENT-1, weeks 1-12)
Infusion-related hypersensitivity reactions were reported in 0.4 % of mirikizumab-treated patients. All infusion-related hypersensitivity reactions were reported as non-serious.

Injection site reactions (LUCENT-2, weeks 12-52)
Injection site reactions were reported in 8.7 % mirikizumab-treated patients. The most frequent reactions were injection site pain, injection site reaction and injection site erythema. These symptoms were reported as non-serious, mild and transient in nature.

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) increased
In the first 12 weeks (LUCENT-1), ALT increased was reported in 0.4 % mirikizumab-treated patients. AST increased was reported by 0.5 % mirikizumab-treated patients. All adverse reactions were reported as mild to moderate in severity and non-serious.

Over all mirikizumab treatment periods in the ulcerative colitis clinical development program (including the placebo-controlled and open label induction and maintenance periods), there have been elevations of ALT to ≥ 3 x upper limit of normal (ULN) (2.0 %), ≥ 5 x ULN (0.7 %) and ≥ 10 x ULN (0.2 %) and AST to ≥ 3 x ULN (2.1 %), ≥ 5 x ULN (1.1 %) and ≥ 10 x ULN (0.1 %) in patients receiving mirikizumab (see section 4.4). These elevations have been noted with and without concomitant elevations in total bilirubin.

Immunogenicity
With 12 months of treatment, up to 23 % of mirikizumab-treated patients developed anti-drug antibodies, most of which were of low titer and tested positive for neutralising activity. Higher antibody titers in approximately 2 % of subjects treated with mirikizumab were associated with lower serum mirikizumab concentrations and reduced clinical response. No association was found between anti-mirikizumab antibodies and hypersensitivity or injection site reactions.

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

Mirikizumab doses up to 2 400 mg intravenously and up to 500 mg subcutaneously have been administered in clinical trials without dose-limiting toxicity. In the event of overdose, the patient must be monitored for signs or symptoms of adverse reactions and appropriate symptomatic treatment must be started immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC24

Mechanism of action

Mirikizumab is a humanised IgG4 monoclonal, anti-interleukin-23 (anti-IL-23) antibody that selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor.

IL-23, a regulatory cytokine, affects the differentiation, expansion, and survival of T cell subsets, (e.g., Th17 cells and Tc17 cells) and innate immune cell subsets, which represent sources of effector cytokines, including IL-17A, IL-17F and IL-22 that drive inflammatory disease. In humans, selective blockade of IL-23 was shown to normalise production of these cytokines.

Pharmacodynamic effects

Inflammatory biomarkers were measured in the phase 3 ulcerative colitis studies. Mirikizumab administered intravenously every 4 weeks during induction dosing significantly reduced levels of fecal calprotectin and C-reactive protein from baseline to week 12. Also, mirikizumab administered subcutaneously every 4 weeks during maintenance dosing sustained significantly reduced levels of fecal calprotectin and C-reactive protein through 40 weeks.

Clinical efficacy and safety

The efficacy and safety of mirikizumab was evaluated in adult patients with moderately to severely active ulcerative colitis in two randomised, double-blind, placebo-controlled, multicentre studies. Enrolled patients had a confirmed diagnosis of ulcerative colitis for at least 3 months and moderately to severely active disease, defined as a modified Mayo score of 4 to 9, including a Mayo endoscopy subscore ≥ 2. Patients had to have failed (defined as loss of response, inadequate response or intolerance) corticosteroids or immunomodulators (6-mercaptopurine, azathioprine) or at least one biologic (a TNFα antagonist and/or vedolizumab) or tofacitinib.

LUCENT-1 was an intravenous induction study with treatment of up to 12 weeks, followed by a 40 week subcutaneous randomised withdrawal maintenance study (LUCENT-2), representing at least 52 weeks of therapy. Mean age was 42.5 years. 7.8 % of patients were ≥ 65 of age and 1.0 % of patients ≥ 75 of age. 59.8 % were men; 40.2 % were women. 53.2 % had severely active disease with a modified Mayo score 7 to 9.

Efficacy results presented for LUCENT-1 and LUCENT-2 were based on central reading of endoscopies and histology.

LUCENT-1
LUCENT-1 included 1 162 patients in the primary efficacy population. Patients were randomised to receive a dose of 300 mg mirikizumab via intravenous infusion or placebo, at week 0, week 4 and week 8 with a 3:1 treatment allocation ratio. The primary endpoint for the induction study was the proportion of subjects in clinical remission [modified Mayo score (MMS) defined as: Stool frequency (SF) subscore = 0 or 1 with a ≥ 1-point decrease from baseline, and rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)] at week 12.

Patients in these studies may have received other concomitant therapies including aminosalicylates (74.3 %), immunomodulatory agents (24.1 % such as azathioprine, 6-mercaptopurine or methotrexate), and oral corticosteroids (39.9 %; prednisone daily dose up to 20 mg or equivalent) at a stable dose prior to and during the induction period. Per protocol oral corticosteroids were tapered after induction.

Of the primary efficacy population, 57.1 % were biologic-naive and tofacitinib-naive. 41.2 % of patients had failed a biologic or tofacitinib. 36.3 % of the patients had failed at least 1 prior anti-TNF therapy, 18.8 % had failed vedolizumab and 3.4 % of patients had failed tofacitinib. 20.1 % had failed more than one biologic or tofacitinib. An additional 1.7 % had previously received but had not failed a biologic or tofacitinib.

In LUCENT-1 a significantly greater proportion of patients were in clinical remission in the mirikizumab treated group compared to placebo at week 12 (Table 2). As early as week 2, mirikizumab-treated patients achieved a greater reduction in RB subscores and decreases in SF subscores.

Table 2: Summary of key efficacy outcomes in LUCENT-1 (week 12 unless indicated otherwise)

	Placebo N = 294		**Mirikizumab IV N = 868**		**Treatment difference and 99.875 % CI**
	N	**%**	**N**	**%**	
Clinical remission*[1]	39	13.3 %	210	24.2 %	11.1 % (3.2 %, 19.1 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	27/171	15.8 %	152/492	30.9 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/118	8.5 %	55/361	15.2 %	- - -
Alternate clinical remission*[2]	43	14.6 %	222	25.6 %	11.1 % (3.0 %, 19.3 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	31/171	18.1 %	160/492	32.5 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/118	8.5 %	59/361	16.3 %	- - -
Clinical response*[3]	124	42.2 %	551	63.5 %	21.4 % (10.8 %, 32.0 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	86/171	50.3 %	345/492	70.1 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	35/118	29.7 %	197/361	54.6 %	- - -
Endoscopic improvement*[4]	62	21.1 %	315	36.3 %	15.4 % (6.3 %, 24.5 %)[c]

Patients who were biologic and JAK-inhibitor naïve [a]	48/171	28.1 %	226/492	45.9 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	12/118	10.2 %	85/361	23.5 %	- - -
Symptomatic remission (week 4)*[5]	38	12.9 %	189	21.8 %	9.2 % (1.4 %, 16.9 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	26/171	15.2 %	120/492	24.4 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/118	8.5 %	67/361	18.6 %	- - -
Symptomatic remission*[5]	82	27.9 %	395	45.5 %	17.5 % (7.5 %, 27.6 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	57/171	33.3 %	248/492	50.4 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	22/118	18.6 %	139/361	38.5 %	- - -
Histo-endoscopic mucosal improvement*[6]	41	13.9 %	235	27.1 %	13.4 % (5.5 %, 21.4 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	32/171	18.7 %	176/492	35.8 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	8/118	6.8 %	56/361	15.5 %	- - -

	Placebo N = 294		**Mirikizumab IV N = 868**		**Treatment difference and 99.875 % CI**
	LS mean	**Standard error**	**LS mean**	**Standard error**	
Bowel urgency severity*[7]	-1.63	0.141	-2.59	0.083	-0.95 (-1.47, -0.44)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	-2.08	0.174	-2.72	0.101	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	-0.95	0.227	-2.46	0.126	- - -

Abbreviations: CI = confidence interval; IV = intravenous; LS = least square

*[1] *Clinical remission is based on the modified Mayo score (MMS) and is defined as: Stool frequency (SF) subscore = 0 or 1 with a ≥ 1-point decrease from baseline, and Rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)*

*[2] *Alternate clinical remission is based on the modified Mayo score (MMS) and is defined as: Stool frequency (SF) subscore = 0 or 1, and Rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)*

*[3] *Clinical response based on the MMS and is defined as: A decrease in the MMS of ≥ 2 points and ≥ 30 % decrease from baseline, and a decrease of ≥ 1 point in the RB subscore from baseline or a RB score of 0 or 1*

*[4] *Endoscopic improvement defined as: ES = 0 or 1 (excluding friability)*

*[5] *Symptomatic remission defined as: SF = 0, or SF = 1 with a ≥ 1-point decrease from baseline, and RB = 0*

*[6] *Histo-endoscopic mucosal improvement defined as achieving both: 1. Histologic improvement, defined using Geboes scoring system with neutrophil infiltration in < 5 % of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue. 2. Endoscopic improvement, defined as ES = 0 or 1 (excluding friability).*

*[7] *Change from baseline in the Urgency Numeric Rating Scale score*

a) *An additional 5 patients on placebo and 15 patients on mirikizumab where previously exposed to but did not fail a biologic or JAK-inhibitor.*

b) Loss of response, inadequate response or intolerance.
c) $p < 0.001$
d) Mirikizumab results in the subgroup of patients who failed more than one biologic or JAK-inhibitor were consistent with results in the overall population.

