PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrOMVOH™

mirikizumab injection

100 mg/mL solution for subcutaneous injection

mirikizumab for injection

20 mg/mL solution for intravenous infusion

Interleukin-23 (IL-23) p19 antagonist

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

OMVOH™ (mirikizumab) is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, loss of response, or were intolerant to conventional therapy, a biologic treatment, or a Janus kinase (JAK) inhibitor.

1.1 Pediatrics

Pediatrics (<18 years of age): Omvoh is not indicated in the pediatric population, as the efficacy and safety of Omvoh have not been evaluated in patients with moderately to severely active ulcerative colitis less than 18 years of age.

1.2 Geriatrics

Geriatrics (≥65 years of age): Limited data are available to Health Canada regarding this age group. Of the 1362 subjects with ulcerative colitis exposed to Omvoh in clinical trials, 99 subjects were 65 years or older, including 11 subjects who were 75 years or older (see 10.3 Pharmacokinetics).

2 CONTRAINDICATIONS

- Omvoh is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- With clinically important active infections (see 7 WARNINGS AND PRECAUTIONS, Infections).

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

Induction Dosing

The recommended induction dosage regimen of Omvoh is 300 mg infused intravenously for at least 30 minutes at Week 0, Week 4, and Week 8 (see 4.4 Administration, Preparation and Administration of Omvoh for Intravenous Infusion).

Only the 300 mg/15 mL Vial presentation of Omvoh should be used for Induction dosing.

Evaluate patients after the 12-week induction dosing, and if there is adequate therapeutic response, transition to maintenance dosing. If patients do not have adequate therapeutic response at Week 12 after induction dosing, consider extended induction dosing by administering 300 mg Omvoh by intravenous infusion at Weeks 12, 16, and 20 (see 14.1 Clinical Trials by Indication). If therapeutic response is achieved with the additional intravenous induction dosing, patients may initiate Omvoh subcutaneous maintenance dosing every 4 weeks. Discontinue Omvoh in patients who do not show evidence of therapeutic benefit to extended induction therapy by Week 24.

Maintenance Dosing

The recommended maintenance dosage regimen of Omvoh is 200 mg (given as two

consecutive subcutaneous injections of 100 mg each) every 4 weeks after completion of induction dosing (see 4.4 Administration, Administration of Omvoh solution for Subcutaneous Injection by Prefilled Pen or Prefilled Syringe).

Only the 100 mg/1 mL Prefilled Pen or Prefilled Syringe presentation of Omvoh should be used for Maintenance dosing.

Pediatrics (< 18 years of age)

Omvoh is not indicated in the pediatric population, as the efficacy and safety of Omvoh have not been evaluated in patients younger than 18 years.

Geriatrics (≥65 years of age)

Limited data are available to Health Canada regarding this age group. No dosage adjustment is required (see 1.2 Geriatrics and 10.3 Pharmacokinetics).

Renal or Hepatic Impairment

No specific studies were conducted to assess the effect of hepatic or renal impairment on the pharmacokinetics of Omvoh (see 10.3 Pharmacokinetics).

4.4 Administration

Preparation and Administration of Omvoh for Intravenous Infusion

Omvoh solution for intravenous infusion must be diluted, prepared and infused by a healthcare professional.

Dilution of Omvoh to prepare solution for infusion

- Each vial is for single use only.
- Prepare the infusion solution using aseptic technique to ensure the sterility of the prepared solution.
- Inspect the content of the vial. The solution should be a clear colourless to slightly yellow solution, and free of visible particles.
- Withdraw 15 mL from the Omvoh vial (300 mg) using an appropriately sized needle (18 to 21 gauge is recommended) and transfer to the infusion bag. Omvoh should be diluted only in intravenous infusion bags (bag size ranging from 50 - 250 mL) containing EITHER 0.9% sodium chloride solution for injection OR 5% dextrose solution for injection. Do not dilute the infusion solution with other solutions or co-infuse with other electrolytes or medications.
- Gently invert the infusion bag to mix the contents. Do NOT shake the prepared bag.

Administration of Omvoh solution for infusion

- Connect the intravenous administration set (infusion line) to the prepared infusion bag and prime the line. Administer the infusion 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 0.9% sodium chloride solution for injection or 5% dextrose solution for injection. The flush should be administered at the same infusion rate as used for Omvoh administration. The time required to flush Omvoh solution from the infusion line is in addition to the minimum 30-minute infusion time.

Storage

It is recommended to start the infusion immediately after preparation. If not used immediately,

store the diluted infusion solution in the refrigerator 2°C to 8°C. The diluted infusion solution must be used within 48 total hours, of which not more than 5 hours are permitted at nonrefrigerated temperatures not to exceed 25°C, starting from the time of vial puncture. Keep drug product away from direct heat or light. Do NOT freeze the diluted solution in the prepared infusion bag (see 11 STORAGE, STABILITY AND DISPOSAL).

Administration of Omvoh solution for Subcutaneous Injection by Prefilled Pen or Prefilled Syringe

- A full maintenance dose will require 2 prefilled pens or 2 prefilled syringes.
- Omvoh is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject Omvoh after training in subcutaneous injection technique. Provide proper training to patients and/or caregivers on the subcutaneous injection technique of Omvoh according to the “Instructions for Use”, included with the packaged product.
- Sites for injection include the abdomen, thigh, and back of the upper arm. Instruct patients to inject in a different injection site with each injection. For example, if the first injection was in the abdomen, the second injection - to complete a full dose - should be in another area of the abdomen, thigh, or back of upper arm. Rotate injection sites.
- Patients and/or caregivers can inject Omvoh into the abdomen and thigh. Only caregivers can inject Omvoh into the back of the upper arm.
- Do not inject into areas where the skin is tender, bruised, erythematous, or indurated.
- Before injection, remove Omvoh prefilled pen or Omvoh prefilled syringe from the refrigerator and leave at room temperature for 30 minutes.
- Inspect Omvoh visually for particulate matter and discolouration prior to administration. Do not use Omvoh if it is cloudy or there are visible particles.
- Omvoh is preservative-free, therefore discard any unused product. Do not reuse.

4.5 Missed Dose

Patients who miss their scheduled infusion should be advised to contact their healthcare professional and to schedule another appointment as soon as possible.

If a maintenance dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regularly scheduled time.

5 OVERDOSAGE

Mirikizumab doses up to 2400 mg intravenously and up to 500 mg subcutaneously have been administered in clinical trials without dose-limiting toxicity. In the event of overdosage, monitor the patient for signs or symptoms of adverse reactions and start appropriate symptomatic treatment immediately.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 - Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous infusion	Solution for intravenous infusion after dilution 20 mg/mL 300 mg/15 mL Vial	citric acid anhydrous, polysorbate 80, sodium chloride, sodium citrate dihydrate, and water for injection
Subcutaneous injection	Solution for injection 100 mg/mL 100 mg/1 mL Syringe	citric acid anhydrous, polysorbate 80, sodium chloride, sodium citrate dihydrate, and water for injection

Omvoh for Intravenous Infusion

Omvoh solution for intravenous infusion after dilution is available as 15 mL solution in a type I glass vial. Omvoh is preservative-free; therefore, each vial is for single use only.

The vial is not made with dry natural rubber latex.

Omvoh 300 mg/15 mL is available in cartons containing 1 vial.

Omvoh Prefilled Pens and Prefilled Syringes

Omvoh prefilled pens and prefilled syringes each contain a 1 mL glass syringe with a fixed 27-gauge ½ inch needle. Omvoh is preservative-free; therefore, each prefilled pen or prefilled syringe is for single use only.

The prefilled pen and prefilled syringe are not made with dry natural rubber latex.

Omvoh 100 mg/mL is available in cartons containing 2 prefilled pens or 2 prefilled syringes.

7 WARNINGS AND PRECAUTIONS

General

Infections

Omvoh may increase the risk of infection. Treatment with Omvoh should not be initiated in patients with any clinically important active infection (including, but not limited to, sepsis, hepatitis B, hepatitis C, HIV/AIDS, and active tuberculosis (TB)). Prior to initiating treatment, patients should be evaluated for active infections. Consider the risks and benefits of treatment prior to initiating use of Omvoh in patients with a chronic infection or a history of recurrent infection. Instruct patients to seek immediate medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops, consider discontinuation of Omvoh until the infection resolves.

No safety data are available in patients with HIV, hepatitis B or hepatitis C. Patients who screened positive for any of these infections were excluded from the clinical trials.

