PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrEBGLYSS™

Lebrikizumab injection

Solution for subcutaneous injection

250 mg/2 mL single use prefilled pen

250 mg/2 mL single use prefilled syringe with needle shield

Immunomodulator, Interleukin inhibitor

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Ebglyss (lebrikizumab injection) is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years of age and older with a body weight of at least 40 kg, whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Ebglyss can be used with or without topical corticosteroids.

1.1 Pediatrics

Adolescents (12 to < 18 years of age who weigh ≥ 40 kg): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Ebglyss in adolescent patients 12 years of age and older who weigh **≥** 40 kg has been established for the treatment of moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable (*see* 4.2 Recommended Dose and Dosage Adjustment, 7.1.3 Pediatrics, and 10.3 Pharmacokinetics).

Pediatrics (< 12 years of age) and Adolescents (12 to < 18 years who weigh < 40 kg): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use in patients < 12 years of age and in adolescents who weigh < 40 kg.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): 123 subjects ≥ 65 years of age were exposed to Ebglyss in moderate-to-severe atopic dermatitis clinical studies (*see* 4.2 Recommended Dose and Dosage Adjustment, 7.1.4 Geriatrics, and 10.3 Pharmacokinetics).

2 CONTRAINDICATIONS

Ebglyss 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.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Ebglyss can be used with or without topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI). TCI may be used but should be reserved for problem areas only, such as the face, neck, intertriginous, and genital areas.

4.2 Recommended Dose and Dosage Adjustment

The recommended dose of Ebglyss is an initial dose of 500 mg (two 250 mg injections) injected subcutaneously at Week 0 and Week 2, followed by 250 mg (one injection) every two weeks until Week 16.

Once clinical response is achieved, the recommended maintenance dose is 250 mg every four weeks starting at Week 16 (*see* 10.3 Pharmacokinetics).

Continued therapy beyond 16 weeks should be carefully considered in a patient who does not

show treatment benefit within this time period.

Special Populations

Renal Insufficiency

No dose adjustment is recommended in patients with renal impairment (*see* 10.3 Pharmacokinetics).

Hepatic Insufficiency

No dose adjustment is recommended in patients with hepatic insufficiency (*see* 10.3 Pharmacokinetics).

Geriatrics (≥ 65 years)

No dose adjustment is required in patients **≥** 65 years of age (*see* 7.1.4 Geriatrics and 10.3 Pharmacokinetics).

Pediatrics (< 12 years of age) and Adolescents (12 to < 18 years who weigh < 40 kg):

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use in patients < 12 years of age and in adolescents who weigh < 40 kg (*see* 1.1 INDICATIONS, Pediatrics).

Adolescents (12 to < 18 years who weigh ≥ 40 kg):

No dose adjustment is required for adolescent patients > 12 years of age and who weigh ≥ 40 kg.

4.4 Administration

Ebglyss is for subcutaneous administration.

Ebglyss is intended for use under the guidance of a healthcare professional. Provide proper training to patients and/or caregivers on the subcutaneous injection technique of Ebglyss according to the Instructions for Use, included with the packaged product. Adult patients may self-inject, or caregivers may give Ebglyss after training in subcutaneous injection technique. For adolescent patients, caregivers may give injections after training in subcutaneous injection technique.

Sites for injection include the abdomen, thigh, and back of the upper arm. Administration of Ebglyss in the back of the upper arm must be performed by a caregiver or healthcare professional.

Rotation of injection sites is recommended. Do not inject into areas where the skin is tender, bruised, red, hard, or in an area of skin that is affected by atopic dermatitis or skin lesions.

Before injection, remove Ebglyss prefilled pen or Ebglyss prefilled syringe from the refrigerator and leave at room temperature for 45 minutes without removing the needle cap. Do not warm by using a heat source such as hot water or microwave.

Inspect Ebglyss visually for particulate matter and discoloration prior to administration. Do not use if the liquid contains visible particles, is discolored or cloudy.

Ebglyss is preservative-free.

4.5 Missed Dose

If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing on the regularly scheduled dosing interval, starting on the new dosing day.

5 OVERDOSAGE

There is no specific treatment for Ebglyss overdose. Single intravenous doses up to 10 mg/kg and two subcutaneous doses up to 500 mg Q2W have been administered to humans in clinical trials without dose-limiting toxicity. In the event of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted 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	Nonmedicinal Ingredients
Subcutaneous Injection (S.C.)	sterile solution for injection, 250 mg/2 mL (prefilled pen or prefilled syringe with needle shield)	Glacial acetic acid, histidine, polysorbate 20, sucrose, water for injection

Ebglyss is a sterile, preservative free, clear, colorless to slightly yellow solution, free of visible particles and is supplied as:

- 250 mg/2 mL single use prefilled pen
- 250 mg/2 mL single use prefilled syringe with needle shield

The prefilled pen contains a 2.25 mL, Type I glass syringe barrel, 27G special thin wall x 8 mm staked needle, and closed with a laminated bromobutyl elastomeric plunger and rigid needle shield.

The prefilled syringe with needle shield contains a 2.25 mL, Type I glass syringe barrel, 27 G special thin wall x 12.7 mm staked needle, and closed with a laminated bromobutyl elastomeric plunger and rigid needle shield.

Ebglyss is for single use and, therefore, contains no antimicrobial preservatives.

Ebglyss prefilled pen and prefilled syringe with needle shield are not made with natural rubber latex.

Ebglyss is available in packs containing 1 prefilled pen or 1 prefilled syringe with needle shield.

7 WARNINGS AND PRECAUTIONS

Immune

Hypersensitivity

Hypersensitivity reactions have been reported following the use of Ebglyss. If a systemic

hypersensitivity reaction (immediate or delayed) occurs, administration of Ebglyss should be discontinued immediately and appropriate therapy initiated.

Helminth Infections

Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if lebrikizumab will influence the immune response against helminth infections by inhibiting IL-13 signaling. Treat patients with the pre-existing helminth infections before initiating treatment with lebrikizumab. If patients become infected while receiving lebrikizumab and do not respond to antihelminth treatment, discontinue treatment with lebrikizumab until the infection resolves.

Conjunctivitis and Keratitis

Conjunctivitis and keratitis occurred more frequently in subjects with atopic dermatitis who received Ebglyss than in subjects who received placebo. Advise patients to report new onset or worsening eye symptoms to their health professional. Patients treated with Ebglyss who develop conjunctivitis that does not resolve following standard treatment should undergo ophthalmological examination, as appropriate (*see* 8 ADVERSE REACTIONS).

Vaccination

Prior to initiating therapy with Ebglyss, consider completion of all age-appropriate immunizations according to current immunization guidelines. Treatment with a live (attenuated) vaccine should be completed before starting the treatment. Avoid concurrent use of live vaccines in patients treated with Ebglyss. No data are available on the response to live or non-live vaccines in patients treated with Ebglyss.

7.1 Special Populations

7.1.1 Pregnant Women

There are no available data on Ebglyss use in pregnant women. Human immunoglobulin G (IgG) is known to cross the placental barrier; therefore, Ebglyss may be transmitted from the mother to the developing fetus. Developmental toxicity studies in pregnant monkeys at doses up to 18 times (adolescents) and 22 times (adults) the human exposure at the recommended human dose revealed no evidence of harm to the developing fetus. Lebrikizumab was detected in fetal serum at concentrations that were approximately 30% of maternal serum concentrations at all tested dose levels (*see* 16 NON-CLINICAL TOXICOLOGY). As a precautionary measure, it is preferable to avoid the use of Ebglyss during pregnancy. Women of reproductive potential should be advised to use effective contraception.

7.1.2 Breast-feeding

There are no data on the presence of Ebglyss in human milk, the effects on the breastfed infant, or the effects on milk production. In a pre- and post-natal developmental toxicity study in pregnant cynomolgus monkeys, lebrikizumab was detected in serum of all offspring at higher concentrations than maternal serum levels until the end of the observation period on post-natal day 180 (*see* 16 NON-CLINICAL TOXICOLOGY). A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue from lebrikizumab therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

7.1.3 Pediatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use in patients < 12 years of age and in adolescents who weigh < 40 kg (*see* 1.1 INDICATIONS, Pediatrics).