LUCENT-2
LUCENT-2 evaluated 544 patients out of the 551 patients who achieved clinical response with mirikizumab in LUCENT-1 at week 12 (see Table 2). Patients were re-randomised in a 2:1 treatment allocation ratio to receive a subcutaneous maintenance regimen of 200 mg mirikizumab or placebo every 4 weeks for 40 weeks (which is 52 weeks from initiation of the induction dose). The primary endpoint for the maintenance study was the proportion of subjects in clinical remission (same definition as in LUCENT-1) at week 40. Corticosteroid tapering was required upon entrance into LUCENT-2 for patients who were receiving corticosteroids during LUCENT-1. Significantly greater proportions of patients were in clinical remission in the mirikizumab-treated group compared to the placebo group at week 40 (see Table 3).

Table 3: Summary of key efficacy measures in LUCENT-2 (week 40; 52 weeks from initiation of the induction dose)

	Placebo N = 179		**Mirikizumab SC N = 365**		**Treatment difference and 95 % CI**
	N	**%**	**N**	**%**	
Clinical remission*[1]	45	25.1 %	182	49.9 %	23.2 % (15.2 %, 31.2 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	35/114	30.7 %	118/229	51.5 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/64	15.6 %	59/128	46.1 %	- - -
Alternate clinical remission*[2]	47	26.3 %	189	51.8 %	24.1 % (16.0 %, 32.2 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	37/114	32.5 %	124/229	54.1 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	10/64	15.6 %	60/128	46.9 %	- - -
Maintenance of clinical remission through week 40*[3]	24/65	36.9 %	91/143	63.6 %	24.8 % (10.4 %, 39.2 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	22/47	46.8 %	65/104	62.5 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	2/18	11.1 %	24/36	66.7 %	- - -
Corticosteroid-free remission*[4]	39	21.8 %	164	44.9 %	21.3 % (13.5 %, 29.1 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	30/114	26.3 %	107/229	46.7 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	9/64	14.1 %	52/128	40.6 %	- - -

Endoscopic improvement*[5]	52	29.1 %	214	58.6 %	28.5 % (20.2 %, 36.8 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	39/114	34.2 %	143/229	62.4 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	13/64	20.3 %	65/128	50.8 %	- - -
Histo-endoscopic mucosal remission*[6]	39	21.8 %	158	43.3 %	19.9 % (12.1 %, 27.6 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	30/114	26.3 %	108/229	47.2 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	9/64	14.1 %	46/128	35.9 %	- - -
Bowel urgency remission*[7]	43/172	25.0 %	144/336	42.9 %	18.1 % (9.8 %, 26.4 %)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	31/108	28.7 %	96/206	46.6 %	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	12/63	19.0 %	43/122	35.2 %	- - -
	Placebo N = 179		**Mirikizumab SC N = 365**		**Treatment difference and 95 % CI**
	LS mean	**Standard error**	**LS mean**	**Standard error**	
Bowel urgency severity*[8]	-2.74	0.202	-3.80	0.139	-1.06 (-1.51, -0.61)[c]
Patients who were biologic and JAK-inhibitor naïve [a]	-2.69	0.233	-3.82	0.153	- - -
Patients who failed [b] at least one biologic or JAK-inhibitor [d]	-2.66	0.346	-3.60	0.228	- - -

Abbreviations: CI = confidence interval; SC = subcutaneous; LS = least square

*[1, 2] *See footnotes on Table 2*

*[3] *The proportion of patients who were in clinical remission at week 40 among patients in clinical remission at week 12, with clinical remission defined as: Stool frequency (SF) subscore = 0 or SF = 1 with a ≥ 1-point decrease from induction baseline, and Rectal bleeding (RB) subscore = 0, and Endoscopic subscore (ES) = 0 or 1 (excluding friability)*

*[4] *Corticosteroid-free remission without surgery, defined as: Clinical remission at week 40, and Symptomatic remission at week 28, and no corticosteroid use for ≥ 12 weeks prior to week 40*

*[5] *Endoscopic improvement defined as: ES = 0 or 1 (excluding friability)*

*[6] *Histo-endoscopic mucosal remission, defined as achieving both: 1. Histologic remission, defined as Geboes subscores of 0 for grades: 2b (lamina propria neutrophils), and 3 (neutrophils in epithelium), and 4 (crypt destruction), and 5 (erosion or ulceration) and 2. Mayo endoscopic score 0 or 1 (excluding friability)*

*[7] *Numeric Rating Scale (NRS) 0 or 1 in patients with urgency NRS ≥ 3 at baseline in LUCENT-1*

*[8] *Change from baseline in the Urgency NRS score*

a) An additional 1 patient on placebo and 8 patients on mirikizumab where previously exposed to but did not fail a biologic or JAK-inhibitor.

b) Loss of response, inadequate response or intolerance.

c) $p < 0.001$

d) Mirikizumab results in the subgroup of patients who failed more than one biologic or JAK-inhibitor were consistent with results in the overall population.

The efficacy and safety profile of mirikizumab was consistent across subgroups, i.e. age, gender, body weight, disease activity severity at baseline and region. The effect size may vary.

At week 40, a greater proportion of patients were in clinical response (defined as decrease in the MMS of ≥ 2 points and ≥ 30 % decrease from baseline, and a decrease of ≥ 1 point in the RB subscore from baseline or a RB score of 0 or 1) in the mirikizumab responder group re-randomised to mirikizumab (80 %) compared to the mirikizumab responder group re-randomised to placebo (49 %).

Week 24 responders to mirikizumab extended induction (LUCENT-2)
For the mirikizumab patients who were not in response at week 12 of LUCENT-1 and received open-label additional 3 doses of 300 mg mirikizumab IV every 4 weeks (Q4W) 53.7 % achieved clinical response at week 12 of LUCENT-2 and 52.9 % mirikizumab patients continued to maintenance receiving 200 mg mirikizumab Q4W SC, and among these patients 72.2 % achieved clinical response and 36.1 % achieved clinical remission at week 40.

Recapture of efficacy after loss of response to mirikizumab maintenance (LUCENT-2)
19 patients who experienced a first loss of response (5.2 %) between week 12 and 28 of LUCENT-2 received open label mirikizumab rescue dosing with 300 mg mirikizumab Q4W IV for 3 doses and 12 of these patients (63.2 %) achieved symptomatic response and 7 patients (36.8 %) achieved symptomatic remission after 12 weeks.

Endoscopic normalisation at week 40
Normalisation of endoscopic appearance of the mucosa was defined as a Mayo endoscopic subscore of 0. At week 40 of LUCENT-2, endoscopic normalisation was achieved in 81/365 (22.2 %) of patients treated with mirikizumab and in 24/179 (13.4 %) of patients in placebo group.

Histologic outcomes
At week 12 greater proportions of patients in the mirikizumab group achieved histologic improvement (39.2 %) compared with patients in the placebo group (20.7 %). At week 40 histologic remission was observed with more patients in the mirikizumab group (48.5 %) as compared to placebo (24.6 %).

Stable maintenance of symptomatic remission
Stable maintenance of symptomatic remission was defined as the proportion of patients in symptomatic remission for at least 7 out of 9 visits from week 4 to week 36 and in symptomatic remission at week 40 among patients in symptomatic remission and clinical response at week 12 of LUCENT-1. At week 40 of LUCENT-2, the proportion of patients achieving stable maintenance of symptomatic remission was greater in patients treated with mirikizumab (69.7 %) versus placebo (38.4 %).

Health-related quality of life
At week 12 of LUCENT-1, patients receiving mirikizumab showed significantly greater clinically relevant improvements on the Inflammatory Bowel Disease Questionnaire (IBDQ) total score ($p \leq 0.001$) when compared to placebo. IBDQ response was defined as at least a 16-point improvement from baseline in IBDQ score and IBDQ remission was defined as a score of at least 170. At week 12 of LUCENT-1, 57.5 % of mirikizumab-treated patients achieved IBDQ remission versus 39.8 % with placebo ($p < 0.001$) and 72.7 % of mirikizumab-treated patients achieved IBDQ response versus 55.8 % in placebo. In LUCENT-2 at week 40, 72.3 % of mirikizumab-treated patients achieved maintenance of IBDQ remission versus 43.0 % placebo treated patients and 79.2 % mirikizumab treated patients achieved IBDQ response versus 49.2 % of placebo treated patients.