Tuberculosis

Omvoh should not be given to patients with active tuberculosis (TB). Evaluate patients for TB prior to initiating treatment with Omvoh. Consider anti-TB therapy prior to initiation of Omvoh in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving Omvoh should be monitored closely for signs and symptoms of active TB during and after treatment.

Hepatic/Biliary/Pancreatic

Hepatic Enzyme Elevation

Elevations of aminotransferases have been reported in patients receiving Omvoh. Evaluate liver enzymes and bilirubin at baseline and every 1-4 months during induction (including extended induction period, if applicable) and thereafter, 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-associated liver injury is suspected, discontinue Omvoh until this diagnosis is excluded (see 8.2 Clinical Trial Adverse Reactions).

Immune

Vaccinations

Prior to initiating therapy with Omvoh, consider completion of all immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with Omvoh. If necessary, live vaccines should be administered at least 4 weeks before initiating Omvoh treatment.

Reproductive Health: Female and Male Potential

- **Fertility**

  The effect of Omvoh on human fertility has not been studied. In addition, no dedicated fertility studies have been conducted in animals (see 16 NON-CLINICAL TOXICOLOGY).

Sensitivity/Resistance

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, may occur with Omvoh administration. If serious hypersensitivity reactions occur, discontinue Omvoh immediately and initiate appropriate treatment (see 8 ADVERSE REACTIONS).

7.1 Special Populations

7.1.1 Pregnant Women

The use of Omvoh in pregnant women has not been studied. Women of childbearing potential should use effective contraception during treatment and for a minimum of 12 weeks after the last administration. A developmental toxicity study in pregnant monkeys revealed no evidence of harm to the developing fetus or infant (see 16 NON-CLINICAL TOXICOLOGY). However, animal studies are not always predictive of human response; therefore, it is unknown whether Omvoh can cause fetal harm when administered to a pregnant woman.

7.1.2 Breast-feeding

There are no data on the presence of Omvoh in human milk, the effects on the breastfed infant, or the effects on milk production. Because human immunoglobulin G (IgG) is secreted into human milk, precaution should be exercised. The developmental and health benefits of breast-feeding should be considered, as well as any potential adverse effects on the breastfed infant.

7.1.3 Pediatrics

Pediatrics (< 18 years of age): Omvoh is not indicated in the pediatric population, as the efficacy and safety of Omvoh have not been evaluated in patients less than 18 years of age.

7.1.4 Geriatrics

Of the 1362 subjects with ulcerative colitis exposed to Omvoh in Phase 2 and Phase 3 studies, 99 subjects were 65 years or older and 11 subjects were 75 years or older. Thus, data in these age groups are limited.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most frequently reported adverse reactions were injection site reactions (8.7%, maintenance period), upper respiratory tract infections (7.9%, frequently nasopharyngitis), headache (3.3%), arthralgia (2.1%), and rash (1.1%) (see Table 2).

The proportion of patients treated with Omvoh who discontinued treatment due to adverse events was 1.8% (7/389).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction frequencies observed in the clinical trials; therefore, may not reflect the frequencies observed in practice and should not be compared to the frequencies in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating frequencies of adverse drug reactions in real-world use.

A total of 1442 subjects were treated with Omvoh in clinical development trials in UC.

In these trials, exposure to Omvoh in 1442 adult ulcerative colitis patients included 1208 exposed for at least 6 months, 926 exposed for at least one year, and 450 exposed for at least 2 years.

Clinical trials excluded patients who had an unstable or uncontrolled illness, including, but not limited to cerebrovascular, cardiovascular, respiratory, gastrointestinal (excluding UC), hepatic, renal, endocrine, hematologic or neurological disorders.

Table 2 summarizes the adverse drug reactions that occurred at a frequency of at least 1% in the Omvoh-treated patients and higher than the placebo group during the 12-week controlled period of LUCENT 1.

Table 2 - Adverse Drug Reactions through Week 12 from LUCENT-1 and through Week 40 from LUCENT-2 occurring in ≥1% of Omvoh-treated patients and higher than placebo

Adverse Drug Reactions in LUCENT-1	OMVOH 300 mg IV at Weeks 0, 4, and 8 N = 958 n (%)	Placebo N = 321 n (%)
Infections and infestations		
Upper respiratory tract infections[a]	76 (7.9)	19 (5.9)
Nervous system disorders		
Headache	32 (3.3)	9 (2.8)
Musculoskeletal disorders		
Arthralgia	20 (2.1)	4 (1.2)
Skin and subcutaneous tissue disorders		
Rash[b]	11 (1.1)	2 (0.6)
Adverse Drug Reactions in LUCENT-2	**OMVOH 200 mg SC Q4W N = 389 N (%)**	**Placebo N = 192 N (%)**
Infections and infestations		
Upper respiratory tract infections[a]	46 (11.8)	19 (9.9)
General disorders and administration site conditions		
Injection site reactions (HLT)[c]	34 (8.7)	8 (4.2)
Musculoskeletal disorders		
Arthralgia	26 (6.7)	8 (4.2)
Nervous system disorders		
Headache	16 (4.1)	2 (1.0)
Skin and subcutaneous tissue disorders		
Rash[b]	16 (4.1)	1 (0.5)

[a] Upper respiratory tract infections contains the preferred terms: acute sinusitis, nasopharyngitis, oropharyngeal discomfort, oropharyngeal pain, pharyngitis, rhinitis, sinusitis, tonsillitis, upper respiratory tract infection, and viral upper respiratory tract infection.

[b] Rash contains the preferred terms: rash, rash macular, rash maculo-papular, rash papular, and rash pruritic.

[c] Injection site reactions contains the preferred terms: injection site pain, injection site reaction, injection site erythema, injection site bruising, injection site pruritus, injection site dermatitis, injection site hematoma, injection site hypersensitivity, injection site oedema, injection site paraesthesia, injection site rash, injection site urticaria.

In the first 12 weeks (LUCENT-1), infusion-related hypersensitivity reactions were reported by 4 (0.4%) Omvoh-treated patients compared to 1 (0.3%) patient in the placebo group.

Increases in alanine aminotransferase (ALT) were reported by 4 (0.4%) Omvoh-treated patients compared to 1 (0.3%) in the placebo group. Increases in aspartate aminotransferase (AST) were reported by 5 (0.5%) Omvoh-treated patients compared to 1 (0.3%) in the placebo group.

Safety in LUCENT-2 (Weeks 12 - 52)

Injection site reactions were reported by 8.7% Omvoh-treated patients compared to 4.2% patients in the placebo group. The most frequently reported events were injection site pain,

injection site reaction, and injection site erythema.

Through Week 52, with the exception of injection site reactions, adverse drug reaction data were consistent with data observed in induction study LUCENT-1.

Hepatic Enzyme Elevations

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

Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity with Omvoh. Immunogenicity tests are generally product-specific and are highly dependent on the sensitivity and specificity of the assay. Comparison of incidence of antibodies between products by different tests may be misleading.

By Week 52, 23% (88/378) of subjects treated with Omvoh at the recommended dose developed antibodies to mirikizumab. Of the 88 subjects who developed antibodies to mirikizumab, 82 subjects (93.1%) had antibodies that were characterized as neutralizing. The antibody titers detected in Omvoh-treated subjects were mostly low. Higher antibody titers (≥ 1:160) were detected in approximately 9% of subjects treated with Omvoh, and these ADA titers were associated with lower serum mirikizumab concentrations and reduced clinical response in 2% of subjects treated with Omvoh.

No association was found between anti-mirikizumab antibodies and hypersensitivity or injection-related events.

8.3 Less Common Clinical Trial Adverse Reactions

Adverse drug reactions from LUCENT-1 and LUCENT-2 occurring in <1% of Omvoh-treated patients:
Immune system disorders: infusion-related hypersensitivity reaction (LUCENT-1, weeks 1-12)
Hepatic and hepatobiliary disorders: alanine aminotransferase increased; aspartate aminotransferase increased

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Specific drug interaction studies have not been conducted in ulcerative colitis patients with Omvoh.

Population pharmacokinetic data analyses indicated that the clearance of Omvoh was not impacted by concomitant administration of Aminosalicyclic acid (5ASAs), corticosteroids or oral immunomodulators (6-mercaptopurine, azathioprine, methotrexate, tioguanine) in patients with ulcerative colitis.

9.4 Drug-Drug Interactions

Live Vaccines

Avoid use of live vaccines in patients treated with Omvoh (see 7 WARNINGS AND PRECAUTIONS, Immune).