7.1.4 Geriatrics

Evidence from 123 patients ≥ 65 years of age who were exposed to Ebglyss in moderate-to-severe atopic dermatitis clinical studies suggests that use in the geriatric population is not associated with differences in safety or efficacy between older and younger subjects (*see* 1.2 INDICATIONS, Geriatrics).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most commonly reported adverse reactions in adolescents weighing at least 40 kg and adults are conjunctivitis (6.5%), injection site reactions (2.6%), conjunctivitis allergic (1.8%), dry eye (1.4%), and herpes zoster (0.6%).

1.3% of Ebglyss-treated patients reported at least one serious adverse event (SAE). The proportion of patients who discontinued treatment due to adverse events was 2.3% in the Ebglyss group and 1.4% in the placebo group during the initial treatment period of up to 16 weeks.

8.2 Clinical Trial Adverse Reactions

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

Adults and Adolescents

The safety of Ebglyss was evaluated across 4 randomized, double-blind, placebo-controlled, multicenter trials in subjects with moderate-to-severe atopic dermatitis including 3 phase 3 trials (ADvocate 1, ADvocate 2, and ADhere), and one phase 2 dose ranging trial (KGAF). In these 4 trials, all subjects (pooled across treatment groups) had a mean age of 37 years; 50% of subjects were men; 62% were White, 13% were Black, and 20% were Asian. In the phase 3 studies, 30% of the subjects had asthma, 50% had allergic rhinitis, 31% had food allergy, and 14% had allergic conjunctivitis at baseline.

ADvocate 1, ADvocate 2, and KGAF compared the safety of Ebglyss monotherapy to placebo. ADhere compared the safety of Ebglyss + TCS to placebo + TCS through 16 weeks. 783 subjects within these studies were treated with Ebglyss in the 16-week placebo-controlled period. A total of 891 subjects within the atopic dermatitis development program were treated with Ebglyss for at least 1 year.

The long-term safety of Ebglyss was assessed in the two monotherapy studies up to Week 52. The long-term safety of Ebglyss in combination with TCS was evaluated for ADhere patients who enrolled in a long-term extension study up to 56 weeks of treatment. In two monotherapy studies, 51.7% of patients treated with lebrikizumab 250 mg Q4W reported a TEAE from Week 16 to Week 52.

Table 2 summarizes the adverse reactions that were reported more frequently in the Ebglyss groups than in the placebo group during the 16-week placebo-controlled period of the clinical trials.

Table 2 – Adverse Reactions Reported by ≥ 1% Ebglyss-Treated Subjects and Higher than Placebo with Moderate-to-Severe Atopic Dermatitis Through Week 16 in Placebo-Controlled Trials

Adverse Reactions	Ebglyss Monotherapy[a]		Ebglyss plus TCS[b]	
	Ebglyss 250 mg Q2W[c] N = 638 n (%)	Placebo N = 338 n (%)	Ebglyss 250 mg Q2W + TCS[c] N = 145 n (%)	Placebo + TCS N = 66 n (%)
Eye Disorders				
Conjunctivitis Allergic	14 (2.2%)	3 (0.9%)	0	0
Dry Eye	8 (1.2%)	4 (1.1%)	3 (2.1%)	0
General disorders and administration site conditions				
Injection Site Reactions[d]	16 (2.6%)	5 (1.5%)	4 (2.8%)	1 (1.5%)
Infections and infestations				
Conjunctivitis	44 (6.8%)	7 (2.1%)	7 (4.8%)	0
Herpes Zoster	3 (0.5%)	0	2 (1.4%)	0

[a] Integrated analysis of the monotherapy trials: ADvocate 1 (KGAB), ADvocate 2 (KGAC), and KGAF.

[b] Analysis of topical corticosteroid (TCS) combination trial: ADhere (KGAD).

[c] Ebglyss 500 mg at Week 0 and Week 2, followed by 250 mg every two weeks (Q2W).

[d] *Injection Site Reactions* includes MedDRA High-Level Term (HLT) which includes (but is not limited to) the most common terms: injection site pain, injection site erythema, and injection site reaction.

Specific Adverse Drug Reactions

Injection Site Reactions

Among the subjects pooled from ADvocate 1, ADvocate 2, KGAF, and ADhere, injection site reaction was reported in 2.6% of the subjects treated with lebrikizumab and 1.5% of the subjects in the placebo group. One subject (0.1%) treated with lebrikizumab reported a severe injection site reaction, and 2 events led to permanent discontinuation of lebrikizumab treatment.

Conjunctivitis and Keratitis

Conjunctivitis was the most frequently reported eye disorder.

Among the subjects pooled from ADvocate 1, ADvocate 2, KGAF, and ADhere, conjunctivitis and conjunctivitis allergic were reported in 6.5% and 1.8% of the subjects treated with lebrikizumab and in 1.8% and 0.7% of the subjects in the placebo group. Conjunctivitis and conjunctivitis allergic events reported were mild or moderate in severity, and 2 events led to

permanent discontinuation of lebrikizumab treatment.

Keratitis events occurred in 0.6% of lebrikizumab-treated patients. All were mild or moderate in severity, and 2 events led to permanent discontinuation of lebrikizumab treatment.

Herpes Zoster

Among the subjects pooled from ADvocate 1, ADvocate 2, KGAF, and ADhere, herpes zoster was reported in 0.6% of the subjects treated with lebrikizumab and none of the subjects in the placebo group. All herpes zoster events reported were mild or moderate in severity and none led to permanent discontinuation of treatment.

Immunogenicity

As with all therapeutic proteins there is a potential for immunogenicity with Ebglyss.

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of Ebglyss or of other drug products.

Anti-drug antibodies were detected during the 12-month treatment period in Ebglyss studies. No definitive conclusions can be drawn regarding the impact of anti-drug antibodies on the pharmacokinetics, efficacy, or safety of lebrikizumab.

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

Adolescents (12 to < 18 years of age who weigh ≥ 40 kg):

The safety of lebrikizumab was assessed in 372 adolescents (age 12 to < 18 years of age who weigh ≥ 40 kg) with moderate-to-severe atopic dermatitis. This includes 270 subjects exposed for at least one year. The observed safety profile of lebrikizumab in these subjects was similar to the observed safety profile in adults with moderate-to-severe atopic dermatitis (*see* 1.1 INDICATIONS, Pediatrics).

Pediatrics (< 12 years of age) and Adolescents (12 to < 18 years who weigh < 40 kg):

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use in patients < 12 years of age and in adolescents who weigh < 40 kg (*see* 1.1 INDICATIONS, Pediatrics).

8.3 Less Common Clinical Trial Adverse Reactions

Adverse drug reactions occurring in <1% of Ebglyss-treated subjects:

Blood and lymphatic system disorders: eosinophilia

Eye disorders: blepharitis, keratitis

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

Eosinophilia
Lebrikizumab-treated subjects had a greater mean increase from baseline in eosinophil count compared to subjects treated with placebo. In lebrikizumab-treated subjects, 20.3% had any increase in eosinophil count compared to 11.7% with placebo. In general, the increase in the lebrikizumab-treated subjects was mild or moderate and transient. Eosinophilia

>5000 cells/mcL was observed in 0.4% in the lebrikizumab-treated subjects and none of the placebo-treated subjects. Adverse reactions of eosinophilia were reported in 0.6% of subjects treated with lebrikizumab and with a similar rate in subjects treated with placebo during the initial treatment period. Eosinophilia did not result in treatment discontinuation and no eosinophil-related disorders were reported (*see* 8.3 Less Common Clinical Trial Adverse Reactions).

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No formal drug interaction studies were conducted. No pharmacokinetic drug interactions are expected based on the characteristics of lebrikizumab.

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established. In atopic dermatitis studies, interactions between lebrikizumab and other systemic immunomodulatory agents or phototherapy have not been evaluated.

Live Vaccines

No data are available on the response to live vaccines. Avoid use of live vaccines in patients treated with Ebglyss (*see* 7 WARNINGS AND PRECAUTIONS, Vaccination).

Non-live Vaccines

No data are available on the response to non-live vaccines.

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

Lebrikizumab is an immunoglobulin G4 (IgG4) monoclonal antibody (MAb) that binds with high affinity and slow off-rate to interleukin (IL)-13 and inhibits IL-13 signaling through the IL-4 receptor alpha (IL-4Rα)/IL-13 receptor alpha 1 (IL-13Rα1) pathway, thereby blocking the downstream effects of IL-13. Lebrikizumab does not prevent the binding of IL-13 to the IL-13 receptor alpha 2 (IL13Rα2 or decoy receptor), which allows the internalization of IL-13 into the cell.