Patient reported outcomes
Decreases in bowel urgency severity were observed as early as week 2 in patients treated with mirikizumab in LUCENT-1. Patients receiving mirikizumab achieved significant bowel urgency

remission compared with patients in the placebo group at week 12 in LUCENT 1 (22.1 % vs 12.3 %), and week 40 in LUCENT-2 (42.9 % vs 25 %). Patients receiving mirikizumab showed significant improvements in fatigue as early as week 2 of LUCENT-1 and the improvements were maintained at week 40 of LUCENT-2. As early as week 4 there was also a significantly greater reduction in abdominal pain.

Hospitalisations and ulcerative colitis related surgeries
Through week 12 of LUCENT-1, the proportion of patients with UC-related hospitalisations were 0.3 % (3/868) in the mirikizumab and 3.4 % (10/294) in the placebo group. UC-related surgeries were reported in 0.3 % (3/868) patients receiving mirikizumab and 0.7 % (2/294) patients in the placebo group. There were no UC-related hospitalisations and no UC-related surgeries in LUCENT-2 in the mirikizumab arm.

Paediatric population

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

5.2 Pharmacokinetic properties

There was no apparent accumulation in serum mirikizumab concentration over time when given subcutaneously every 4 weeks.

Mean (coefficient variation [CV %]) C_{max} and area under the curve (AUC) after induction dosing (300 mg every 4 weeks administered by intravenous infusion) in patients with ulcerative colitis were 99.7 (22.7) µg/mL and 538 (34.4) µg*day/mL, respectively. The mean (CV %) C_{max} and AUC after maintenance dosing (200 mg every 4 weeks by subcutaneous injection) were 10.1 (52.1) µg/mL and 160 (57.6) µg*day/mL, respectively.

Absorption

Following subcutaneous dosing of mirikizumab, peak serum concentrations were achieved 2-3 days post dose with an estimated absolute bioavailability of 44 %.
Injection site location did not significantly influence absorption of mirikizumab.

Distribution

The mean total volume of distribution was 4.83 L.

Biotransformation

Mirikizumab is a humanised IgG4 monoclonal antibody and is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgGs.

Elimination

In the population PK analysis, mean apparent clearance was 0.0229 L/hr and the mean elimination half-life is approximately 9.3 days in patients with ulcerative colitis. Clearance is independent of dose.

Dose proportionality

Mirikizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure over a dose range of 5 to 2 400 mg given as an intravenous infusion or over a dose range of 120 to 400 mg given as a subcutaneous injection in patients with ulcerative colitis or in healthy volunteers.

Special populations

Population pharmacokinetic analysis showed that age, sex, weight, or race/ethnicity did not have a clinically meaningful effect on the pharmacokinetics of mirikizumab (see also section 4.8, "immunogenicity"). Among the 1 362 subjects with ulcerative colitis exposed to mirikizumab in Phase 2 and Phase 3 studies, 99 (7.3 %) patients were 65 years or older and 11 (0.8 %) patients were 75 years or older.

Renal or hepatic impairment
Specific clinical pharmacology studies to evaluate the effects of renal impairment and hepatic impairment on the pharmacokinetics of mirikizumab have not been conducted. Population pharmacokinetic analysis showed that creatinine clearance (range of 36.2 to 291 mL/min) or total bilirubin (range of 1.5 to 29 µmol/L) did not affect mirikizumab pharmacokinetics.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction and development.

Carcinogenesis / mutagenesis

Non-clinical studies have not been conducted to evaluate the carcinogenic or mutagenic potential of mirikizumab.

Impairment of fertility

No reproductive organ weight or histopathology effects were observed in sexually mature cynomolgus monkeys that received mirikizumab once weekly for 26 weeks, at a dose of 100 mg/kg (at least 30 times the human maintenance dose).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate dihydrate
Citric acid, anhydrous
Sodium chloride
Polysorbate 80
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store in a refrigerator (2 ºC – 8 ºC).
Do not freeze.
Store in the original package in order to protect from light.

Omvoh may be stored unrefrigerated for up to 2 weeks at a temperature not above 30 ºC.
If these conditions are exceeded, Omvoh must be discarded.

6.5 Nature and contents of container

Omvoh 100 mg solution for injection in pre-filled syringe

1 mL solution in a type I clear glass syringe.
The syringe is encased in a disposable, single-dose syringe with bromobutyl rubber plunger.
Pack sizes of 2 or 6 pre-filled syringes.
Not all pack sizes may be marketed.

Omvoh 100 mg solution for injection in pre-filled pen

1 mL solution in a type I clear glass syringe.
The syringe is encased in a disposable, single-dose pen with bromobutyl rubber plunger.
Pack sizes of 2, 4 or 6 pre-filled pen.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

For single use only. Omvoh should not be used if particles appear or if the solution is cloudy and/or distinctly brown.
Do not use Omvoh that has been frozen.

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

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Papendorpseweg 83
3528 BJ Utrecht
The Netherlands.

8. MARKETING AUTHORISATION NUMBER(S)

Omvoh 100 mg solution for injection in pre-filled syringe

EU/1/23/1736/002
EU/1/23/1736/003

Omvoh 100 mg solution for injection in pre-filled pen

EU/1/23/1736/004
EU/1/23/1736/005
EU/1/23/1736/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 May 2023

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

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

Name and address of the manufacturer of the biological active substance

Eli Lilly Kinsale Limited, Dunderrow, Kinsale, Co. Cork, Ireland

Name and address of the manufacturer responsible for batch release

Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France

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 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 - VIAL

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 300 mg concentrate for solution for infusion
mirikizumab

2. STATEMENT OF ACTIVE SUBTANCE(S)

Each vial contains 300 mg of mirikizumab in 15 mL (20 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Concentrate for solution for infusion
300 mg/15 mL
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous use after dilution.
For single use only.
Do not shake.
Read 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

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the vial in the outer carton in order to protect from light

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

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.,
Papendorpseweg 83, 3528 BJ Utrecht,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
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NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

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

Omvoh 300 mg sterile concentrate
mirikizumab
For IV use after dilution

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

300 mg/15 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON - PRE-FILLED SYRINGE (pack of 2)

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 100 mg solution for injection in pre-filled syringe
mirikizumab

2. STATEMENT OF ACTIVE SUBTANCE(S)

Each pre-filled syringe contains 100 mg of mirikizumab in 1 mL solution.

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
2 pre-filled syringes of 1 mL solution

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only.
Read the package leaflet before use.
Subcutaneous use
Do not shake.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package 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

Eli Lilly Nederland B.V.,
Papendorpseweg 83, 3528 BJ Utrecht,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omvoh 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR MULTIPACK (with Blue Box)

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 100 mg solution for injection in pre-filled syringe
mirikizumab

2. STATEMENT OF ACTIVE SUBTANCE(S)

Each pre-filled syringe contains 100 mg of mirikizumab in 1 mL solution.

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
Multipack: 6 (3 packs of 2) pre-filled syringes.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only.
Read the package leaflet before use.
Subcutaneous use.
Do not shake.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package 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

Eli Lilly Nederland B.V.,
Papendorpseweg 83, 3528 BJ Utrecht,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omvoh 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (without Blue Box)

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 100 mg solution for injection in pre-filled syringe
mirikizumab

2. STATEMENT OF ACTIVE SUBTANCE(S)

Each pre-filled syringe contains 100 mg of mirikizumab in 1 mL solution.

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
2 pre-filled syringes of 1 mL solution. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only.
Read the package leaflet before use.
Subcutaneous use.
Do not shake.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package 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

Eli Lilly Nederland B.V.,
Papendorpseweg 83, 3528 BJ Utrecht,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omvoh 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

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

Omvoh 100 mg injection
mirikizumab
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 (pack of 2)

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 100 mg solution for injection in pre-filled pen
mirikizumab

2. STATEMENT OF ACTIVE SUBTANCE(S)

Each pre-filled pen contains 100 mg of mirikizumab in 1 mL solution.

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
2 pre-filled pens of 1 mL solution

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only.
Read the package leaflet before use.
Subcutaneous use.
Do not shake.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package 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

Eli Lilly Nederland B.V.,
Papendorpseweg 83, 3528 BJ Utrecht,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omvoh 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (with Blue Box)

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 100 mg solution for injection in pre-filled pen
mirikizumab

2. STATEMENT OF ACTIVE SUBTANCE(S)

Each pre-filled pen contains 100 mg of mirikizumab in 1 mL solution.

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
Multipack: 4 (2 packs of 2) pre-filled pens of 1 mL solution
Multipack: 6 (3 packs of 2) pre-filled pens of 1 mL solution

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only.
Read the package leaflet before use.
Subcutaneous use.
Do not shake.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package 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

Eli Lilly Nederland B.V.,
Papendorpseweg 83, 3528 BJ Utrecht,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/005 (4 pre-filled pens)
EU/1/23/1736/006 (6 pre-filled pens)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omvoh 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (without Blue Box)

1. NAME OF THE MEDICINAL PRODUCT

Omvoh 100 mg solution for injection in pre-filled pen
mirikizumab

2. STATEMENT OF ACTIVE SUBTANCE(S)

Each pre-filled pen contains 100 mg of mirikizumab in 1 mL solution.