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Mirikizumab is a humanized IgG4 monoclonal antibody that binds with high affinity and specificity to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor. It has no observed cross-reactivity to other members of the IL-12 cytokine family (that is, IL-12, IL-27, and IL-35).

IL-23 is a naturally occurring cytokine that 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, that drive inflammatory disease.

10.2 Pharmacodynamics

No formal Pharmacodynamic studies have been performed with mirikizumab.

10.3 Pharmacokinetics

Mirikizumab exhibited linear pharmacokinetics with a dose-proportional increase in exposure over a dose range of 5 to 2400 mg given as an intravenous injection or over a dose range of 120 to 400 mg given as a subcutaneous injection, in patients with ulcerative colitis or in healthy volunteers. There was no apparent accumulation in serum mirikizumab concentration over time when given intravenously or subcutaneously every 4 weeks.

Table 3 - Summary of mirikizumab Pharmacokinetic Parameters in adult patients with Ulcerative Colitis[a]

	$C_{max, ss}$ µg/mL	$t_{½}$ days	$AUC_{tau, ss}$ µg*day/mL	CL L/hr	V L	CL/F L/hr	V/F L
Induction (300 mg every 4 weeks administered by intravenous infusion)	99.7 (23%)	9.3 (40%)	538 (34%)	0.0229 (34%)	4.83 (21%)	--	--

	$C_{max, ss}$ µg/mL	$t_{½}$ days	$AUC_{tau, ss}$ µg*day/mL	CL L/hr	V L	CL/F L/hr	V/F L
Maintenance (200 mg every 4 weeks administered by subcutaneous injection)	10.1 (52%)	9.3 (40%)	160 (58%)	--	--	0.0487 (54%)	11.1 (42%)

[a] Abbreviations: $AUC_{tau, ss}$ = area under concentration-time curve at a dosing interval at steady state; $C_{max, ss}$ = peak concentration at steady state; CL = clearance; CL/F= apparent clearance; V= volume of distribution; V/F=apparent volume of distribution; $t_{1/2}$ = half life.

Parameter estimates following intravenous and subcutaneous administration are based on population PK analysis using data from phase 3 induction and maintenance study, respectively. Parameter estimates were reported as geometric mean (% coefficient variation).

Absorption

Following subcutaneous dosing of mirikizumab, peak serum concentrations were achieved approximately 3 days post dose. The absolute bioavailability was estimated to be 44% based on population PK modeling.

Injection site location had no clinically meaningful effect on mirikizumab exposure.

Distribution:

The mean total volume of distribution of mirikizumab was 4.83 L.

Metabolism:

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

Elimination

Based on population pharmacokinetic analysis, the mean systemic clearance of mirikizumab was 0.0229 L/hr and the mean half-life was 9.3 days in patients with ulcerative colitis. Clearance was independent of dose.

Special Populations and Conditions

- **Pediatrics**

  The pharmacokinetics of mirikizumab in pediatric patients has not been evaluated.

- **Geriatrics**

  Of the 1362 subjects with ulcerative colitis exposed to mirikizumab in Phase 2 and Phase 3 studies, 99 subjects were 65 years or older and 11 subjects were 75 years or older. Population pharmacokinetic analysis showed no overall differences in mirikizumab exposure between older and younger subjects.

- **Sex**

  Population pharmacokinetic analysis showed that sex did not have a significant effect on the pharmacokinetics of mirikizumab.

- **Ethnic Origin**

Population pharmacokinetic analysis showed that race/ethnicity did not have a significant effect on the pharmacokinetics of mirikizumab.

- **Hepatic Insufficiency**

  Specific clinical pharmacology studies to evaluate the effects of hepatic impairment on the pharmacokinetics of mirikizumab have not been conducted.

  Population pharmacokinetic analysis showed that total bilirubin (range of 1.5 to 29 µmol/L) was not identified as a clinically relevant covariate on mirikizumab pharmacokinetics.

- **Renal Insufficiency**

  Specific clinical pharmacology studies to evaluate the effects of renal 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) was not identified as a clinically relevant covariate on mirikizumab pharmacokinetics.

- **Obesity**

  Population pharmacokinetic analysis showed that weight was a covariate on mirikizumab exposure; however no clinically meaningful effects of weight were observed.

11 STORAGE, STABILITY AND DISPOSAL

- Store refrigerated at 2°C to 8°C.
- Do NOT freeze. Do not use Omvoh if it has been frozen.
- Do NOT shake.
- Keep Omvoh in the original carton to protect from light until the time of use.
- If needed, the prefilled syringe or prefilled pen may be stored outside of refrigeration at not more than 30°C for up to 2 weeks in the original carton to protect from light. Once Omvoh has been stored at room temperature, do not return to the refrigerator. If these conditions are exceeded, Omvoh must be discarded.

12 SPECIAL HANDLING INSTRUCTIONS

Omvoh is sterile and preservative-free. Discard any unused portion.

The prefilled syringe and prefilled pen should be disposed of in a puncture-resistant container for syringes and needles. Patients or caregivers should be instructed in the technique as well as proper syringe and needle disposal, and not to reuse these items.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	mirikizumab
Chemical name:	Immunoglobulin G4, anti-(human interleukin 23 p19 subunit) (human monoclonal LY3074828 γ4-chain), disulfide with human monoclonal LY3074828 κ-chain, dimer
Molecular formula:	$C_{6380}H_{9842}N_{1686}O_{2004}S_{48}$ (protein backbone without pyroglutamation, tetramer)
Molecular mass:	The overall molecular weight is approximately 147 kDa
Structural formula:	Mirikizumab is a humanized immunoglobulin G4 (IgG4) isotype monoclonal antibody composed of two identical immunoglobulin kappa light chains and two identical immunoglobulin gamma heavy chains.
Physicochemical properties:	Mirikizumab is clear to opalescent, colorless to slightly yellow to slightly brown solution.

Product Characteristics:

Mirikizumab drug substance manufacture begins with the thawing of the working cell bank, that is scaled-up prior to seeding a production bioreactor. The culture is harvested, clarified, and purified via a downstream purification process. Mirikizumab drug product is formulated, sterile filtered and filled into vials or syringes prior to final packaging.

Mirikizumab for Injection, 300 mg/15 mL is supplied as a sterile, non-pyrogenic, preservative-free solution in a 20-mL glass vial intended for single use. The mirikizumab drug product is diluted with 0.9% Sodium Chloride Injection or 5% Dextrose Injection prior to administration by intravenous infusion.

Mirikizumab Injection, 100 mg/mL is supplied as a 100 mg/mL prefilled syringe and prefilled pen, non-pyrogenic parenteral solution for subcutaneous administration, intended for single use.

The prefilled pen and prefilled syringe each contain a 1 mL-long, clear, Type I glass syringe barrel with small round flange, 27G special thin wall x 1/2" staked needle, and closed with a barrier film laminated elastomeric plunger.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Ulcerative Colitis

The efficacy and safety of Omvoh in adult subjects with moderately to severely active ulcerative colitis was evaluated in two multicentre, randomized, double-blind, placebo-controlled clinical studies (LUCENT-1 and LUCENT-2). LUCENT-1 was a 12-week induction phase study that evaluated the ability of Omvoh administered by intravenous (IV) injection to achieve clinical remission. LUCENT-2 was a subsequent 40-week withdrawal maintenance phase study

(52 weeks of continuous treatment) that evaluated the ability of Omvoh administered by subcutaneous (SC) injection to achieve clinical remission in subjects who achieved clinical response after 12 weeks of Omvoh treatment in the induction study. All subjects had previously had an inadequate response, loss of response, or failed to tolerate corticosteroids, immunomodulators (i.e., 6-mercaptopurine, azathioprine), biologic therapy (i.e., TNF blocker, vedolizumab), or a Janus Kinase inhibitor (i.e., tofacitinib).

Enrolled subjects were 18 years of age or older with a modified Mayo score (mMS) ≥4 including an endoscopy subscore (ES) ≥2. The mMS is a composite endpoint scored from 0 (normal) to 9 (most severe) consisting of three subscores each scored from 0 (normal) to 3 (most severe), including stool frequency, rectal bleeding, and findings on centrally read endoscopy. An ES of 2 was defined by marked erythema, absent vascular pattern, friability, and erosions; an ES of 3 was defined by spontaneous bleeding and ulceration.