10.2 Pharmacodynamics

In a clinical study, lebrikizumab reduced the levels of the following downstream regulated molecules: serum periostin, total immunoglobulin E (IgE), CCL18 (pulmonary and activation-regulated chemokine [PARC]), and CCL13 (monocyte chemotactic protein 4 [MCP 4]).

10.3 Pharmacokinetics

Lebrikizumab exhibited linear pharmacokinetics with a dose-proportional increase in exposure over the dose range of 37.5 to 500 mg given as a subcutaneous injection in subjects with moderate-to-severe atopic dermatitis or in healthy volunteers.

Table 3 – Summary of Lebrikizumab Pharmacokinetic Parameters in Healthy Adult Participants after a Single Subcutaneous Dose with the Prefilled Pen

	C_{max} [a] (µg/mL)	t_{max} [b] (day)	$t_{½}$ [c] (day)	$AUC_{0\text{-}inf}$ [a] (µg*day/mL)	CL/F [a] (L/day)	V_{ss}/F [a] (L)
250 mg SC	41.9 (31%)	7.07 (2.00-20.83)	28.0 (8.90-79.1)	1450 (26%)	0.173 (26%)	6.57 (22%)

[a] Geometric mean (geometric CV%)

[b] Median (minimum-maximum)

[c] Geometric mean (minimum-maximum)

Following the 500 mg loading doses at Week 0 and Week 2, steady-state serum concentrations were achieved with the first 250 mg Q2W dose at Week 4. The median (5^{th} - 95^{th}) accumulation ratio from first loading dose to steady state (Week 16) based on population pharmacokinetic (PK) predicted C_{trough} was 1.53 (1.04 – 2.12).

Based on a population PK analysis, the estimated steady-state maximum concentration ($C_{max,ss}$), the steady-state average concentration ($C_{avg,ss}$), and the steady-state trough concentration ($C_{trough,ss}$) at Week 16 following the 250 mg Q2W subcutaneous dose in subjects with moderate-to-severe atopic dermatitis were 109 µg/mL, 100 µg/mL, and 86 µg/mL, respectively. The $C_{max,ss}$, the $C_{avg,ss}$, and the $C_{trough,ss}$ at Week 52 following the transition to 250 mg Q4W subcutaneous maintenance dosing in subjects with moderate-to-severe atopic dermatitis were 63 µg/mL, 51 µg/mL, and 36 µg/mL, respectively.

Absorption

Following a single subcutaneous 250 mg dose of lebrikizumab, peak serum concentrations were achieved approximately 7 to 8 days post dose. The absolute bioavailability for a subcutaneous dose was estimated as 86%.

Injection site locations did not consistently influence the absorption of lebrikizumab.

Distribution

Based on a population PK analysis, the total volume of distribution at steady-state was 5.14 L.

Metabolism

Lebrikizumab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Elimination

In the population PK analysis, clearance was 0.154 L/day and was independent of dose. The mean elimination half-life was 24.5 days.

Special Populations and Conditions

- **Pediatrics**

  Adolescents (12 to < 18 years of age who weigh ≥ 40 kg):
  At Week 16, estimated median steady-state maximum concentration ($C_{max,ss}$), steady-state average concentration ($C_{avg,ss}$), and steady-state trough concentration ($C_{trough,ss}$) in adolescent subjects following 250 mg Q2W dosing were 121 µg/mL, 111 µg/mL, and 96 µg/mL, respectively. Corresponding estimated steady-state concentrations following 250 mg Q4W dosing were 71 µg/mL, 56 µg/mL, and 38 µg/mL, respectively.

  Pediatrics (< 12 years of age) and Adolescents (12 to < 18 years who weigh < 40 kg):
  The pharmacokinetics of lebrikizumab in these subjects have not been studied.

- **Geriatrics**

  Age did not have a clinically meaningful effect on the pharmacokinetics of lebrikizumab.

- **Sex**

  Sex did not have a clinically meaningful effect on the pharmacokinetics of lebrikizumab.

- **Ethnic Origin**

  Race did not have a clinically meaningful effect on the pharmacokinetics of lebrikizumab.

- **Renal and Hepatic Insufficiency**

  Specific clinical pharmacology studies to evaluate the effects of renal impairment and hepatic impairment on the pharmacokinetics of lebrikizumab have not been conducted. Lebrikizumab, as a monoclonal antibody, is not expected to undergo significant renal and hepatic elimination.

  Population PK analysis showed that markers of renal function (eGFR) had no clinically meaningful effect on lebrikizumab pharmacokinetics over a range of 27.4 to 335 mL/min/1.73 m^2.

  Markers of hepatic function (AST ranged from 6 to 105 IU/L, and ALT ranged from 5 to 178 IU/L) were not identified as covariates on lebrikizumab pharmacokinetics.

- **Body Weight**

  Lebrikizumab C_{max}, C_{avg}, and C_{trough} concentrations decreased with increasing body weight as determined by population PK analysis. No dose adjustments are necessary in patients with higher body weight.

11 STORAGE, STABILITY AND DISPOSAL

Ebglyss is sterile and preservative-free.

Store refrigerated at 2°C to 8°C in the original carton to protect from light.

If necessary, Ebglyss may be kept at room temperature up to 30°C for up to 7 days in the original carton. Throw away Ebglyss if not used within 7 days at room temperature.

Do not freeze. Do not use Ebglyss if it has been frozen.

Do not shake.

Discard the Ebglyss single use prefilled pen or prefilled syringe with needle shield after use in a puncture-resistant container.

12 SPECIAL HANDLING INSTRUCTIONS

For special handling instructions on how to properly dispose of Ebglyss following an injection, refer to the PATIENT MEDICATION INFORMATION, INSTRUCTIONS FOR USE section of the product monograph.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: lebrikizumab

Molecular formula: H chain: $C_{2177}H_{3373}N_{567}O_{672}S_{18}$ L chain: $C_{1040}H_{1617}N_{283}O_{345}S_{7}$

Molecular mass: Approximately 145,285 Daltons for the non-glycosylated protein backbone of the molecule.

Structural formula: Lebrikizumab is a recombinant Immunoglobulin G4 (IgG4) monoclonal antibody composed of 2 identical gamma heavy chains (445 amino acid residues each) and 2 identical light chains (218 amino acid residues each) with inter- and intra-chain disulfide bonds.

Physicochemical properties: lebrikizumab solution is clear, colorless to slightly yellow, free of visible particles with a pH of 5.4 – 6.0.

Product Characteristics:

Lebrikizumab is produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. Lebrikizumab 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. Lebrikizumab drug product is formulated, sterile filtered and filled into syringes prior to final packaging.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The efficacy and safety of Ebglyss were evaluated in monotherapy studies ADvocate 1 and ADvocate 2 and concomitant TCS study, ADhere. All three studies were randomized, double-blind, placebo-controlled, and involved a total of 1062 adults and adolescents (aged 12 to < 18 years and weighing ≥ 40 kg) with moderate-to-severe atopic dermatitis, defined by an Eczema Area and Severity Index (EASI) ≥ 16; Investigator's Global Assessment (IGA) score ≥ 3; and a body surface area (BSA) involvement of ≥ 10%. Patients enrolled into the three studies previously had an inadequate response to topical medication or determination that topical treatments are otherwise medically inadvisable.

Patients with active hepatitis, endoparasitic infections, a history of invasive opportunistic infections, history of human immunodeficiency virus (HIV) infection, severe uncontrolled asthma, and a history of malignancy, including mycosis fungoides, within 5 years before the screening visit (except completely treated in situ carcinoma of the cervix, completely treated and resolved non-metastatic squamous or basal cell carcinoma of the skin) were excluded from clinical studies.

At baseline, the monotherapy studies ADvocate 1 and ADvocate 2 enrolled 424 and 427 patients, respectively. Across studies, the mean age was 35.8 years, the mean weight was 77.1 kg, 49.9% were female, 63.7% were white, 22.6% were Asian, 9.9% were black, and 12.0% were adolescents (12 to < 18 years). Overall, 61.5% of patients had a baseline IGA score of 3 (moderate atopic dermatitis), 38.5% of patients had a baseline IGA score of 4 (severe atopic dermatitis), and 54.8% of patients had received prior systemic treatment. The mean baseline EASI score was 29.6, the mean baseline Pruritus Numeric Rating Scale (NRS) was 7.2, the mean baseline Dermatology Life Quality Index (DLQI) was 15.5.