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
2 pre-filled pens of 1 mL solution. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only.
Read the package leaflet before use.
Subcutaneous use.
Do not shake.

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original package 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

Eli Lilly Nederland B.V.,
Papendorpseweg 83, 3528 BJ Utrecht,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1736/005 (4 pre-filled pens)
EU/1/23/1736/006 (6 pre-filled pens)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Omvoh 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL

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

Omvoh 100 mg solution for injection
mirikizumab
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

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Omvoh 300 mg concentrate for solution for infusion
mirikizumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 Omvoh is and what it is used for

Omvoh contains the active substance mirikizumab, a monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind specifically to certain target proteins in the body. Omvoh works by attaching to and blocking a protein in the body called IL-23 (interleukin-23), which is involved in inflammation. By blocking the action of IL-23, Omvoh reduces inflammation and other symptoms associated with ulcerative colitis.

Ulcerative colitis is a chronic inflammatory disease of the large bowel. If you have ulcerative colitis, you will first be given other medicines. If you do not respond well enough or cannot tolerate these medicines, you may be given Omvoh to reduce signs and symptoms of ulcerative colitis such as diarrhoea, abdominal pain, urgency and rectal bleeding.

2. What you need to know before you receive Omvoh

Do not use Omvoh
- if you are allergic to mirikizumab or any of the other ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice before using Omvoh.
- If you have important active infections (active tuberculosis).

Warnings and precautions
- Talk to your doctor or pharmacist before using this medicine.
- Your doctor will check how well you are before treatment.
- Make sure you tell your doctor about any illness you have before treatment.

Infections

- Omvoh can potentially cause serious infections.
- Treatment with Omvoh should not be started if you have an active infection until the infection is gone.
- After starting the treatment, tell your doctor right away if you have any symptoms of an infection such as:
    - fever
    - chills
    - muscle aches
    - cough
    - shortness of breath
    - runny nose
    - sore throat
    - pain during urination

- Also tell your doctor if you have recently been near anyone who might have tuberculosis.
- Your doctor will examine you and may do a test for tuberculosis before you have Omvoh.
- If your doctor thinks you are at risk of an active tuberculosis, you may be given medicines to treat it.

Vaccinations

Your doctor will check to see if you need any vaccinations before starting treatment. Tell your doctor, pharmacist or nurse if you have recently had or are going to have a vaccination. Some types of vaccines (live vaccines) should not be given while using Omvoh.

Allergic reactions

- Omvoh can potentially cause serious allergic reactions.
- Stop using Omvoh and get emergency medical help right away if you develop any of the following symptoms of a serious allergic reaction:
    - rash
    - fainting
    - dizziness
    - low blood pressure
    - swelling of the face, lips, mouth, tongue or throat, trouble breathing
    - sensation of throat tightening or chest tightness.

Liver blood test

Your doctor will conduct blood tests before starting and during treatment with Omvoh to check if your liver is functioning normally. If blood tests are abnormal, your doctor might interrupt therapy with Omvoh and do additional tests on your liver to determine the cause.

Children and adolescents

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

Other medicines and Omvoh

Tell your doctor, pharmacist or nurse

- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. Some types of vaccines (live vaccines) should not be given while using Omvoh.

Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before using this medicine. It is preferable to avoid the use of Omvoh in pregnancy. The effects of Omvoh in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and should use effective contraception while using Omvoh and for at least 10 weeks after the last Omvoh dose.

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

Driving and using machines
Omvoh is unlikely to influence your ability to drive and use machines.

Omvoh contains sodium
This medicine contains 60 mg sodium (main component of cooking/table salt) in each 300 mg dose. This is equivalent to 3 % of the recommended maximum daily dietary intake of sodium for an adult. Before Omvoh is given to you, it is mixed with a solution that might contain sodium. Talk to your doctor if you are on a low salt diet.

3. How Omvoh is used

Omvoh is intended for use under the guidance and supervision of a doctor experienced in the diagnosis and treatment of ulcerative colitis.

How much Omvoh is given and for how long
Your doctor will decide how much Omvoh you need and for how long. Omvoh is for long-term treatment. Your doctor or nurse will regularly monitor your condition to check that the treatment is having the desired effect.

- Treatment start: The first dose of Omvoh is 300 mg and will be given by your doctor by intravenous infusion (drip in a vein in your arm) over at least 30 minutes. After the first dose, you will receive another dose of Omvoh 300 mg 4 weeks later and again after an additional 4 weeks.
  If you do not have adequate therapeutic response after these 3 infusions, your doctor might consider continuing intravenous infusions at weeks 12, 16 and 20.

- Maintenance therapy: 4 weeks after the last intravenous infusion, a maintenance dose of Omvoh 200 mg will be given by an injection under the skin ('subcutaneously') and then every 4 weeks. The maintenance dose of 200 mg will be given by using 2 injections each containing 100 mg of Omvoh.
  If you lose response after receiving the maintenance dose of Omvoh, your doctor may decide to give you 3 doses of Omvoh by intravenous infusions.
  Your doctor or nurse will tell you when to switch to subcutaneous injections.
  During maintenance therapy you and your doctor or nurse should decide if you should inject Omvoh yourself after training in subcutaneous injection technique. It is important not to try to inject yourself until you have been trained by your doctor or nurse. Your doctor or nurse will offer the necessary training.

If you receive more Omvoh than you should
If you have received more Omvoh than you should or the dose has been given sooner than prescribed, inform your doctor.

If you forget to use Omvoh
If you missed a dose of Omvoh, talk to your doctor.

If you stop using Omvoh
You should not stop using Omvoh without speaking to your doctor first. If you stop treatment, symptoms of ulcerative colitis may come back.

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

4. Possible side effects

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

Common (may affect up to 1 in 10 people)
- Upper respiratory tract infections (nose and throat infections)
- Joint pain
- Headache
- Rash
- Injection site reactions (e.g. red skin, pain)

Uncommon (may affect up to 1 in 100 people)
- Shingles
- Infusion-related allergic reaction (e.g. itch, hives)
- Increase in the level of liver enzymes in your blood

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 Omvoh

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

Do not use this medicine after the expiry date which is stated on the vial label and on the outer carton after "EXP". The expiry date refers to the last day of that month.

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

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

Do not use this medicine if you notice that the vial is damaged, or the medicine is cloudy, distinctly brown, or has particles in it.

This medicine is for single use only.

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

Diluted solution
It is recommended to start the infusion immediately after dilution. If not immediately used, the diluted solution prepared with sodium chloride 9 mg/mL (0.9 %) solution for injection may be stored refrigerated (2 ºC – 8 ºC) for not more than 96 hours or at room temperature not exceeding 25 ºC for not more than 10 hours (total time must not exceed 96 hours) starting from the time of vial puncture. The diluted infusion solution prepared with 5 % glucose must be used within 48 hours, of which not more than 5 hours are permitted at nonrefrigerated temperature not to exceed 25 °C, starting at the time of vial puncture.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Keep the diluted solution away from direct heat or light.
Do not freeze the diluted solution.

6. Contents of the pack and other information

What Omvoh contains
- The active substance is mirikizumab.
  Each vial contains 300 mg mirikizumab in 15 mL (20 mg/mL).
- The other ingredients are sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections.

What Omvoh looks like and contents of the pack
Omvoh is a solution in a clear glass vial. Its colour may vary from colourless to slightly yellow.

Pack size of 1 vial.

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

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Omvoh 300 mg concentrate for solution for infusion
mirikizumab

The following information is intended for healthcare professionals only:

Do not use Omvoh that has been frozen.

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

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.

Dilution prior to intravenous infusion

1. Each vial is for single use only.
2. Prepare the infusion solution using aseptic technique to ensure the sterility of the prepared solution.
3. Inspect the content of the vial. The concentrate should be clear, colourless to slightly yellow and free of visible particles. Otherwise, it should be discarded.
4. Withdraw 15 mL of the mirikizumab vial (300 mg) using an appropriately sized needle (18 to 21 gauge is recommended) and transfer to the infusion bag. The concentrate should be diluted only in infusion bags (bag size ranging from 50-250 mL) containing either sodium chloride 9 mg/mL (0.9 %) solution for injection or 5% glucose solution for injection. The final concentration after dilution is approximately 1.2 mg/mL to approximately 6 mg/mL.
5. Gently invert the infusion bag to mix. Do not shake the prepared bag.

Administration of the diluted solution

6. The intravenous administration set (infusion line) should be connected to the prepared intravenous bag and the line should be primed. The infusion should be administered for at least 30 minutes.
7. At the end of the infusion, to ensure a full dose is administered, the infusion line should be flushed with sodium chloride 9 mg/mL (0.9 %) solution or 5 % glucose solution for injection. The flush should be administered at the same rate as used for Omvoh administration. The time required to flush Omvoh solution from the infusion line is in addition to the minimum 30 minutes infusion time.