Table 4 - Summary of subject demographics for clinical trials in ulcerative colitis

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex n (%)
LUCENT-1 (Induction)	Multicentre, double-blinded, randomized, placebo-controlled	Placebo IV at Weeks 0, 4 and 8	294	42.5 years (18-79)	Male 695 (59.8%)
		Mirikizumab 300 mg IV at Weeks 0, 4 and 8	868		Female 467 (40.2%)
LUCENT-2 (Maintenance)	Multicentre, double-blinded, randomized, placebo-controlled	Placebo SC Q4W	179	42.7 years (18-79)	Male 318 (58.5%)
		Mirikizumab 200 mg SC Q4W	365		Female 226 (41.5%)

IV = intravenous; SC = subcutaneous; Q4W = every 4 weeks.

Induction Phase Study: LUCENT-1

In LUCENT-1, 1162 subjects were randomized 3:1 to receive 300 mg Omvoh or placebo by intravenous infusion at Week 0, Week 4, and Week 8. Randomization was stratified by (a) biologic-failed status (yes/no), (b) baseline corticosteroid use (yes/no), (c) baseline disease activity (mMS: [4-6, moderate] or [7-9, severe]), and (d) region (North America/Europe/Other). Subjects who were on concomitant ulcerative colitis therapies prior to enrollment continued on stable doses during the study, including 39.9% of subjects receiving oral corticosteroids, 24.1% receiving immunomodulators and 74.3% receiving aminosalicylates.

At baseline, 57.1% of subjects were biologic and Janus Kinase inhibitor (JAKi) naive, 41.0% had failed at least one biologic and 3.4% had failed a JAKi. An additional 1.7% had previously received but had not failed a biologic or JAKi.

Subjects had a median mMS of 7.0 and 53.2% had severely active disease (mMS ≥7).

The primary efficacy endpoint was the proportion of subjects in clinical remission at Week 12. Key secondary endpoints included the proportion of subjects in clinical response, endoscopic improvement, and histologic-endoscopic mucosal improvement.

Study Results

The results of the primary and key secondary endpoints are shown in Table 5.

Table 5 - Proportion of Patients Meeting Efficacy Endpoints at Week 12 in LUCENT-1[a]

	Placebo N=294		OMVOH N=868		Treatment difference and 99.875% CI[b]
	N	%	N	%	
Primary endpoint					
Clinical remission[c], Week 12	39	13.3%	210	24.2%	11.1% (3.2%, 19.1%)[d]
Biologic and JAKi naive[e]	27/171	15.8%	152/492	30.9%	
Prior biologic or JAKi failed[f]	10/118	8.5%	55/361	15.2%	
Key secondary endpoints					
Clinical response[g], Week 12	124	42.2%	551	63.5%	21.4% (10.8%, 32.0%)[d]
Biologic and JAKi naive[e]	86/171	50.3%	345/492	70.1%	
Prior biologic or JAKi failed[f]	35/118	29.7%	197/361	54.6%	
Endoscopic improvement[h], Week 12	62	21.1%	315	36.3%	15.4% (6.3%, 24.5%)[d]
Biologic and JAKi naive[e]	48/171	28.1%	226/492	45.9%	
Prior biologic or JAKi failed[f]	12/118	10.2%	85/361	23.5%	
Histologic-endoscopic mucosal improvement[i], Week 12	41	13.9%	235	27.1%	13.4% (5.5%, 21.4%)[d]
Biologic and JAKi naive[e]	32/171	18.7%	176/492	35.8%	
Prior biologic or JAKi failed[f]	8/118	6.8%	56/361	15.5%	

[a] Abbreviations: CI = confidence interval; ES = endoscopic subscore; IV = intravenous; MMS = modified Mayo score; RB = rectal bleeding; SF = stool frequency; UC = ulcerative colitis.
[b] Treatment difference (99.875% CI) adjusted for randomization stratification factors.
[c] Clinical remission is based on the MMS defined as an SF subscore = 0, or an SF subscore = 1 with a ≥1-point decrease from baseline; and an RB subscore = 0; and an ES = 0 or 1 (excluding friability).
[d] p<0.00125 based on the Cochran-Mantel-Haenszel chi-square test adjusted for randomization stratification factors. Non-responder imputation was used to impute missing data.
[e] An additional 5 patients on placebo and 15 patients on Omvoh were previously exposed to but did not fail a biologic or JAKi.
[f] Prior biologic or JAKi failed is defined as loss of response, inadequate response or intolerance to biologic therapy (TNF blocker or vedolizumab), or tofacitinib.
[g] Clinical response is defined as a decrease in the MMS of ≥2 points with ≥30% decrease from baseline, and either a decrease of ≥1 point in the RB subscore from baseline or an RB subscore of 0 or 1.
[h] Endoscopic improvement is defined as an ES = 0 (normal or inactive disease) or 1 (erythema, decreased vascular pattern), excluding friability.
[i] Histologic-endoscopic mucosal improvement is defined as achieving both endoscopic improvement (ES = 0 or 1, excluding friability) and histologic improvement (Geboes scoring system with neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue).

Symptomatic Remission Subscore

Symptomatic remission (defined as a rectal bleeding subscore = 0 and a stool frequency subscore = 0 or a stool frequency subscore = 1 with a ≥1 point decrease from baseline) was

observed at Week 12 in 45.5% of subjects receiving Omvoh and 27.9% of subjects receiving placebo. Symptomatic remission was observed at Week 4 in 21.8% of subjects receiving Omvoh and 12.9% of subjects receiving placebo.

Maintenance Phase Study: LUCENT-2

LUCENT-2 was a randomized withdrawal maintenance study in which 544 subjects who received Omvoh and achieved clinical response at Week 12 in study LUCENT-1 were randomized 2:1 to receive 200 mg Omvoh or placebo subcutaneously every 4 weeks for 40 weeks (i.e., 52 weeks of continuous treatment in LUCENT-1 and LUCENT-2 in total). Randomization was stratified by (a) biologic-failed status (yes/no), (b) baseline corticosteroid use (yes/no), (c) baseline disease activity (mMS: [4-6, moderate] or [7-9, severe]), and (d) region (North America/Europe/Other). Subjects who were on concomitant ulcerative colitis therapies during LUCENT-1 were required to continue on stable doses during the study; subjects who were receiving corticosteroids at LUCENT-1 baseline and who achieved clinical response in study LUCENT-1 required corticosteroid tapering at start of LUCENT-2.

The primary endpoint was the proportion of subjects in clinical remission at Week 40 (52 weeks of continuous treatment in LUCENT-1 and LUCENT-2). Key secondary endpoints included the proportion of subjects achieving endoscopic improvement, histo-endoscopic mucosal remission, corticosteroid-free clinical remission without surgery, and bowel urgency response at Week 40. An additional key secondary endpoint was maintenance of clinical remission at Week 40 of LUCENT-2 among subjects who achieved clinical remission at Week 12 in LUCENT-1.

Study Results

The results of primary and key secondary endpoints are provided in Table 6.

Table 6- Proportion of Patients Meeting Efficacy Endpoints in LUCENT-2 at Week 40 (52 weeks of continuous treatment)[a]

	Placebo[b] SC every 4 weeks N=179		OMVOH SC 200 mg every 4 weeks N=365		Treatment difference and 95% CI[c]
	N	%	N	%	
Primary endpoint					
Clinical remission[d, e]	45	25.1%	182	49.9%	23.2% (15.2%, 31.2%)[f]
Biologic and JAKi naive[g]	35/114	30.7%	118/229	51.5%	
Prior biologic or JAKi failed[h]	10/64	15.6%	59/128	46.1%	
Key secondary endpoints					
Endoscopic improvement[d, i]	52	29.1%	214	58.6%	28.5% (20.2%, 36.8%)[f]
Biologic and JAKi naive[g]	39/114	34.2%	143/229	62.4%	
Prior biologic or JAKi failed[h]	13/64	20.3%	65/128	50.8%	
Maintenance of clinical remission[e, j]	24/65	36.9%	91/143	63.6%	24.8% (10.4%, 39.2%)[f]
Biologic and JAKi naive[g]	22/47	46.8%	65/104	62.5%	
Prior biologic or JAKi failed[h]	2/18	11.1%	24/36	66.7%	
Corticosteroid-free remission[d, k]	39	21.8%	164	44.9%	21.3%