The concomitant TCS study, ADhere, enrolled 211 patients. The mean age was 37.2 years, the mean weight was 76.2 kg, 48.8% were female, 61.6% were white, 14.7% were Asian, 13.3% were black, and 21.8% were adolescents. In this study, 69.2% of patients had a baseline IGA score of 3 (moderate atopic dermatitis), 30.8% of patients had a baseline IGA score of 4 (severe atopic dermatitis), and 47.4% of patients had received prior systemic treatment. The mean baseline EASI score was 27.3, the mean baseline Pruritus NRS was 7.1, the mean baseline DLQI was 14.4.

In all three studies, patients received subcutaneous injection of the initial dose of 500 mg of Ebglyss (two 250 mg injections) at Weeks 0 and 2, followed by 250 mg every other week (Q2W) until Week 16, or matching placebo in a 2:1 ratio. In ADhere, study patients also received concomitant low-to-mild potency TCS or TCI on active lesions on sensitive areas only, such as the face, neck, intertriginous, and genital areas.

Patients were permitted to receive rescue treatment at the discretion of the investigator to control intolerable symptoms of atopic dermatitis. Patients requiring systemic rescue treatment were discontinued from study treatment.

In ADvocate-1 and 2, patients achieving IGA 0 or 1 or at least a 75% reduction in EASI (EASI 75) at Week 16 without having received any rescue therapy were re-randomised in a blinded manner to (i) Ebglyss 250 mg Q2W; (ii) Ebglyss 250 mg every 4 weeks (Q4W); or (iii) matching placebo (Ebglyss withdrawal) up to 52 weeks.

In all the three studies, the co-primary endpoints were the proportion of patients with IGA 0 or 1 with at least a 2-point reduction in IGA score from baseline and EASI 75 from baseline to Week 16. Key secondary endpoints included the proportion of patients achieving EASI 90, reduction in itch as defined by at least 4-point improvement in Pruritus NRS, and change in DLQI from baseline to Week 16.

Table 4 – Summary of Patient Demographics for Clinical Trials in Moderate-to-Severe Atopic Dermatitis

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex n (%)
ADvocate 1	Multicentre, double blinded, randomized, placebo-controlled	Induction (0-16 weeks) • Ebglyss: 250 mg SC administration Q2W[a] • Placebo: SC administration Q2W Maintenance (16-52 weeks) • Ebglyss: 250 mg SC administration Q2W[b] • Ebglyss: 250 mg SC administration Q4W[b] • Placebo (Ebglyss withdrawal): SC administration Q2W • Escape arm	Total 424	35.5 (12-93)	Male 210 (49.5%) Female 214 (50.5%)
			Adult 369	38.6 (18-93)	
			Adolescent 55	14.4 (12-17)	
ADvocate 2	Multicentre, double blinded, randomized, placebo-controlled		Total 427	36.2 (12-85)	Male 216 (50.6%) Female 211 (49.4%)
			Adult 380	38.8 (18-85)	
			Adolescent 47	14.8 (12-17)	
ADhere	Multicentre, double blinded, randomized, placebo-controlled	Induction (0-16 weeks) • Ebglyss: 250 mg SC administration Q2W[a] + topical corticosteroids • Placebo: SC administration Q2W + topical corticosteroids	Total 211	37.2 (12-82)	Male 108 (51.2%) Female 103 (48.8%)
			Adult 165	43.6 (18-82)	
			Adolescent 46	14.6 (12-17)	

[a] Participants randomly assigned to Ebglyss 250 mg Q2W at Baseline received 500 mg loading doses at Week 0 and Week 2.

[b] Participants who received PBO during the first 16 weeks of the study and who were re-randomized to Ebglyss treatment received a loading dose of either 500 mg at Weeks 16 and 18 if randomized to Ebglyss 250 mg Q2W or 500 mg at Week 16 if randomized to Ebglyss 250 mg Q4W.

14.2 Study Results

Clinical Response at Week 16 (ADvocate 1, ADvocate 2, and ADhere) in Moderate-to-Severe Atopic Dermatitis Patients

The results of the Ebglyss monotherapy trials (ADvocate 1 and ADvocate 2) and the Ebglyss + TCS trial (ADhere) are presented in Table 5.

Table 5 – Efficacy Results of Ebglyss at Week 16[a] In ADvocate 1 (monotherapy), ADvocate 2 (monotherapy), and ADhere (combination therapy with TCS)

	ADvocate 1		ADvocate 2		ADhere	
	Ebglyss[b] 250 mg Q2W	Placebo	Ebglyss[b] 250 mg Q2W	Placebo	Ebglyss[b] 250 mg Q2W + TCS	Placebo + TCS
Number of subjects	283	141	281	146	145	66
Co-primary endpoints[c]						
IGA 0 or 1	43%	13%	33%	11%	41%	22%
Treatment Effect (95% CI)	29.7 (21.6, 37.8)		21.9 (14.2, 29.6)		18.3 (5.1, 31.5)	
p-value vs PBO	<.001		<.001		.011	
EASI-75	59%	16%	52%	18%	70%	42%
Treatment Effect (95% CI)	42.0 (33.3, 50.6)		33.3 (24.4, 42.2)		26.4 (12.1, 40.8)	
p-value vs PBO	<.001		<.001		<.001	
Key secondary endpoints[d]						
EASI-90	38%	9%	31%	10%	41%	22%
Treatment Effect (95% CI)	28.8 (21.3, 36.3)		20.7 (13.3, 28.1)		18.9 (6.1, 31.7)	
p-value vs PBO	<.001		<.001		.008	
Number of subjects with baseline Pruritus NRS score ≥4	263	130	253	134	130	57
Pruritis NRS ≥4-point improvement	46%	13%	40%	12%	51%	32%
Treatment Effect (95% CI)	32.9 (24.6, 41.3)		28.3 (20.0, 36.5)		19.2 (4.3, 34.1)	
p-value vs PBO	<.001		<.001		.017	

[a] Subjects who received rescue therapy or discontinued treatment due to lack of efficacy were analyzed as non-responders. Data after treatment discontinuation due to any other reason were considered missing. Any missing data was imputed using MCMC-MI. The categorical primary and key secondary endpoints were analyzed using the Cochran-Mantel-Haenszel test.

[b] Subjects received 500 mg of Ebglyss at Week 0 and Week 2, and 250 mg Q2W up to Week 16.

[c] Responder was defined as a subject with an IGA 0 or 1 (“clear” or “almost clear”) and a reduction of ≥ 2 points on a 0-4 IGA scale, or a 75% reduction in EASI from Baseline to Week 16, respectively.

[d] A prespecified graphical multiple testing procedure was used to control the overall Type I error rate at a 2-sided alpha of 0.05 for all primary and key secondary endpoints.

A greater proportion of patients randomized to Ebglyss achieved improvement in Pruritus NRS ($p < 0.01$) or in EASI 90 ($p < 0.05$) as early as Week 4 compared to placebo. The proportion of patients responding on Pruritus NRS or EASI 90 continued to increase through the treatment period.

In the monotherapy trials ADvocate 1 and ADvocate 2 (pooled), 291 Ebglyss-treated patients who were responders at Week 16 were re-randomized to 36 weeks of treatment, with 118 patients re-randomized to treatment with Ebglyss 250 mg Q4W dose regimen. 59/77 (76.9%) patients who were IGA 0,1 responders at Week 16 and 94/115 (81.7%) patients who were EASI 75 responders at Week 16 maintained their response through Week 52.

Quality of Life/Patient-Reported Outcomes

In both monotherapy studies (ADvocate 1 and ADvocate 2) and in the TCS combination study (ADhere), improvements in patient reported outcomes were associated with Ebglyss 250 mg Q2W.

In ADvocate 1, the proportion of Ebglyss-treated responders for Sleep-Loss Scale (with baseline Sleep-Loss Scale ≥ 2) and DLQI (with baseline DLQI ≥ 4) was 39% and 76%, respectively, compared to 5% and 34% for placebo at Week 16.