Package leaflet: Information for the patient

Omvoh 100 mg solution for injection in pre-filled syringe

mirikizumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 Omvoh is and what it is used for

Omvoh contains the active substance mirikizumab, a monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind specifically to certain target proteins in the body. Omvoh works by attaching to and blocking a protein in the body called IL-23 (interleukin-23), which is involved in inflammation. By blocking the action of IL-23, Omvoh reduces inflammation and other symptoms associated with ulcerative colitis.

Ulcerative colitis is a chronic inflammatory disease of the large bowel. If you have ulcerative colitis, you will first be given other medicines. If you do not respond well enough or cannot tolerate these medicines, you may be given Omvoh to reduce signs and symptoms of ulcerative colitis such as diarrhoea, abdominal pain, urgency and rectal bleeding.

2. What you need to know before you use Omvoh

Do not use Omvoh
- if you are allergic to mirikizumab or any of the other ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice before using Omvoh.
- If you have important active infections (active tuberculosis).

Warnings and precautions
- Talk to your doctor or pharmacist before using this medicine.
- Your doctor will check how well you are before treatment.
- Make sure you tell your doctor about any illness you have before treatment.

Infections

- Omvoh can potentially cause serious infections. Treatment with Omvoh should not be started if you have an active infection until the infection is gone.
- After starting the treatment, tell your doctor right away if you have any symptoms of an infection such as:
    - fever
    - chills
    - muscle aches
    - cough
    - shortness of breath
    - runny nose
    - sore throat
    - pain during urination

- Also tell your doctor if you have recently been near anyone who might have tuberculosis.
- Your doctor will examine you and may do a test for tuberculosis before you have Omvoh.
- If your doctor thinks you are at risk of an active tuberculosis, you may be given medicines to treat it.

Vaccinations

Your doctor will check to see if you need any vaccinations before starting treatment. Tell your doctor, pharmacist or nurse if you have recently had or are going to have a vaccination. Some types of vaccines (live vaccines) should not be given while using Omvoh.

Allergic reactions

- Omvoh can potentially cause serious allergic reactions.
- Stop using Omvoh and get emergency medical help right away if you develop any of the following symptoms of a serious allergic reaction:
    - rash
    - fainting
    - dizziness
    - low blood pressure
    - swelling of the face, lips, mouth, tongue or throat, trouble breathing
    - sensation of throat tightening or chest tightness.

Liver blood test

Your doctor will conduct blood tests before starting and during treatment with Omvoh to check if your liver is functioning normally. If blood tests are abnormal, your doctor might interrupt therapy with Omvoh and do additional tests on your liver to determine the cause.

Children and adolescents

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

Other medicines and Omvoh

Tell your doctor, pharmacist or nurse

- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. Some types of vaccines (live vaccines) should not be given while using Omvoh.

Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before using this medicine. It is preferable to avoid the use of Omvoh in pregnancy. The effects of Omvoh in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and should use effective contraception while using Omvoh and for at least 10 weeks after the last Omvoh dose.

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

Driving and using machines
Omvoh is unlikely to influence your ability to drive and use machines.

Omvoh contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium -free".

3. How to use Omvoh

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

How much Omvoh is given and for how long
Your doctor will decide how much Omvoh you need and for how long. Omvoh is for long-term treatment. Your doctor or nurse will regularly monitor your condition to check that the treatment is having the desired effect.

- Treatment start: The first dose of Omvoh is 300 mg and will be given by your doctor by intravenous infusion (drip in a vein in your arm) over at least 30 minutes. After the first dose, you will receive another dose of Omvoh 300 mg 4 weeks later and again after an additional 4 weeks.
  If you do not have adequate therapeutic response after these 3 infusions, your doctor might consider continuing intravenous infusions at weeks 12, 16 and 20.

- Maintenance therapy: 4 weeks after the last intravenous infusion, a maintenance dose of Omvoh 200 mg will be given by an injection under the skin ('subcutaneously') and then every 4 weeks. The maintenance dose of 200 mg will be given by using 2 injections each containing 100 mg of Omvoh.
  If you lose response after receiving the maintenance dose of Omvoh, your doctor may decide to give you 3 doses of Omvoh by intravenous infusions.

  Your doctor or nurse will tell you when to switch to subcutaneous injections.
  During maintenance therapy you and your doctor or nurse should decide if you should inject Omvoh yourself after training in subcutaneous injection technique. It is important not to try to inject yourself until you have been trained by your doctor or nurse. Your doctor or nurse will offer the necessary training.
  A caregiver may also give you your Omvoh injection after proper training.
  Use a reminder method such as notes in a calendar or diary to help you remember when to take your next dose so that you avoid missing or repeating doses.

If you receive more Omvoh than you should
If you have received more Omvoh than you should or the dose has been given sooner than prescribed, inform your doctor.

If you forget to use Omvoh
If you have forgotten to inject a dose of Omvoh, inject as soon as possible. Thereafter, resume dosing every 4 weeks.

If you stop using Omvoh
You should not stop using Omvoh without speaking to your doctor first. If you stop treatment, symptoms of ulcerative colitis may come back.

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

4. Possible side effects

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

Common (may affect up to 1 in 10 people):
- Upper respiratory tract infections (nose and throat infections)
- Joint pain
- Headache
- Rash
- Injection site reactions (e.g. red skin, pain)

Uncommon (may affect up to 1 in 100 people):
- Shingles
- Infusion-related allergic reaction (e.g. itch, hives)
- Increase in the level of liver enzymes in your blood.

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 Omvoh

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

Do not use this medicine after the expiry date which is stated on the label and on the outer carton after "EXP". The expiry date refers to the last day of that month.

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

Do not microwave the syringes, run hot water over them, or leave them in direct sunlight.
Do not shake your pre-filled syringe.

Store in the original packaging in order to protect from light.
Omvoh may be stored unrefrigerated for up to 2 weeks at a temperature not above 30 ºC.
If these conditions are exceeded, Omvoh must be discarded.

Do not use this medicine if you notice that the pre-filled syringe is damaged, or the medicine is cloudy, distinctly brown, or has particles in it.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your doctor, nurse or 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 Omvoh contains
- The active substance is mirikizumab.
  Each pre-filled syringe contains 100 mg of mirikizumab in 1 mL solution.
- The other ingredients are sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections.

What Omvoh looks like and contents of the pack

Omvoh is a solution in a clear glass cartridge encased in a disposable, single-use syringe. Its colour may vary from colourless to slightly yellow.

Pack sizes of 2 or 6 pre-filled syringes. Not all pack sizes may be available in your country.

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This leaflet was last revised in

Other sources of information

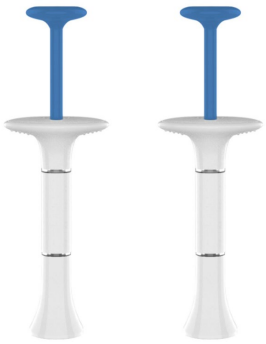
Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

Instructions for use

Omvoh 100 mg solution for injection in pre-filled syringe

mirikizumab

2 pre-filled syringes



Read this before you inject Omvoh. Follow all the step-by-step instructions.

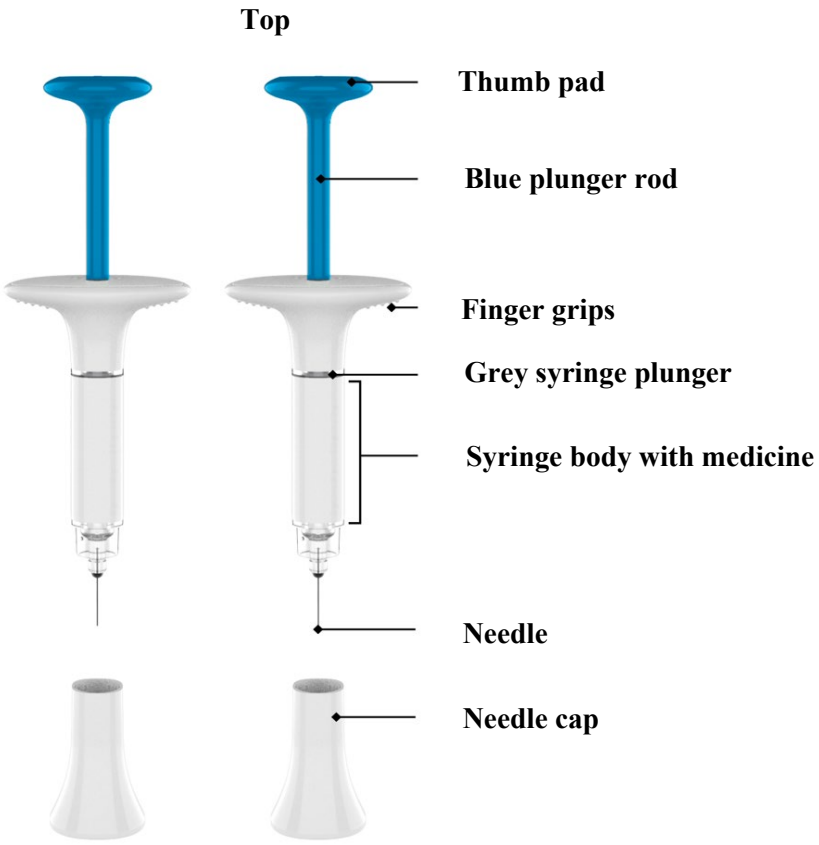
- **2 Omvoh injections are required for a full dose.**
- Inject 1 Omvoh pre-filled syringe followed right away by the other Omvoh pre-filled syringe.