					(13.5%, 29.1%)[f]
Biologic and JAKi naive[g]	30/114	26.3%	107/229	46.7%	
Prior biologic or JAKi failed[h]	9/64	14.1%	52/128	40.6%	
Histo-endoscopic mucosal remission[d, l]	39	21.8%	158	43.3%	19.9% (12.1%, 27.6%)[f]
Biologic and JAKi naive[g]	30/114	26.3%	108/229	47.2%	
Prior biologic or JAKi failed[h]	9/64	14.1%	46/128	35.9%	
Bowel urgency response[m]	43/172	25.0%	144/336	42.9%	18.1 (9.8%, 26.4%)[f]
Biologic and JAKi naive[g]	31/108	28.7%	96/206	46.6%	
Prior biologic or JAKi failed[h]	12/63	19.0%	43/122	35.2%	

[a] Abbreviations: CI = confidence interval; ES = endoscopic subscore; MMS = modified Mayo score; RB = rectal bleeding; SC = subcutaneous; SF = stool frequency.
[b] The placebo arm includes those patients who received Omvoh during the induction study (LUCENT-1) and were randomized to receive placebo through Week 40.
[c] Treatment difference (95% CI) adjusted for randomization stratification factors.
[d] Among patients who achieved clinical response with Omvoh induction treatment.
[e] Clinical remission is based on the MMS defined as an SF subscore = 0, or an SF subscore = 1 with a ≥1-point decrease from UC-1 baseline; and an RB subscore = 0; and an ES = 0 or 1 (excluding friability).
[f] $p<0.05$ based on the Cochran-Mantel-Haenszel chi-square test adjusted for randomization stratification factors. Non-responder imputation was used to impute missing data.
[g] An additional 1 patient on placebo and 8 patients on Omvoh were previously exposed to but did not fail a biologic or JAKi.
[h] Prior biologic or JAKi failed is defined as loss of response, inadequate response or intolerance to biologic therapy (TNF blocker or vedolizumab), or tofacitinib.
[i] Endoscopic improvement is defined as a modified Mayo ES = 0 (normal or inactive disease) or 1 (erythema, decreased vascular pattern) excluding friability.
[j] Among patients who achieved clinical remission at week 12 in LUCENT-1 with Omvoh induction treatment.
[k] Corticosteroid free remission is defined as clinical remission at Week 40; and symptomatic remission at Week 28; and no corticosteroid use for ≥12 weeks prior to Week 40.
[l] Histo-endoscopic mucosal remission is defined as both endoscopic improvement (ES = 0 or 1, excluding friability); and histologic remission [Geboes scoring system with subscores of 0 for grades: 2b (lamina propria neutrophils), and 3 (neutrophils in epithelium), and 4 (crypt destruction), and 5 (erosion or ulceration)].
[m] Bowel urgency response is defined as NRS 0 or 1 in patients with urgency NRS ≥3 at baseline in LUCENT-1.

Omvoh Extended Induction

Subjects who did not achieve clinical response after induction with Omvoh in LUCENT-1 were eligible to receive extended induction with Omvoh by intravenous infusion at Weeks 0, 4, and 8 of LUCENT-2. Of these subjects, 146/272 (53.7%) achieved clinical response at Week 12 (24 weeks total induction including LUCENT-1) and were eligible to receive maintenance Omvoh subcutaneously every 4 weeks during LUCENT-2. At Week 40, of the subjects who achieved clinical response after extended induction and transitioned to maintenance regimen, 72.2% maintained clinical response, including 36.1% who achieved clinical remission.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Cynomolgus monkeys were administered mirikizumab two times per

week at IV doses of 100 or 300 mg/kg (i.e., 200 or 600 mg/kg/week), formulated in 10 mM sodium citrate, 150 mM sodium chloride, 0.03% polysorbate 80, pH 5.5, or vehicle control, for 6 months. One animal in the 300 mg/kg/dose group exhibited hematologic, clinical chemistry, and morphologic changes indicative of immune-mediated hemolytic effect of mirikizumab administration. This animal also exhibited a ~90% reduction in NK cell activity and a ~75% reduction in NK cell absolute counts. The no observed adverse effect level (NOAEL) was 100 mg/kg/dose, corresponding to 30X and 100X the human exposure based on AUC at the mirikizumab induction dose (300 mg IV) and the mirikizumab maintenance dose (200 mg SC), respectively.

Sexually mature cynomolgus monkeys were administered mirikizumab once per week at SC doses of 10 and 100 mg/kg formulated in 10 mM sodium citrate, 150 mM sodium chloride, 0.02% polysorbate 80, pH 6.0, or vehicle control, for 6 months. No organ weight or histopathology effects were observed in the male or female reproductive tract. The NOAEL was 100 mg/kg, corresponding to 6.6X and 22X the human exposure based on AUC at the mirikizumab induction dose of 300 mg IV and maintenance dose of 200 mg SC, respectively.

Carcinogenicity: Carcinogenicity studies have not been conducted with mirikizumab

Genotoxicity: Genotoxicity studies have not been conducted with mirikizumab.

Reproductive and Developmental Toxicology: A developmental toxicity study in pregnant monkeys revealed no adverse developmental effects to the fetus or infant. Pregnant cynomolgus monkeys were administered mirikizumab two times per week at an IV dose of 300 mg/kg (i.e., 600 mg/kg/week), formulated in 10 mM sodium citrate, 150 mM sodium chloride, 0.02% polysorbate 80, pH 5.5, or vehicle control, from gestation day 21 ± 1 until birth. There were no mirikizumab-related adverse effects in mothers, fetuses, or infants followed for 6 months after birth. Mirikizumab was detected in all infants for at least 28 days after birth. The overall incidence of embryo/fetal loss was 6.7% (1/15) in the control group and was 26.7% (4/15) at 300 mg/kg mirikizumab, with both values within the range of historical control data at the Testing Facility. The NOAEL for developmental effects was 300 mg/kg/dose, with a corresponding maternal AUC of 127000 µg·hr/mL (69X and 232X the human exposure based on AUC at the mirikizumab induction dose of 300 mg IV and the mirikizumab maintenance dose of 200 mg SC, respectively). The concentration of mirikizumab in maternal milk was not determined. Animal studies are not always predictive of human response, therefore, it is unknown whether mirikizumab could cause fetal harm when administered to a pregnant woman.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrOMVOH™

mirikizumab injection

Read this carefully before you start taking OMVOH and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about Omvoh.

What is Omvoh used for?

- Omvoh contains the active substance 'mirikizumab', a monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind specifically to certain proteins in the body.
- Omvoh works by stopping a protein in the body called 'IL-23', which causes inflammation.
- Ulcerative colitis is an 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 diarrhea, rectal bleeding, and urgency.

How does Omvoh work?

Omvoh contains the active substance 'mirikizumab', a monoclonal antibody. Monoclonal antibodies are proteins that recognize and bind specifically to certain proteins in the body.

Omvoh works by stopping a protein in the body called 'IL-23', which causes inflammation.

What are the ingredients in Omvoh?

Medicinal ingredients: mirikizumab

Non-medicinal ingredients: citric acid anhydrous, polysorbate 80, sodium chloride, sodium citrate dihydrate, and water for injection.

Omvoh comes in the following dosage forms:

Intravenous Infusion:
- Single-use vial: 20 mg/mL (300 mg/15 mL)

Subcutaneous Injection
- Prefilled syringe: 100 mg/mL
- Prefilled pen: 100 mg/mL

Do not use Omvoh if:

- You are allergic to mirikizumab or any of the other ingredients of this medicine. See **What are the ingredients in Omvoh?**
- If you have important active infections.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Omvoh. Talk about any health conditions or problems you may have, including if you:

- currently have an infection or if you have an infection that keeps coming back. Omvoh may lower your ability to fight infections and may increase your risk of infections.
- have tuberculosis (TB) or have been in close contact with someone with TB.
- have recently received or plan to receive an immunization (vaccine). You should not be given certain types of vaccines (called 'live vaccines') while using Omvoh.
- have liver problems.
- experience signs of an allergic reaction or other reaction to an infusion such as wheezing, difficulty breathing, hives, itching, swelling or dizziness. These could occur during or several hours after the infusion.

Other warnings you should know about:

Your healthcare professional may check blood tests while taking Omvoh to help tell if your liver is functioning normally. If blood tests are abnormal, your healthcare professional might interrupt therapy with Omvoh and do additional tests on your liver to determine the cause.

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

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your healthcare professional for advice before using this medicine. This is because it is not known if Omvoh can harm your unborn baby. If you are a woman of childbearing potential, use adequate contraception while using Omvoh. Talk to your healthcare professional about your contraception options.