In ADvocate 2, the proportion of Ebglyss-treated responders for Sleep-Loss Scale (with baseline Sleep-Loss Scale ≥ 2) and DLQI (with baseline DLQI ≥ 4) was 28% and 66%, respectively, compared to 8% and 34% for placebo at Week 16.

In ADhere, the proportion of Ebglyss-treated responders for Sleep-Loss Scale (with baseline Sleep-Loss Scale ≥ 2) and DLQI (with baseline DLQI ≥ 4) was 35% and 77%, respectively, compared to 18% and 59% for placebo at Week 16.

Adolescents (12 to < 18 years of age)

In the monotherapy studies ADvocate 1 and ADvocate 2, the mean age of adolescent subjects was 14.6 years, the mean weight was 68.2 kg, and 56.9% were female. In these studies, 63.7% had a baseline IGA of 3 (moderate atopic dermatitis), 36.3% had a baseline IGA of 4 (severe atopic dermatitis), and 47.1% had received prior systemic treatment.

In the concomitant study with TCS ADhere, the mean age of adolescent subjects was 14.6 years, mean weight was 62.2 kg, and 50.0% were female. In this study, 76.1% had a baseline IGA of 3 (moderate atopic dermatitis), 23.9% had a baseline IGA of 4 (severe atopic dermatitis), and 23.9% had received prior systemic treatment.

By week 16, clinically meaningful efficacy results were demonstrated in adolescent subjects treated with Ebglyss and Ebglyss + TCS and were consistent with the results observed in the adult population.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Repeat dose studies and safety pharmacology evaluations administering

lebrikizumab to primarily sexually-immature cynomolgus monkeys did not reveal lebrikizumab-related adverse effects. Lebrikizumab was administered once weekly to male and female cynomolgus monkeys (3/sex/group; 2.4-3.4 years of age) at dose levels of 0, 5, and 25 mg/kg by subcutaneous (SC) injection for 3 months (13 doses) or once weekly by intravenous (IV) injection to male and female monkeys (4/sex/group; 2.5-4.5 years of age) for up to 9 months (39 doses) at dose levels of 0, 1, 5, and 25 mg/kg. There were no deaths or treatment-related adverse clinical signs or findings noted during physical or ophthalmic examinations. There were no adverse effects on ECG parameters, body weight, food consumption, clinical chemistry, hematology, coagulation or urinalysis parameters, peripheral blood immunophenotype, organ weights, or tissue morphology attributed to lebrikizumab. The NOAEL was the high dose of 25 mg/kg/week IV. Margins of exposure were not calculated based on a lack of toxicokinetic data from the pivotal 9-month study. However, $C_{avg,ss}$ at the NOAEL is expected to approximate the $C_{avg,ss}$ observed in a 9-month female monkey fertility study on the basis of similar peak serum concentrations in both males and females. At the NOAEL of 25 mg/kg administered once a week, systemic exposure is approximately 15 to 18 times higher than adolescents and adults at the recommended human dose (500 mg SC W0 and W2, then 250 mg SC Q2W), based on $C_{avg,ss}$.

Carcinogenicity: Nonclinical studies have not been conducted to evaluate the carcinogenic potential of lebrikizumab.

Genotoxicity: Nonclinical studies have not been conducted to evaluate the mutagenic or genotoxic potential of lebrikizumab.

Reproductive and Developmental Toxicology: No lebrikizumab-related adverse effects on reproductive organs, reproductive hormones, menstrual cycles, spermatogenesis or sperm were observed in sexually mature cynomolgus monkeys that received lebrikizumab at a dose of 25 mg/kg weekly for 37 weeks (females; intravenous route) or 13 weeks (males; subcutaneous route). Exposure at 25 mg/kg once a week in male and female cynomolgus monkeys is 11 to 14 or 15 to 18 times the adolescent and adult exposure at the recommended human dose (500 mg SC W0 and W2, then 250 mg SC Q2W), respectively, based on $C_{avg,ss}$.

In an embryofetal development study, no malformations or embryofetal toxicity were observed in fetuses from pregnant cynomolgus monkeys administered lebrikizumab during organogenesis (GD 20 to GD 48) at an initial dose of 150 mg/kg followed by 50 mg/kg per week by subcutaneous injection, 22 times (adults) the human exposure ($C_{avg,ss}$) at the recommended dose (500 mg/kg SC W0 and W2, then 250 mg SC Q2W) based on $C_{avg,ss}$. Lebrikizumab was detected in fetal serum at concentrations that were approximately 30% of maternal serum concentrations at all tested dose levels indicating that lebrikizumab crossed the placenta in monkeys.

In a pre- and post-natal development study, pregnant cynomolgus monkeys were administered lebrikizumab from GD 35 to parturition at 150 mg/kg initial followed by 50 mg/kg per week by subcutaneous injection. No embryofetal toxicity or malformations, or effects on morphological, functional, or immunological development were observed in the infants from birth through 6 months of age. Serum lebrikizumab concentrations in all offspring were higher than maternal serum concentrations until the end of the observation period on post-natal day (PND) or lactation day (LD) 180. The NOAEL was 150 mg/kg followed by 50 mg/kg/week (leading dose followed by maintenance dose). Margins of exposure were not calculated based on a lack of toxicokinetic data. However, $C_{avg,ss}$ at the NOAEL is expected to approximate the $C_{avg,ss}$ observed in the embryofetal development study on the basis of similar trough serum concentrations in females. At the NOAEL of 150 mg/kg followed by 50 mg/kg/week, systemic

exposure is approximately 22 times (adults) the human exposure ($C_{avg,ss}$) at the recommended human dose (500 mg SC W0 and W2, then 250 mg SC Q2W) based on $C_{avg,ss}$

Juvenile Toxicity: Juvenile toxicity studies were not conducted with lebrikizumab.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrEbglyss™

lebrikizumab injection

Read this carefully before you start taking **Ebglyss** 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 **Ebglyss**.

What is Ebglyss used for?

- Ebglyss is a prescription medicine used to treat adults and adolescents 12 years of age and older who weigh at least 40 kg with moderate-to-severe atopic dermatitis (eczema) that is not well controlled with prescription therapies used on the skin (topical), or who cannot use topical therapies. Ebglyss can be used with or without topical corticosteroids.
- It is not known if Ebglyss is safe and effective in adolescents with atopic dermatitis who weigh less than 40 kg or in children under 12 years of age.

How does Ebglyss work?

Ebglyss contains the active substance lebrikizumab.

Lebrikizumab is a monoclonal antibody. Monoclonal antibodies are a type of specialized protein that recognizes and binds specifically to certain proteins in the body.

Ebglyss works by blocking a protein called IL-13, which is found in higher amounts in people with atopic dermatitis. This can result in reduced inflammation, improved condition of your skin, and reduced itch, redness and scaling.

What are the ingredients in Ebglyss?

Medicinal ingredients: lebrikizumab

Nonmedicinal ingredients: glacial acetic acid, histidine, polysorbate 20, sucrose, and water for injection.

Ebglyss comes in the following dosage forms:

- 250 mg/2 mL single use prefilled pen
- 250 mg/2 mL single use prefilled syringe with needle shield
- Ebglyss prefilled pen and prefilled syringe with needle shield are not made with natural rubber latex.

Do not use Ebglyss if:

You are allergic to lebrikizumab or to any of the other ingredients of this medicine.

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

- have eye problems (e.g., itching, redness)
- have a parasitic worm (helminth) infection
- are scheduled to receive any vaccinations. You should not receive a "live vaccine" if you are treated with Ebglyss.
- are pregnant or plan to become pregnant. It is not known if Ebglyss will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Ebglyss passes into your breast milk.

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

The following may interact with Ebglyss:

- Inform your healthcare professional if you have recently had or are going to have a vaccination. You should not receive "live vaccines" while using Ebglyss.