Also keep in mind:

- Your healthcare provider should show you how to prepare and inject Omvoh using the pre-filled syringe. **Do not** inject yourself or someone else until you have been shown how to inject Omvoh.
- Each Omvoh pre-filled syringe is for one-time use only. Do not share or reuse your syringe. You may give or get an infection.
- Your healthcare provider may help you decide where on your body to inject your dose. You can also read the "Choose your injection site" section of these instructions to help you choose which area can work best for you.
- If you have vision problems, do not use Omvoh pre-filled syringe without help from a caregiver.
- Keep the Instructions for use and refer to them as needed.

Before you use the Omvoh pre-filled syringes, read and carefully follow all the step-by-step instructions.

Parts of the Omvoh pre-filled syringe



100 mg/mL + 100 mg/mL = 1 Full dose

IMPORTANT:

• 2 injections are required for a full dose.

• Inject 1 syringe followed right away by the other syringe.

Preparing to inject Omvoh

Take the syringes from the refrigerator

Take 2 syringes from the refrigerator.
Leave the needle caps on until you are ready to inject.
Leave the syringes at room temperature for 30 minutes before injecting.
Do not microwave the syringe, run hot water over them, or leave them in direct sunlight.
Do not use the syringes if the medicine is frozen.
Do not shake the syringes.

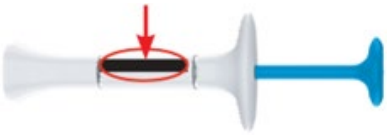
Gather supplies

Supplies:
• 2 alcohol wipes
• 2 cotton balls or pieces of gauze
• 1 sharps container (see "Disposing of Omvoh syringe")

Inspect the syringes and the medicine

Make sure you have the right medicine. The medicine inside should be clear. It may be colourless to slightly yellow.

Expiry date

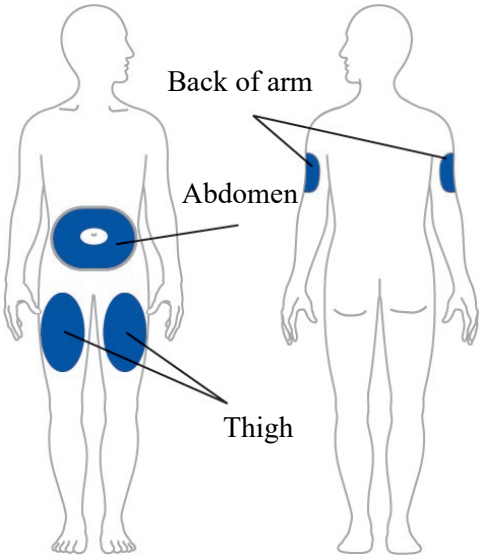


Do not use the syringe, and dispose of as directed by your healthcare provider if:
• it looks damaged
• the medicine is cloudy, is discoloured, or has particles
• the expiry date printed on the label has passed
• the medicine is frozen

Prepare for injection

Wash your hands with soap and water before you inject Omvoh.

Choose your injection site



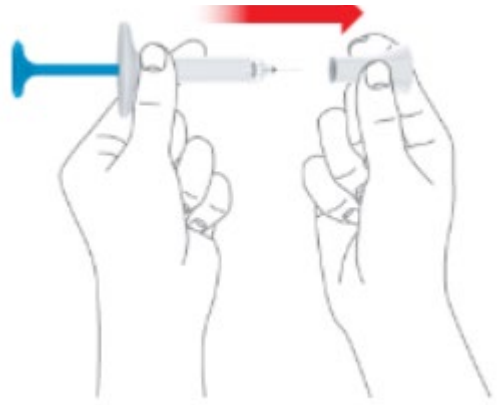
Your healthcare provider can help you choose the injection site that is best for you.

- **You or another person** may inject the medicine into your stomach area (abdomen). **Do not** inject within 5 centimetres of the belly button (navel).
- **You or another person** may inject the medicine in the front of your thighs. This area should be at least 5 centimetres above the knee and 5 centimetres below the groin.
- **Another person** may give you the injection in the back of your upper arm.
- **Do not** inject in the exact same spot every time. For example, if your first injection was in your abdomen, your second injection - to complete a full dose - could be in another spot in your abdomen.
- **Do not** inject into areas where the skin is tender, bruised, red or hard.

Clean the injection site with an alcohol wipe. Let the injection site dry before you inject your medicine.

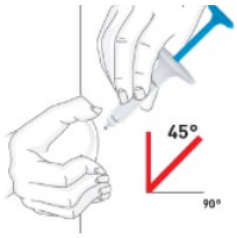
Injecting Omvoh

1 Uncap the syringe



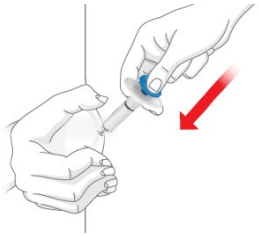
- **Leave the needle cap on until you are ready to inject.**
- Pull the needle cap off and throw it away in your household waste.
- **Do not** put the needle cap back on. You could damage the needle or stick yourself by accident.
- **Do not** touch the needle.

2 Insert

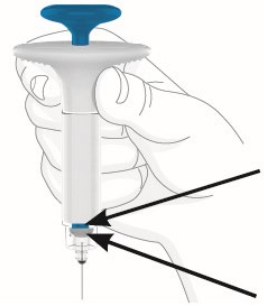


- Gently pinch and hold a fold of skin where you will inject.
- Insert the needle at a 45 degree angle

3 Inject



- Slowly push on the thumb pad to push the plunger all the way in until all the medicine is injected.
- The grey syringe plunger should be pushed all the way to the needle end of the syringe.



Blue plunger rod

Grey syringe plunger

- You should see the blue plunger rod show through the syringe body when the injection is complete as shown.
- Remove the needle from your skin and gently let go of your skin.
- If you have bleeding at the injection site, press a cotton ball or gauze over the injection site.
- **Do not** rub the injection site.
- **Do not** put the needle cap back on the pre-filled syringe.

2 injections are required for a full dose. Inject one syringe immediately followed by the other syringe.

Disposing of Omvoh syringe

Throw away the used syringe

- Put the used syringe in a sharps disposal container right away after use. Do not throw the syringe directly into your household waste.

- If you do not have a sharps disposal container, you may use a household container that is:

  – made of a heavy-duty plastic,
  – can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  – upright and stable during use,
  – leak-resistant,
  – properly labelled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be local laws about how you should throw away needles and syringes.

- Do not recycle your used sharps disposal container.

- For more information on how to dispose of the container properly, ask your healthcare provider about options available in your area.

Commonly asked questions

Q. What if I let my syringe warm up for longer than 30 minutes before injecting?
A. Your syringe can stay at room temperature up to 30 °C for up to 2 weeks.

Q. What if I see air bubbles in the syringe?
A. It is normal to have air bubbles in the syringe. They will not harm you or affect your dose.

Q. What if there is a drop of liquid on the tip of the needle when I remove the needle cap?
A. It is okay to see a drop of liquid on the tip of the needle. This will not harm you or affect your dose.

Q. What if I cannot push in the plunger?
A. If the plunger is stuck or damaged:
- **Do not** continue to use the syringe
- Remove the needle from your skin
- Do not use the syringe. Talk to your doctor or pharmacist to get a new one.

Q. What if there is a drop of liquid or blood on my skin after my injection?
A. This is normal. Press a cotton ball or gauze over the injection site. **Do not** rub the injection site.

Q. How can I tell if my injection is complete?
A. When your injection is complete:
- The blue plunger rod should show through the body of the syringe.
- The grey syringe plunger should be pushed all the way to the needle end of the syringe.

Read the full package leaflet for Omvoh inside this box to learn more about your medicine.

Last revised in

Package leaflet: Information for the patient

Omvoh 100 mg solution for injection in pre-filled pen

mirikizumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 Omvoh is and what it is used for

Omvoh contains the active substance mirikizumab, a monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind specifically to certain target proteins in the body. Omvoh works by attaching to and blocking a protein in the body called IL-23 (interleukin-23), which is involved in inflammation. By blocking the action of IL-23, Omvoh reduces inflammation and other symptoms associated with ulcerative colitis.

Ulcerative colitis is a chronic inflammatory disease of the large bowel. If you have ulcerative colitis, you will first be given other medicines. If you do not respond well enough or cannot tolerate these medicines, you may be given Omvoh to reduce signs and symptoms of ulcerative colitis such as diarrhoea, abdominal pain, urgency and rectal bleeding.