If you are breastfeeding or are planning to breastfeed, talk to your healthcare professional before using this medicine. It is not known if Omvoh passes into breast milk. You and your healthcare professional should decide if you will breastfeed while using Omvoh.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Omvoh may change the way the body responds to live vaccines.

How to take Omvoh:

- You will first receive Omvoh through a vein in the arm (intravenous infusion or IV) given by a healthcare professional every 4 weeks for a total of 3 doses.
- Your healthcare professional may decide that you may benefit from an additional 3 doses of Omvoh by intravenous infusion.
- You will then continue to receive Omvoh as an injection under the skin (subcutaneous injection) every 4 weeks as described below.

Treatment Start: Intravenous Infusion

- Omvoh will be given to you by a healthcare professional in a healthcare setting.
- You will be given Omvoh through a needle placed in a vein (intravenous infusion or IV) in your arm over a period of about 30 minutes.
- Your healthcare professional will monitor you closely during the infusion.

Maintenance Treatment: Subcutaneous Injection by prefilled pen or prefilled syringe

- Use Omvoh exactly as your healthcare professional tells you to.
- Omvoh comes as 2 different types of devices:
    - a single-patient-use (1 time use only) prefilled pen
    - a single-patient-use (1 time use only) prefilled syringe
- Your healthcare professional will decide with you which type of device is best for you.
- For your full dose, you will need either 2 injections with the prefilled pen or 2 injections with the prefilled syringe. Inject 1 Omvoh pen or syringe followed right away by the other Omvoh pen or syringe.
- Omvoh is intended for use under the guidance and supervision of your healthcare professional. If your healthcare professional decides that you or a caregiver may give your injections of Omvoh at home, you should receive training on the correct way to prepare and inject Omvoh. Do not try to inject Omvoh yourself until you or your caregiver have been shown how to inject Omvoh.
- Omvoh can be injected by patients and/or caregivers under the skin in your stomach area (abdomen) or upper leg (thigh). Omvoh can be injected only by caregivers in the back of the upper arm.
- Use a different injection site each time you use Omvoh. For example, if the first injection was in the abdomen, the second injection - to complete a full dose - should be in another area of the abdomen, thigh, or back of upper arm. Rotate injection sites.
- Do not give an injection in an area that is tender, bruised, red, or hard.
- Do not use this medication if it looks cloudy or is leaking.
- **Read the detailed Instructions for Use that come with Omvoh prefilled pen or prefilled syringe about how to use Omvoh the correct way.**

Usual dose:

The recommended dosing schedule is as follows:

Treatment	Time of treatment	Dose and Route of administration
Treatment Start	Weeks 0, 4 and 8	300 mg intravenous infusion
If you do not have adequate therapeutic response after these 3 infusions, your healthcare professional might consider continuing intravenous infusions at weeks 12, 16 and 20.		
Maintenance Treatment	4 weeks after Treatment Start and then every 4 weeks there after	200 mg subcutaneous injection Given either as: • 2 injections of 100 mg prefilled pens, or • 2 injections of 100 mg prefilled syringes

Overdose:

If you think you, or a person you are caring for, have taken too much Omvoh, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

Intravenous Infusion

- If you forget or miss an appointment to receive the Omvoh infusion, make another appointment as soon as possible.

Subcutaneous Injection

- If you miss a dose of Omvoh, inject the missed dose as soon as you remember. Then, take your next dose at your regularly scheduled time. If you have questions about your schedule, ask your healthcare professional.

What are possible side effects from using Omvoh?

These are not all the possible side effects you may have when taking Omvoh. If you experience any side effects not listed here, tell your healthcare professional.

The most common side effects of Omvoh include:

- Injection site reactions
- Upper respiratory infections
- Headache
- Joint pain
- Rash

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNCOMMON			
Infection Symptoms include: fever, chills, muscle aches, cough, shortness of breath, or pain during urination		x	
RARE			
Serious allergic reactions Symptoms include: fainting, dizziness, feeling lightheaded (low blood pressure); swelling of your face, eyelids, lips, mouth, tongue or throat; trouble breathing or throat tightening; chest tightness		x	x
Liver problems. Symptoms include tiredness, loss of appetite, pain on the right side of your stomach, dark urine, or yellowing of the skin and eyes (jaundice) or itching of the skin		x	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough

to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store refrigerated at 2°C to 8°C.
- Do NOT freeze. Do not use Omvoh if it has been frozen.
- Do NOT shake.
- Keep Omvoh in the original carton to protect from light until the time of use.
- Throw away (dispose of) your prefilled pens or prefilled syringes, as described in the Instructions for Use, if any of the above conditions are not followed.
- If needed, your prefilled syringes or prefilled pens may be stored at room temperature up to 30°C for up to 2 weeks in the original carton to protect from light. Once Omvoh has been stored at room temperature, do not return it to the refrigerator and discard any unused Omvoh after 2 weeks.

Keep Omvoh and all medicines out of the reach of children.

If you want more information about Omvoh:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html), the manufacturer's website (www.lilly.ca), or by calling 1-888-545-5972.
- Instructions for Use can be found on www.lilly.ca

This leaflet was prepared by Eli Lilly Canada, Inc.

Last Revised JUL 20, 2023

A4.01-MIR-NL0000-PM-YYYYMMDD

INSTRUCTIONS FOR USE

PrOMVOH™ (ahm-VOH)

mirikizumab injection
for subcutaneous use

Prefilled Syringe

This Instructions for Use contains information on how to inject OMVOH.

For subcutaneous injection only.

Before you use OMVOH prefilled syringes, read and carefully follow all the step-by-step instructions. Two injections are required for a full dose.

Important information you need to know before injecting OMVOH

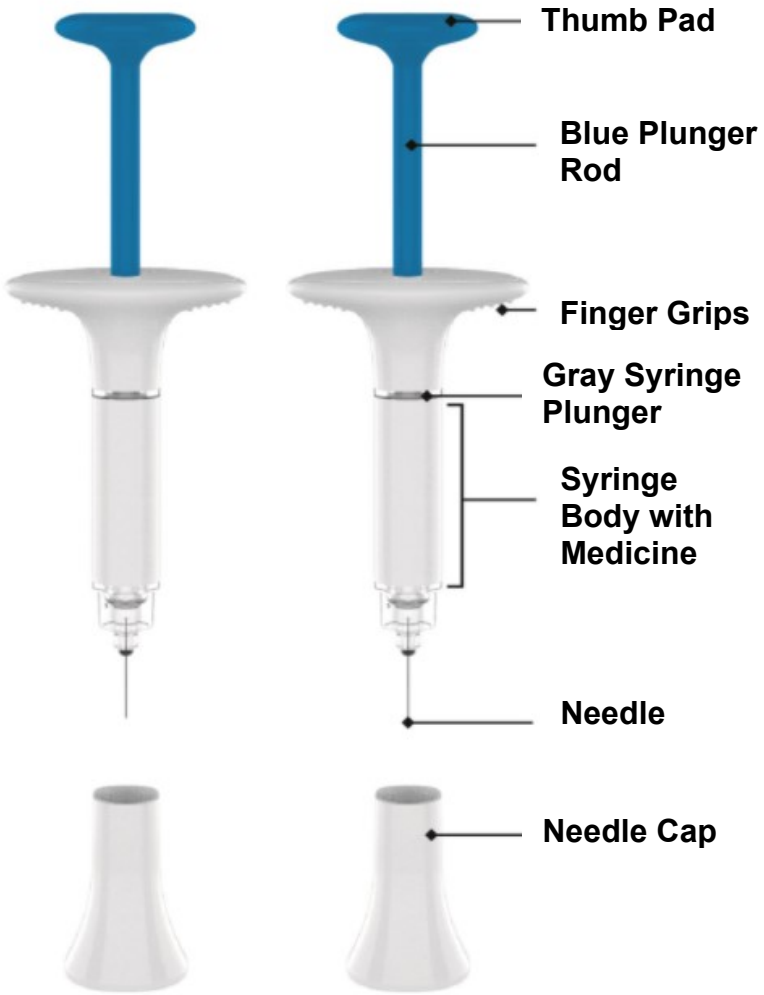
- Your healthcare provider should show you how to prepare and inject OMVOH using the prefilled syringe. **Do not** inject yourself or someone else until you have been shown how to inject OMVOH.
- Keep this Instructions for Use and read it as needed.
- 2 OMVOH injections are required for a full dose.
- Inject 1 OMVOH prefilled syringe followed right away by the other OMVOH prefilled syringe.
- Each OMVOH prefilled syringe is for **one-time use only**. **Do not** share or reuse your OMVOH prefilled 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 prefilled syringe without help from a caregiver.
- See **Storing OMVOH Prefilled Syringes** for important storage information.