How to take Ebglyss:

- **See the Instructions for Use that comes with this Patient Medication Information about how to prepare and inject Ebglyss and how to properly store and throw away (dispose of) used Ebglyss prefilled pens and prefilled syringes.**
- Use Ebglyss exactly as prescribed by your healthcare professional.
- Ebglyss comes as a single use prefilled pen or prefilled syringe with needle shield.
- Ebglyss is given by injection under the skin (subcutaneous injection).
- If your healthcare professional decides that you or a caregiver can give the injections of Ebglyss, you or a caregiver should receive training on the right way to prepare and inject Ebglyss.
- Do not try to inject Ebglyss until you have been shown the right way by your healthcare professional. In people under the age of 18 years, Ebglyss should be given by an adult.
- Inject Ebglyss in your stomach area (abdomen) or thigh, or have a caregiver inject Ebglyss in the back of your upper arm.
- Your healthcare professional may prescribe other medicines to use with Ebglyss. Use the other prescribed medicines exactly as your healthcare professional tells you to.
- If you have questions about when you should use Ebglyss, ask your healthcare professional.
- Do not use this medication if it looks cloudy or is leaking.

Usual dose:

Each prefilled pen and prefilled syringe with needle shield contain 250 mg of Ebglyss to be injected under the skin (subcutaneously).

- The initial dose of Ebglyss is 500 mg (two injections) at Week 0 and Week 2, followed by 250 mg (one injection) every two weeks until Week 16.
- The maintenance dose is 250 mg every four weeks starting at Week 16.

Overdose:

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

Missed Dose:

If you miss a dose, inject the missed dose as soon as possible, then continue dosing at your regularly scheduled time, starting on the new dosing day.

What are possible side effects from using Ebglyss?

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

The most common side effects of Ebglyss include:

- Eye and eyelid inflammation, including redness, swelling, itching, and dryness
- Injection site reactions
- Shingles (herpes zoster)
- High count of certain white blood cells

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 in the original carton to protect from light.

If necessary, Ebglyss may be kept at room temperature up to 30°C for up to 7 days in the original carton. Throw away Ebglyss if not used within 7 days at room temperature.

Do not freeze. Do not use Ebglyss if it has been frozen.

Do not shake.

Discard the Ebglyss single use prefilled pen or prefilled syringe with needle shield after use in a

puncture-resistant container.

Keep out of reach and sight of children.

If you want more information about Ebglyss:

- 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 1-800-545-5972.

Ebglyss is a trademark owned by or licensed to Eli Lilly and Company, its subsidiaries or affiliates.

This leaflet was prepared by Eli Lilly Canada, Inc.

Last Revised MON DD, YYYY

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INSTRUCTIONS FOR USE

PrEBGLYSS™ [EHB-glihs]

(lebrikizumab)

injection, for subcutaneous use

Single Use Prefilled Syringe with Needle Shield

Read these Instructions for Use before you use Ebglyss and carefully follow all the step-by-step instructions.

Important information for the Ebglyss Prefilled Syringe with Needle Shield:

Do not inject yourself or someone else until you have been shown how to inject Ebglyss. Your healthcare professional should show you or your caregiver how to prepare and inject Ebglyss before you do it yourself the first time. You and your caregiver should read these Instructions for Use before you start using Ebglyss and each time you get a refill. Keep these instructions and refer to them as needed. Call your healthcare professional if you have any questions.

Each **single use** prefilled syringe with needle shield (called “Ebglyss Prefilled Syringe” in these instructions) contains 250 mg of lebrikizumab for injection under the skin (subcutaneous injection). Do not share or reuse syringes.

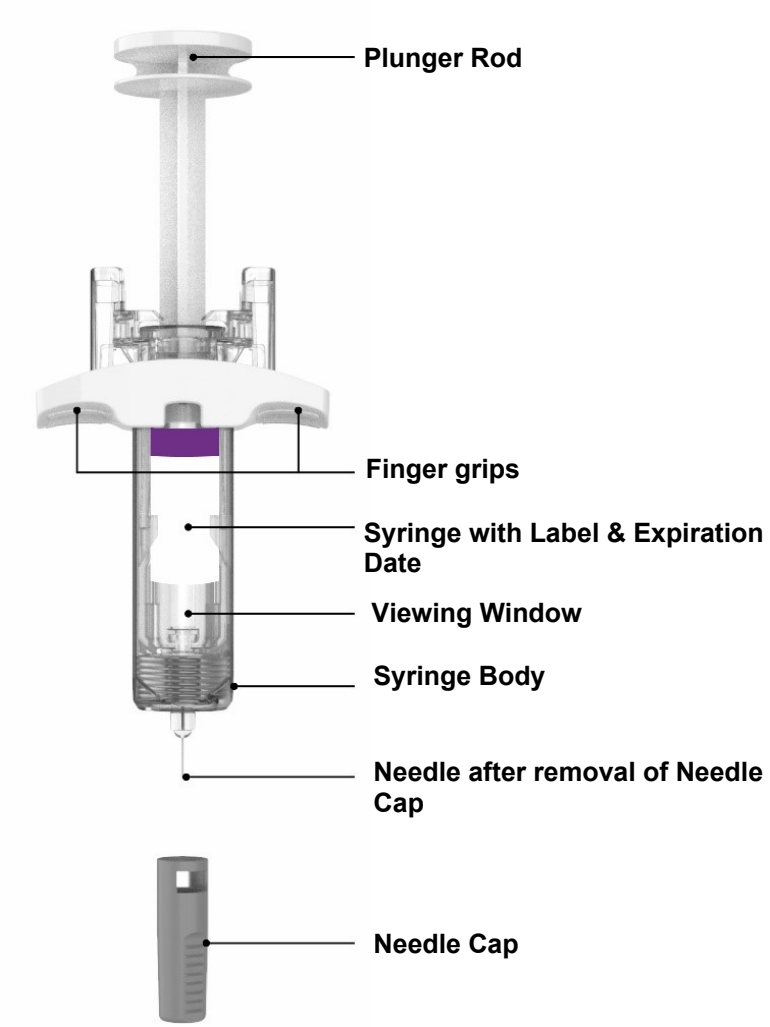
When using the Ebglyss Prefilled Syringe

- Talk to your healthcare professional about how often you will need to inject the medicine.
- Use a different injection site each time you inject.
- If you have vision problems, do not use Ebglyss Prefilled Syringe without help from a caregiver.
- To reduce the risk of accidental needle sticks, each Prefilled Syringe has a Needle Shield that is automatically activated to cover the needle after you have given your injection.
- Throw away (dispose of) your used Ebglyss single use prefilled syringe immediately after use (*see* **Dispose of the Syringe Safely**).
- **Do not** use the Ebglyss Prefilled Syringe if it has been dropped on a hard surface or damaged.
- **Do not** use the Ebglyss Prefilled Syringe if the Needle Cap is missing or not securely attached.
- **Do not** touch the Plunger Rod until you are ready to inject.
- **Do not** get rid of any air bubble in the Ebglyss Prefilled Syringe.
- **Do not** pull back on the Plunger Rod at any time.
- **Do not** inject through clothes.
- **Do not** remove the Needle Cap until right before you are ready to give the injection.
- **Do not re-use an Ebglyss Single Use Prefilled Syringe.**