2. What you need to know before you use Omvoh

Do not use Omvoh
- if you are allergic to mirikizumab or any of the other ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice before using Omvoh.
- If you have important active infections (active tuberculosis).

Warnings and precautions
- Talk to your doctor or pharmacist before using this medicine.
- Your doctor will check how well you are before treatment.
- Make sure you tell your doctor about any illness you have before treatment.

Infections

- Omvoh can potentially cause serious infections. Treatment with Omvoh should not be started if you have an active infection until the infection is gone.
- After starting the treatment, tell your doctor right away if you have any symptoms of an infection such as:
    - fever
    - chills
    - muscle aches
    - cough
    - shortness of breath
    - runny nose
    - sore throat
    - pain during urination

- Also tell your doctor if you have recently been near anyone who might have tuberculosis.
- Your doctor will examine you and may do a test for tuberculosis before you have Omvoh.
- If your doctor thinks you are at risk of an active tuberculosis, you may be given medicines to treat it.

Vaccinations

Your doctor will check to see if you need any vaccinations before starting treatment. Tell your doctor, pharmacist or nurse if you have recently had or are going to have a vaccination. Some types of vaccines (live vaccines) should not be given while using Omvoh.

Allergic reactions

- Omvoh can potentially cause serious allergic reactions.
- Stop using Omvoh and get emergency medical help right away if you develop any of the following symptoms of a serious allergic reaction:
    - rash
    - fainting
    - dizziness
    - low blood pressure
    - swelling of the face, lips, mouth, tongue or throat, trouble breathing
    - sensation of throat tightening or chest tightness.

Liver blood test

Your doctor will conduct blood tests before starting and during treatment with Omvoh to check if your liver is functioning normally. If blood tests are abnormal, your doctor might interrupt therapy with Omvoh and do additional tests on your liver to determine the cause.

Children and adolescents

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

Other medicines and Omvoh

Tell your doctor, pharmacist or nurse

- if you are using, have recently used or might use any other medicines.
- if you have recently had or are going to have a vaccination. Some types of vaccines (live vaccines) should not be given while using Omvoh.

Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before using this medicine. It is preferable to avoid the use of Omvoh in pregnancy. The effects of Omvoh in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and should use effective contraception while using Omvoh and for at least 10 weeks after the last Omvoh dose.

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

Driving and using machines
Omvoh is unlikely to influence your ability to drive and use machines.

Omvoh contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium -free".

3. How to use Omvoh

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

How much Omvoh is given and for how long
Your doctor will decide how much Omvoh you need and for how long. Omvoh is for long-term treatment. Your doctor or nurse will regularly monitor your condition to check that the treatment is having the desired effect.

- Treatment start: The first dose of Omvoh is 300 mg and will be given by your doctor by intravenous infusion (drip in a vein in your arm) over at least 30 minutes. After the first dose, you will receive another dose of Omvoh 300 mg 4 weeks later and again after an additional 4 weeks.
  If you do not have adequate therapeutic response after these 3 infusions, your doctor might consider continuing intravenous infusions at weeks 12, 16 and 20.

- Maintenance therapy: 4 weeks after the last intravenous infusion, a maintenance dose of Omvoh 200 mg will be given by an injection under the skin ('subcutaneously') and then every 4 weeks. The maintenance dose of 200 mg will be given by using 2 injections each containing 100 mg of Omvoh.
  If you lose response after receiving the maintenance dose of Omvoh, your doctor may decide to give you 3 doses of Omvoh by intravenous infusions.

  Your doctor or nurse will tell you when to switch to subcutaneous injections.
  During maintenance therapy you and your doctor or nurse should decide if you should inject Omvoh yourself after training in subcutaneous injection technique. It is important not to try to inject yourself until you have been trained by your doctor or nurse. Your doctor or nurse will offer the necessary training.
  A caregiver may also give you your Omvoh injection after proper training.
  Use a reminder method such as notes in a calendar or diary to help you remember when to take your next dose so that you avoid missing or repeating doses.

If you receive more Omvoh than you should
If you have received more Omvoh than you should or the dose has been given sooner than prescribed, inform your doctor.

If you forget to use Omvoh
If you have forgotten to inject a dose of Omvoh, inject as soon as possible. Thereafter, resume dosing every 4 weeks.

If you stop using Omvoh
You should not stop using Omvoh without speaking to your doctor first. If you stop treatment, symptoms of ulcerative colitis may come back.

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

4. Possible side effects

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

Common (may affect up to 1 in 10 people):
- Upper respiratory tract infections (nose and throat infections)
- Joint pain
- Headache
- Rash
- Injection site reactions (e.g. red skin, pain)

Uncommon (may affect up to 1 in 100 people):
- Shingles
- Infusion-related allergic reaction (e.g. itch, hives)
- Increase in the level of liver enzymes in your blood.

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 Omvoh

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

Do not use this medicine after the expiry date which is stated on the label and on the outer carton after "EXP". The expiry date refers to the last day of that month.

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

Do not microwave the pens, run hot water over them, or leave them in direct sunlight.
Do not shake your pre-filled pen.

Store in the original packaging in order to protect from light.
Omvoh may be stored unrefrigerated for up to 2 weeks at a temperature not above 30 ºC.
If these conditions are exceeded, Omvoh must be discarded.

Do not use this medicine if you notice that the pre-filled pen is damaged, or the medicine is cloudy, distinctly brown, or has particles in it.

This medicine is for single use only.

Do not throw away any medicines via wastewater. Ask your doctor, nurse or 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 Omvoh contains
- The active substance is mirikizumab.
  Each pre-filled pen contains 100 mg of mirikizumab in 1 mL solution.
- The other ingredients are sodium citrate dihydrate; citric acid, anhydrous; sodium chloride; polysorbate 80; water for injections.

What Omvoh looks like and contents of the pack

Omvoh is a solution in a clear glass cartridge encased in a disposable, single-use pen. Its colour may vary from colourless to slightly yellow.

Pack sizes of 2, 4 or 6 pre-filled pens. Not all pack sizes may be available in your country.

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3528 BJ Utrecht
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Manufacturer
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Rue du Colonel Lilly
67640 Fegersheim
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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

Instructions for use

Omvoh 100 mg solution for injection in pre-filled pen

mirikizumab

2 pre-filled pens

Read this before you inject Omvoh. Follow all the step-by-step instructions.

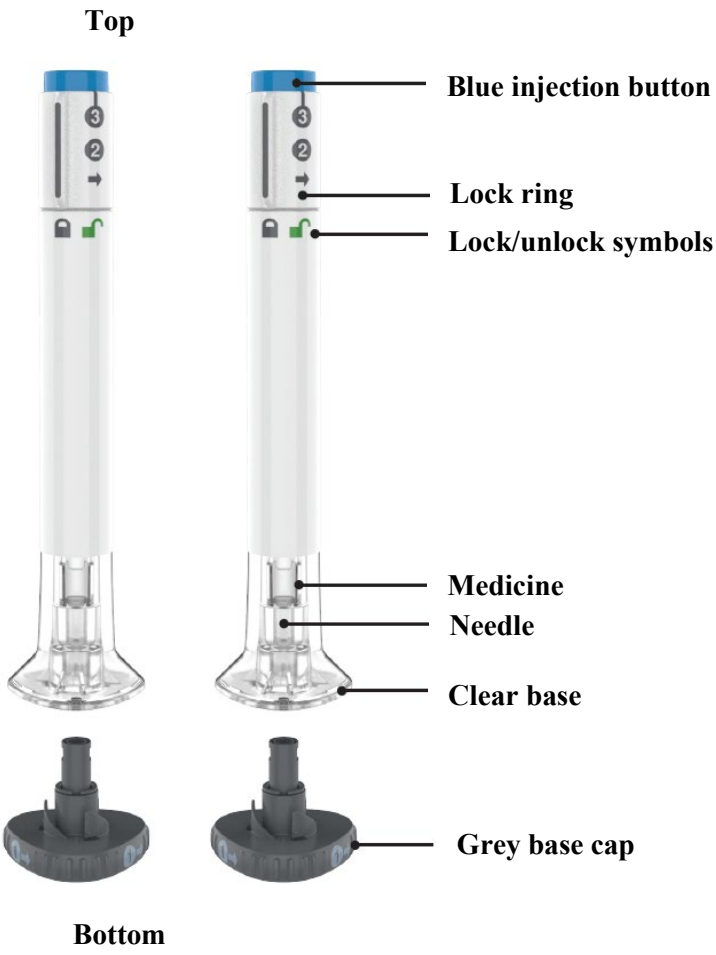
- **2 Omvoh injections are required for a full dose.**
- Inject 1 Omvoh pen followed right away by the other Omvoh pen.

Also keep in mind:

- Your healthcare provider should show you how to prepare and inject Omvoh using the pen. **Do not** inject yourself or someone else until you have been shown how to inject Omvoh.
- Each Omvoh pen is for one-time use only. Do not share or reuse your pen. You may give or get an infection.
- Your healthcare provider may help you decide where on your body to inject your dose. You can also read the "Choose your injection site" section of these instructions to help you choose which area can work best for you.
- If you have vision or hearing problems, do not use Omvoh pen without help from a caregiver.
- Keep the Instructions for use and refer to them as needed.