INSTRUCTIONS FOR USE

Before you use OMVOH prefilled syringes, read and carefully follow all the step-by-step instructions.

Parts of the OMVOH Prefilled Syringe

Top



Bottom

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

IMPORTANT:
- 2 OMVOH injections are required for a full dose.
- Inject 1 OMVOH prefilled syringe followed right away by the other OMVOH prefilled syringe.

Preparing to inject OMVOH

Take the Prefilled Syringes from the refrigerator

Take 2 OMVOH prefilled syringes from the refrigerator.

Leave the needle caps on until you are ready to inject.

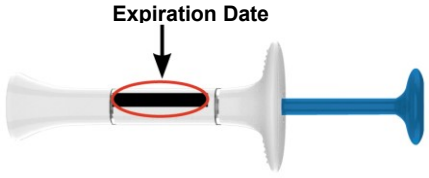
Leave the prefilled syringes at room temperature for 30 minutes before injecting.
Do not microwave the prefilled syringes, or run hot water over them, or leave them in direct sunlight.
Do not use the prefilled syringes if the medicine is frozen.

Do not shake the prefilled syringes.

Gather supplies

Supplies:
- 2 alcohol wipes
- 2 cotton balls or pieces of gauze
- 1 sharps container (see **Disposing of OMVOH Prefilled Syringes**)

Inspect the Prefilled Syringes and the medicine



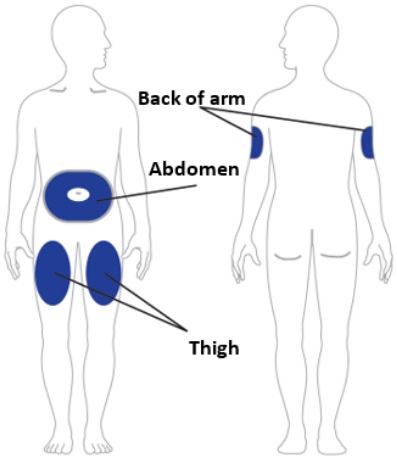
Make sure you have the right medicine. The medicine inside should be clear. It may be colourless to slightly yellow.
Do not use the prefilled syringes and throw away (dispose of) as directed by your healthcare provider or pharmacist if:
- one or both prefilled syringes look damaged
- the medicine is cloudy, is discoloured, or has particles
- the expiration 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.

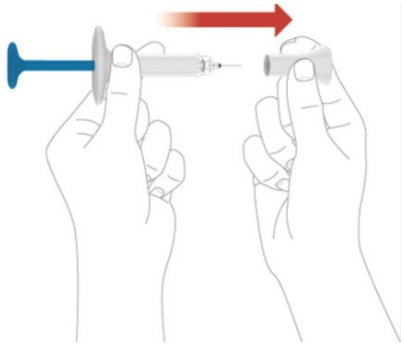


- **You or another person** may inject the medicine into your stomach area (abdomen). **Do not** inject within 2 inches of the belly button (navel).
- **You or another person** may inject the medicine in the front of your thighs. This area should be at least 2 inches above the knee and 2 inches below 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 sites with an alcohol wipe. Let the injection sites dry before you inject the medicine.

Injecting OMVOH

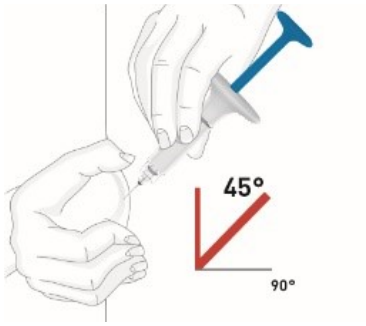
1 Uncap



- **Leave the needle cap on until you are ready to inject.**
- Pull the needle cap off and throw it away in your household trash.
- **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

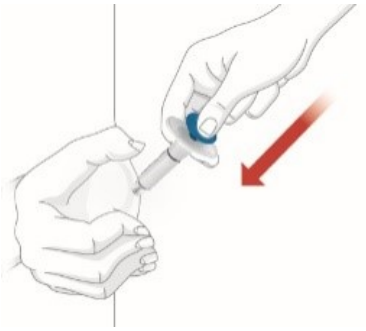
- Gently pinch and hold a fold of skin where you will inject.



- Insert the needle at a 45-degree angle.

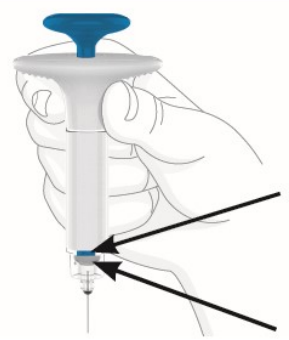
3 Inject

- Slowly push on the thumb pad to push the plunger all the way in until all the medicine is injected.



- The gray syringe plunger should be pushed all the way to the needle end of the syringe.

- 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, as this may cause bruising.
- **Do not** put the needle cap back on the prefilled syringe.



Blue Plunger Rod

Gray Syringe Plunger

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

Disposing of OMVOH Prefilled Syringes

Throw away the used prefilled syringes

- Put the used OMVOH prefilled syringes in a sharps disposal container right away after use. **Do not** throw away (dispose of) the OMVOH prefilled syringes in your household trash.

- 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, and
  - properly labeled 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.

Commonly Asked Questions

Q. What if I let my OMVOH prefilled syringe warm up for longer than 30 minutes before injecting?

A. Your prefilled syringe can stay at room temperature up to 30°C for up to 2 weeks.

Q. What if I see air bubbles in the OMVOH prefilled syringe?

A. It is normal to have air bubbles in the prefilled 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
- Dispose of the syringe and 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 gray syringe plunger should be pushed all the way to the needle end of the syringe.

If you have more questions about how to use the OMVOH prefilled syringe:

- Call your healthcare provider or
- Call Lilly at 1-888-545-5972
- Visit www.lilly.ca

Storing OMVOH Prefilled Syringes

- Store your prefilled syringes in the refrigerator between 2ºC to 8ºC.
- Your prefilled syringes may be stored at room temperature for up to 2 weeks. **Do not** store above 30°C. Throw away (dispose of) OMVOH if not used within 2 weeks at room temperature.
- **Do not** freeze your prefilled syringes.
- Store your prefilled syringes in the original to protect from light until use.
- **Do not** microwave your prefilled syringes, or run hot water over them, or leave them in direct sunlight.

- **Do not** shake your prefilled syringes.
- Throw away (dispose of) your prefilled syringes if any of the above conditions are not followed.
- **Keep your prefilled syringes and all medicines out of the sight and reach of children.**

Read the Patient Medication Information for OMVOH inside this box to learn about your medicine.

Eli Lilly Canada Inc., P.O. Box 73, Toronto, Ontario, M5X 1B1

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INSTRUCTIONS FOR USE

PrOMVOH™ (ahm-VOH)

mirikizumab injection
for subcutaneous use
Prefilled Pen

This Instructions for Use contains information on how to inject OMVOH.

For subcutaneous injection only.

Before you use the OMVOH prefilled pens (Pens), read and carefully follow all the step-by-step instructions. Two injections are required for a full dose.