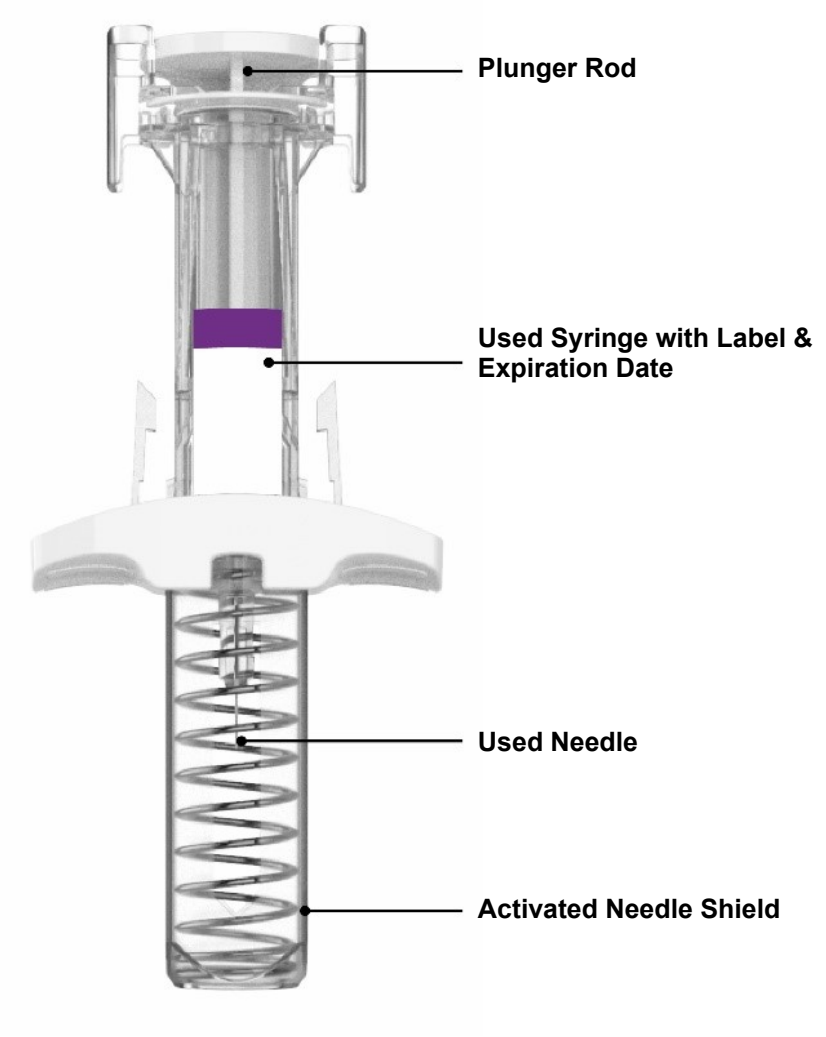
INSTRUCTIONS FOR USE

Read these Instructions for Use before you use Ebglyss and carefully follow all the step-by-step instructions.

Parts of the Ebglyss Prefilled Syringe with Needle Shield Before Use



After Use



How should I store Ebglyss?

- **Keep Ebglyss Prefilled Syringes and all medicines out of the reach and sight of children.**
- Store Ebglyss in a refrigerator, at 2°C to 8°C.
- Keep Ebglyss in the original carton until ready for use to protect from light.
- Ebglyss Prefilled Syringes can be stored at room temperature up to 30°C for up to 7 days. Throw away (dispose of) any Ebglyss Prefilled Syringes that have been left at room temperature for longer than 7 days.
- **Do not** heat or freeze the Ebglyss Prefilled Syringe.
- **Do not** shake the Ebglyss Prefilled Syringe.
- **Do not** put the Ebglyss Prefilled Syringe into direct sunlight.

Preparing to inject Ebglyss

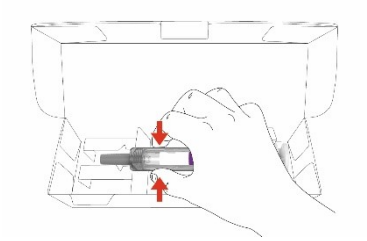
Prepare Supplies

Make sure you have the following:

- 1 Ebglyss Prefilled Syringe with Needle Shield
- 1 alcohol wipe*
- 1 cotton ball or gauze*
- 1 sharps disposal container*

*Items not included with the product.

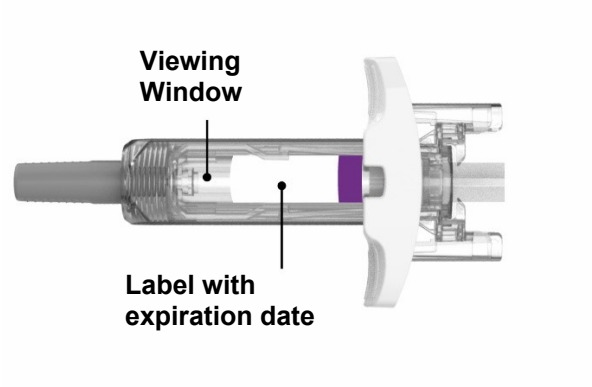
Remove Syringe from Carton



Remove the Ebglyss Prefilled Syringe from the carton by holding the middle of the Syringe Body.

Leave the Needle Cap on until you are ready to inject.

Inspect Prefilled Syringe



When you receive your Ebglyss Prefilled Syringes, **always check to see that you have the correct medicine and dose and visually inspect the syringe**.

Note: You may gently rotate the Plunger Rod to view the syringe label.

The label should read "Ebglyss".

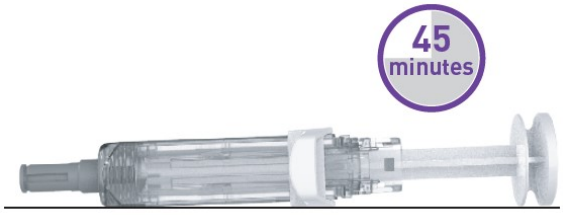
Do not use the Ebglyss Prefilled Syringe if the expiration date has passed.

Do not use the Ebglyss Prefilled Syringe if it has been damaged.

Look at the medicine through the Viewing Window on the Ebglyss Prefilled Syringe. The liquid should be clear and colorless to slightly yellow. *Note: some air bubbles are normal.*

Do not use the Ebglyss Prefilled Syringe if the liquid is discolored or cloudy, or it contains visible flakes or particles, or the syringe shows signs of damage, or the syringe has been dropped, or the medicine is frozen.

Bring to Room Temperature



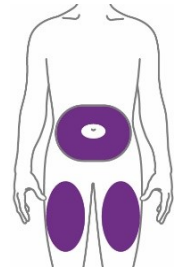
Place the Ebglyss Prefilled Syringe on a flat surface and let it warm to room temperature naturally for at least 45 minutes.

Do not heat the Ebglyss Prefilled Syringe with a microwave or hot water.

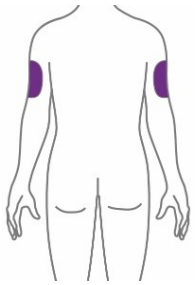
Do not put the Ebglyss Prefilled Syringe into direct sunlight.

Do not keep Ebglyss Prefilled Syringes at room temperature above 30°C for more than 7 days. Throw away (dispose of) any Ebglyss Prefilled Syringes that have been left at room temperature for longer than 7 days.

Choose Your Injection Site



You or another person may inject into these areas.



Another person must inject into this area.

- You can inject into your thigh or stomach area (abdomen), except for 5 centimeters around your belly button (navel).
- If you chose the front of your thigh, you should inject at least 5 centimeters above the knee and 5 centimeters below the groin.
- If you choose the outer area of the upper arm, you will need a caregiver to help you.
- Choose a different injection site each time you inject Ebglyss.

Do not inject into areas where the skin is tender, bruised, red, hard or in an area of skin that is affected by atopic dermatitis or other skin lesions**.**

Prepare Your Skin

Wash your hands thoroughly. Clean the injection site with an alcohol wipe. Let the injection site dry before injecting.

Do not touch the injection site again or blow on it before the injection.

Injecting Ebglyss

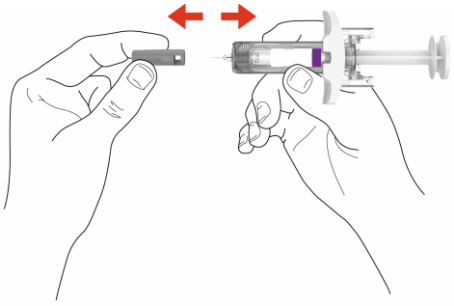
1 **Remove Needle Cap**

Hold the Ebglyss Prefilled Syringe in the middle of the Syringe Body with the Needle pointing away from you, and pull off the Needle Cap.

Do not put the Needle Cap back on.

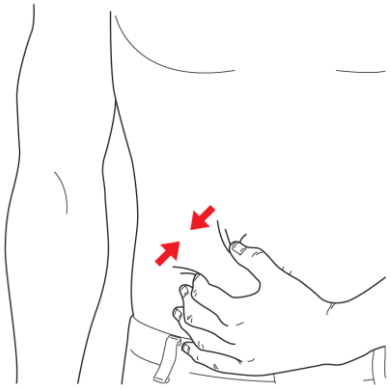
Do not touch the Needle.

Inject your medicine immediately after removing the Needle Cap.