Before you use the Omvoh pens, read and carefully follow all the step-by-step instructions.

Parts of the Omvoh pen



100 mg/mL + 100 mg/mL = 1 Full dose

IMPORTANT:

• 2 injections are required for a full dose.

• Inject 1 pen followed right away by the other pen.

Preparing to inject Omvoh

Take the pens from the refrigerator

Take 2 Omvoh pens from the refrigerator.
Leave the grey base caps on until you are ready to inject.
Leave the pens at room temperature for 30 minutes before injecting.
Do not microwave the pens, run hot water over them, or leave them in direct sunlight.
Do not use the pens if the medicine is frozen.
Do not shake.

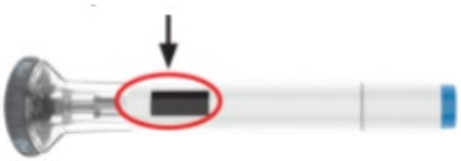
Gather supplies

Supplies:
• 2 alcohol wipes
• 2 cotton balls or pieces of gauze
• 1 sharps container (see "Disposing of Omvoh pens")

Inspect the pens and the medicine

Make sure you have the right medicine. The medicine inside should be clear. It may be colourless to slightly yellow.

Expiry date

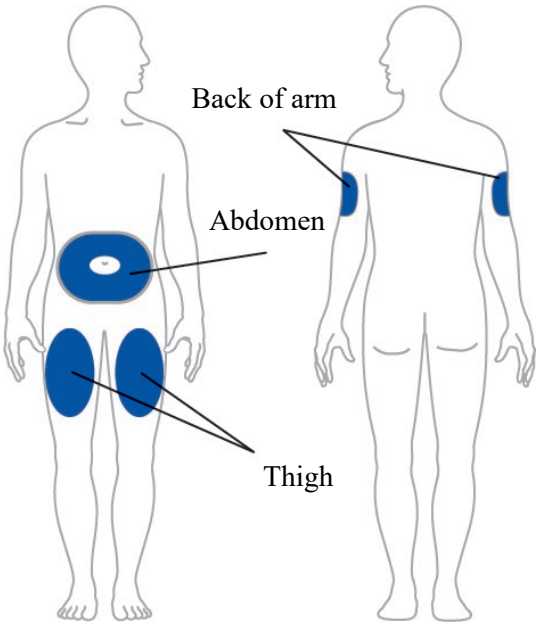


Do not use the pens, and dispose of as directed by your healthcare provider if:
• it looks damaged
• the medicine is cloudy, is discoloured, or has particles
• the expiry date printed on the label has passed
• the medicine is frozen

Prepare for injection

Wash your hands with soap and water before you inject Omvoh.

Choose your injection site



Your healthcare provider can help you choose the injection site that is best for you.

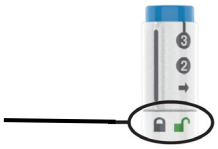
- **You or another person** may inject the medicine into your stomach area (abdomen). **Do not** inject within 5 centimetres of the belly button (navel).
- **You or another person** may inject the medicine in the front of your thighs. This area should be at least 5 centimetres above the knee and 5 centimetres below the groin.
- **Another person** may give you the injection in the back of your upper arm.
- **Do not** inject in the exact same spot every time. For example, if your first injection was in your abdomen, your second injection - to complete a full dose - could be in another spot in your abdomen.
- **Do not** inject into areas where the skin is tender, bruised, red or hard.

Clean the injection site with an alcohol wipe. Let the injection site dry before you inject your medicine.

Injecting Omvoh

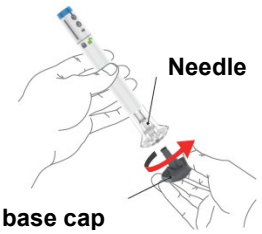
1 **Uncap the pen**

Make sure the pen is locked.



Leave the grey base cap on until you are ready to inject.

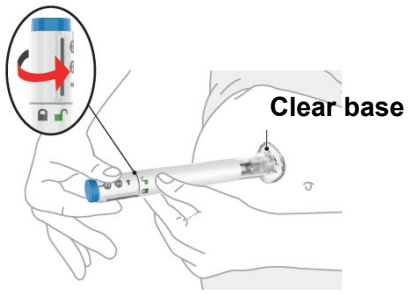
- Twist off the grey base cap and throw it away in your household waste.
- **Do not** put the grey base cap back on – this could damage the needle.
- **Do not** touch the needle.



2 **Place and Unlock**

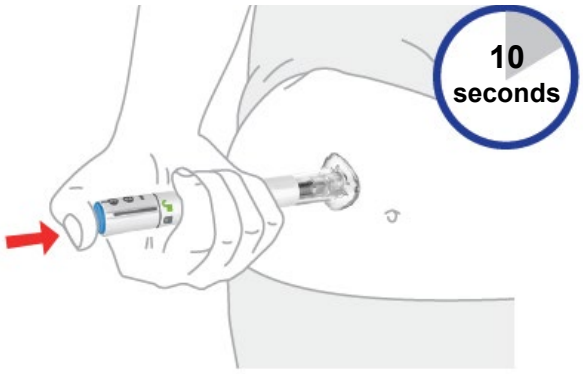
- Place and hold the clear base flat and firmly against your skin.

Keep the base on your skin and turn the lock ring to the **unlock** position.

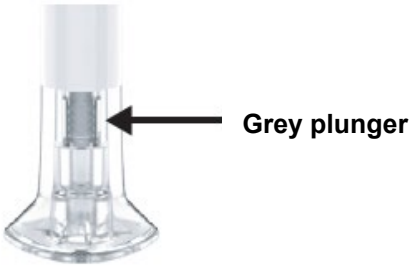


3 **Press and Hold for up to 10 Seconds**

- Press and hold the blue injection button. You will hear a loud click (injection started).
- **Keep holding the clear base firmly against your skin.** You will hear a second loud click in about 10 seconds after the first one (injection completed).



- You will know the injection is complete when the grey plunger is visible.
- Remove the pen from your skin.
- If you have bleeding at the injection site, press a cotton ball or gauze over the injection site.
- **Do not** rub the injection site.

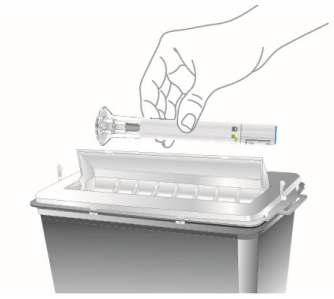


2 injections are required for a full dose. Inject one pen immediately followed by the other pen.

Disposing of Omvoh pens

Throw away the used pens

- Put the used pen in a sharps disposal container right away after use. Do not throw the pen directly into your household waste.



- If you do not have a sharps disposal container, you may use a household container that is:

  – made of a heavy-duty plastic,
  – can be closed with a tight fitting, puncture-resistant lid, without sharps being able to come out,
  – upright and stable during use,
  – leak-resistant,
  – properly labelled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be local laws about how you should throw away needles and syringes.

- Do not recycle your used sharps disposal container.

- For more information on how to dispose of the container properly, ask your healthcare provider about options available in your area.

Commonly asked questions

Q. What if I let my pens warm up for longer than 30 minutes before injecting?
A. Your pen can stay at room temperature up to 30 °C for up to 2 weeks.

Q. What if I see air bubbles in the pen?
A. It is normal to have air bubbles in the pen. They will not harm you or affect your dose.

Q. What if there is a drop of liquid on the tip of the needle when I remove the grey base cap?
A. It is okay to see a drop of liquid on the tip of the needle. This will not harm you or affect your dose.

Q. What if I unlocked the pen and pressed the blue injection button down until the injection is complete?
A. Do not remove the grey base cap. Do not use the pen. Talk to your doctor or pharmacist to get a new one.

Q. Do I need to hold the blue injection button down until the injection is complete?
A. You do not need to hold the blue injection button down, but it may help you keep the pen steady and firm against your skin.

Q. What if the needle did not retract after my injection?
A. Do not touch the needle or replace the grey base cap. Store the pen in a safe place to avoid an accidental needlestick and contact your doctor, pharmacist or nurse.

Q. What if there is a drop of liquid or blood on my skin after my injection?

A. This is normal. Press a cotton ball or gauze over the injection site. **Do not** rub the injection site.

Q. What if I heard more than 2 clicks during my injection – 2 loud clicks and a soft one. Did I get my complete injection?

A. Some patients may hear a soft click right before the second loud click. That is the normal operation of the pen. **Do not** remove the pen from your skin until you hear the second loud click.

Q. How can I tell if my injection is complete?

A. After you press the blue injection button, you will hear 2 loud clicks. The second loud click tells you that your injection is complete. You will also see the grey plunger at the top of the clear base.

Read the full package leaflet for Omvoh inside this box to learn more about your medicine.

Last revised in