Important information you need to know before injecting OMVOH

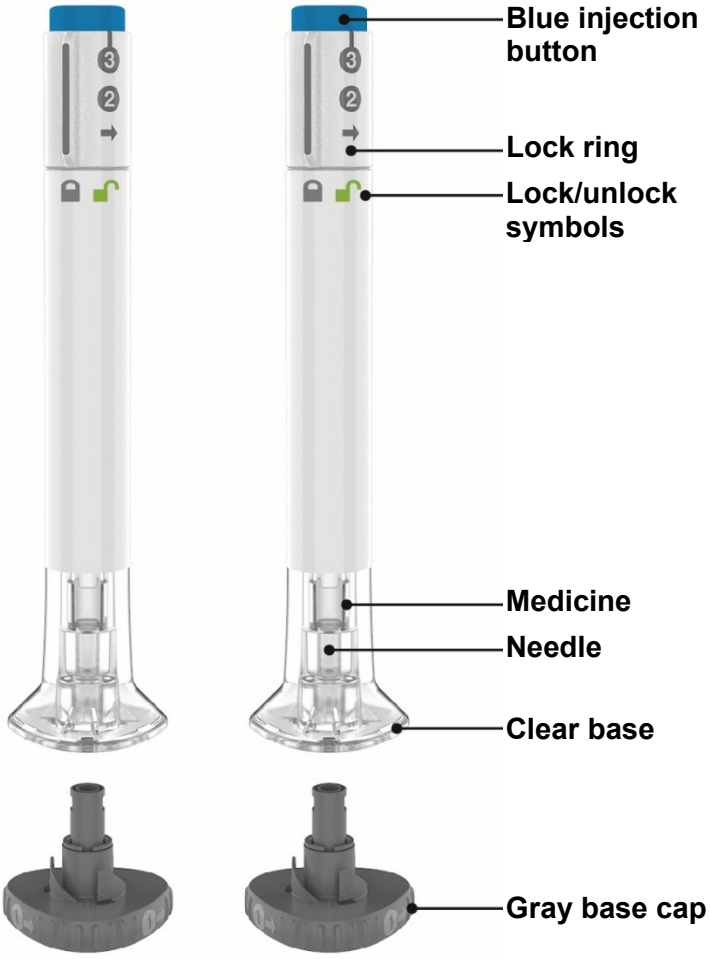
- Your healthcare provider should show you how to prepare and inject OMVOH using the Pen. **Do not** inject yourself or someone else until you have been shown how to inject OMVOH.
- Keep this Instructions for Use and read it as needed.
- 2 OMVOH injections are required for a full dose.
- Inject 1 OMVOH Pen followed right away by the other OMVOH Pen.
- Each OMVOH Pen is for **one-time use only**.
- The OMVOH Pen contains glass parts. Handle it carefully. If you drop it on a hard surface do not use it. Use a new OMVOH Pen for your injection.
- 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.
- See **Storing OMVOH Pens** for important storage information.

INSTRUCTIONS FOR USE

Before you use the OMVOH Pens, read and carefully follow all the step-by-step instructions.

Parts of the OMVOH Pen

Top



Bottom

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

IMPORTANT:
- 2 OMVOH injections are required for a full dose.
- Inject 1 OMVOH Pen followed right away by the other OMVOH Pen.

Preparing to inject OMVOH

Take the Pens from the refrigerator

Take 2 OMVOH Pens from the refrigerator.

Leave the gray 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, or run hot water over them, or leave them in direct sunlight.

Do not use the Pens if the medicine is frozen.

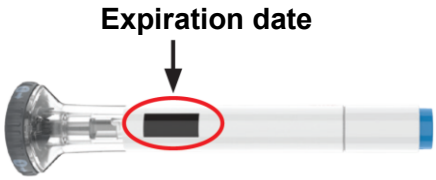
Do not shake the Pens.

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.



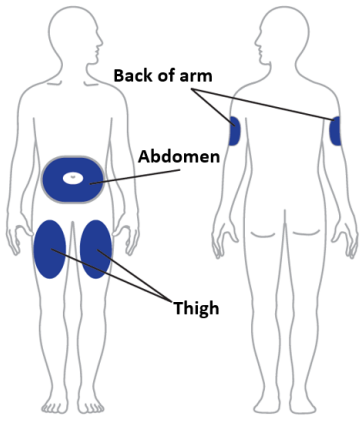
Do not use the Pens and throw away (dispose of) as directed by your healthcare provider or pharmacist if:
- one or both Pens look damaged
- the medicine is cloudy, is discoloured, or has particles
- the expiration date printed on the label has passed
- the medicine is frozen

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.



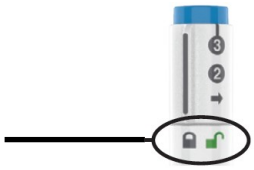
- **You or another person** may inject the medicine into your stomach area (abdomen). **Do not** inject within 2 inches of the belly button (navel).
- **You or another person** may inject the medicine in the front of your thighs. This area should be at least 2 inches above the knee and 2 inches below 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 sites with an alcohol wipe. Let the injection sites dry before you inject the medicine.

Injecting OMVOH

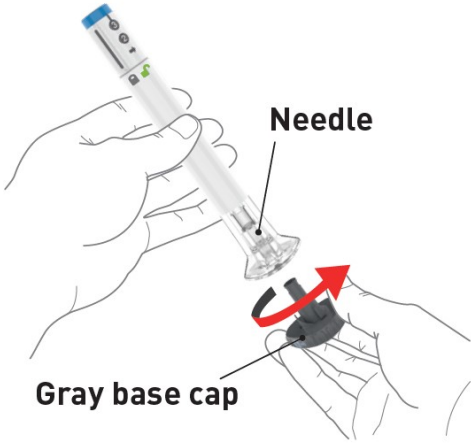
1 Uncap the Pen

Make sure the Pen is **locked**.



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

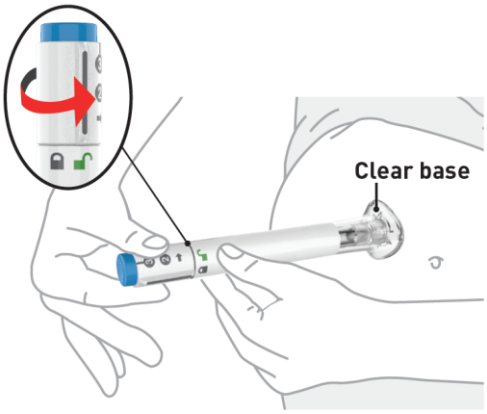
- Twist off the gray base cap and throw it away in your household trash.
- **Do not** put the gray base cap back on – this could damage the needle.
- **Do not** touch the needle.



2 Place and Unlock

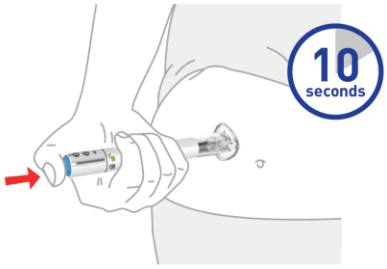
- Place and hold the clear base flat and firmly against the skin.

Keep the clear base on the skin, then 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 the skin.** You will hear a second loud click in about 10 seconds after the first one (injection completed).



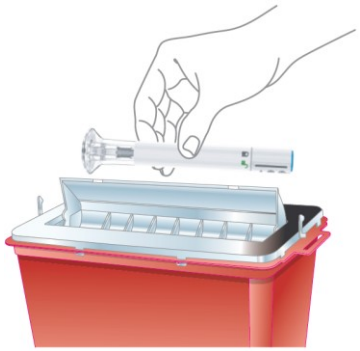
- You will know the injection is complete when the gray plunger is visible.
- Remove the Pen from the skin.
- If you have bleeding at the injection site, press a cotton ball or gauze over the injection site.
- **Do not** rub the injection site, as this may cause bruising.

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 OMVOH Pens in a sharps disposal container right away after use. **Do not** throw away (dispose of) the OMVOH Pens in your household trash.



- 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, and
  - properly labeled 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.

Commonly Asked Questions

Q. What if I let my Pen warm up for longer than 30 minutes before injecting?

A. Your Pen can stay at room temperature up to 86°F (30°C) for up to 2 weeks.

Q. What if I see 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 gray 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 before I twisted off the gray base cap?

A. **Do not** remove the gray base cap. Throw away (dispose of) the Pen and 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 gray base cap. Store the Pen in a safe place to avoid an accidental needlestick and contact 1-800-Lilly-Rx (1-800-545-5979) for instructions on how to return the Pen.

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 gray plunger at the top of the clear base.

If you have more questions about how to use the OMVOH Pen:

- Call your healthcare provider or
- Call Lilly at 1-888-545-5972
- Visit www.lilly.ca

Storing OMVOH Pens

- Store your Pens in the refrigerator between 2ºC to 8ºC.
- Your Pens may be stored at room temperature for up to 2 weeks. **Do not** store above 30°C. Throw away (dispose of) OMVOH if not used within 2 weeks at room temperature.
- **Do not** freeze your Pens.
- Store your Pens in the original carton to protect from light until use.

- **Do not** microwave your Pens, or run hot water over them, or leave them in direct sunlight.
- **Do not** shake your Pens.
- Throw away (dispose of) your Pens if any of the above conditions are not followed.
- **Keep your Pens and all medicines out of the sight and reach of children.**

Read the Patient Medication Information for OMVOH inside this box to learn more about your medicine.

Eli Lilly Canada Inc., P.O. Box 73, Toronto, Ontario, M5X 1B1

OMVOH™ is a trademark of Eli Lilly and Company.

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The OMVOH Pen meets the current dose accuracy and functional requirements of ISO 11608-1 and 11608-5.

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