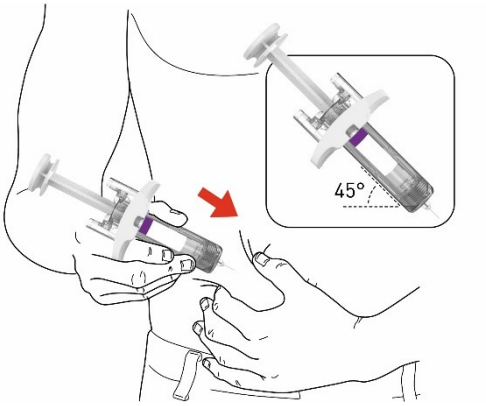
2 **Pinch the Injection Site**

Gently pinch a fold of skin at the injection site (thigh or stomach, except for 5 centimeters around your belly button, or outer area of the upper arm if injected by your caregiver).



3 **Insert the Needle**

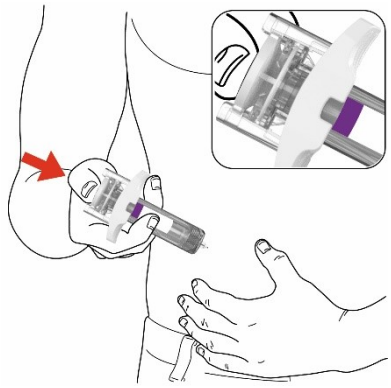
Insert the Needle completely into the fold of skin at about a 45º angle.



4 Push in the Plunger Rod

Gently relax the pinch while keeping the needle in place. Slowly and steadily push the Plunger Rod down all the way until it stops and the syringe is empty**.**

Note: It is normal to feel some resistance.



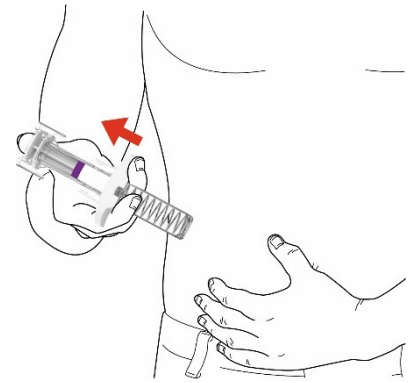
5 Release and Remove

Lift your thumb to release the Plunger Rod until the Needle is covered by the Needle Shield, and then remove the Syringe from the injection site.

Lightly press a cotton ball or gauze on the injection site if you see any blood.

Do not put the Needle Cap back on.

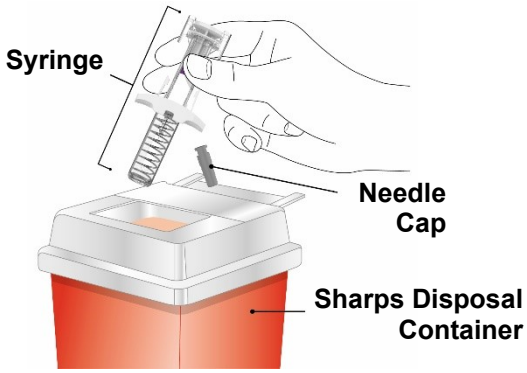
Do not rub your skin after injection.



Dispose of the Syringe Safely

Put your used Ebglyss Prefilled Syringe and Needle Cap in a sharps disposal container immediately after use.

Do not dispose of (throw away) Ebglyss Prefilled Syringes and Needle Caps 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,
- able to be closed with a tight-fitting, puncture resistant lid to keep sharps from falling 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, follow your community guidelines for the right way to dispose of it. There may be provincial or local laws regarding the disposal of used needles and syringes.

For more information about safe sharps disposal, ask your healthcare professional about options available in your area.

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this.

Do not recycle your used sharps disposal container.

Do not put the Needle Cap back on.

If you have more questions about how to use the Ebglyss Prefilled Syringe:

- Call your healthcare professional
- Call 1-888-545-5972
- Visit www.lilly.ca

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

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INSTRUCTIONS FOR USE

PrEBGLYSS™ [EHB-glihs]

(lebrikizumab)

injection, for subcutaneous use

Prefilled Pen (250 mg/2 mL)

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

Before you use the Ebglyss prefilled pen (Pen), read and carefully follow all the step-by-step instructions.

Important Information You Need to Know Before Injecting Ebglyss

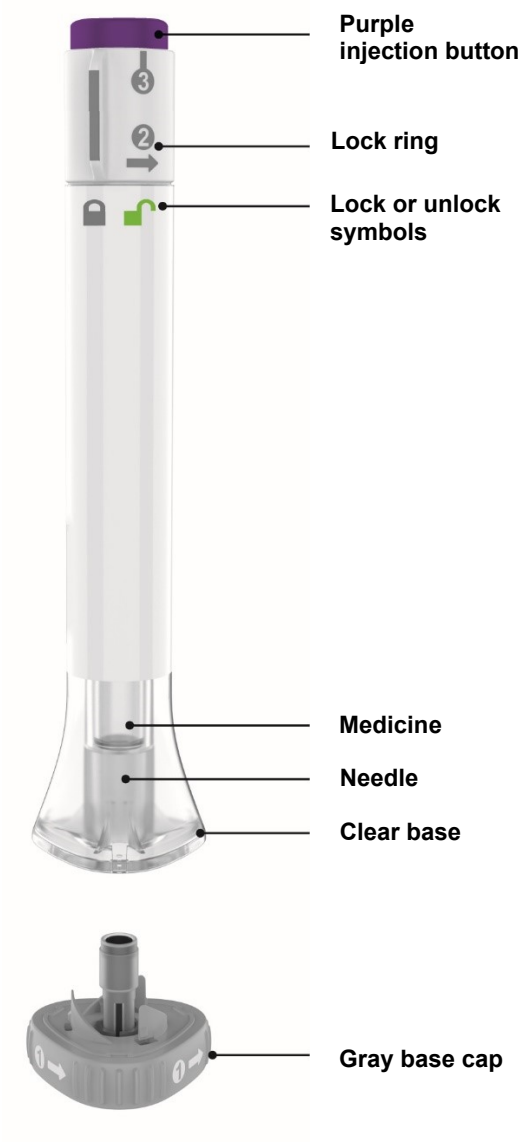
- Your healthcare professional should show you how to prepare and inject Ebglyss using the Pen. **Do not** inject yourself or someone else until you have been shown how to inject Ebglyss.
- Keep this Instructions for Use and read it as needed.
- Each Ebglyss Pen contains 1 dose (250 mg) of Ebglyss. **The Pen is for one-time use only.**
- The Ebglyss Pen contains glass parts. Handle it carefully. If you drop it on a hard surface, **do not** use it. Use a new Ebglyss Pen for your injection.
- Your healthcare professional may help you decide where on your body to inject your dose. You can also read the **Choose and Clean 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 Ebglyss Pen without help from a caregiver.
- See **Storing Ebglyss** for important storage information.

INSTRUCTIONS FOR USE

Before you use the Ebglyss Pen, read and carefully follow all the step-by-step instructions.

Parts of the Ebglyss Pen

Top



Bottom

Preparing to inject Ebglyss

Gather supplies:

- Ebglyss Pen from the refrigerator
- alcohol wipe
- cotton ball or piece of gauze
- sharps disposal container

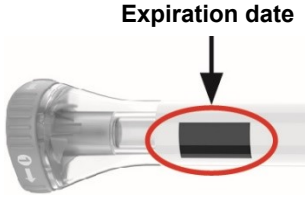
Wait 45 minutes

With the gray base cap on, allow the Pen to warm up to room temperature for 45 minutes before injecting.

- **Do not** warm up the Pen with a microwave, or hot water, or direct sunlight.
- **Do not** use the Pen if the medicine is frozen.

Inspect the Pen and the medicine

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



Do not use the Pen (see **Disposing of Ebglyss**) if the:

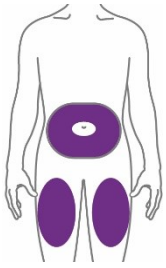
- Pen looks damaged
- medicine is cloudy, is discolored, or has particles
- expiration date printed on the label has passed

Wash your hands with soap and water

Choose and Clean your injection site

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

Clean the injection site with an alcohol wipe and let dry.



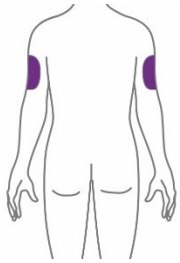
You or another person may inject into these areas.

- **Stomach area (abdomen) —**

  At least 5 centimeters away from the belly button (navel).

- **Front of thigh —**

  At least 5 centimeters above the knee and 5 centimeters below the groin.



Another person must inject into this area.

- **Back of upper arm —**

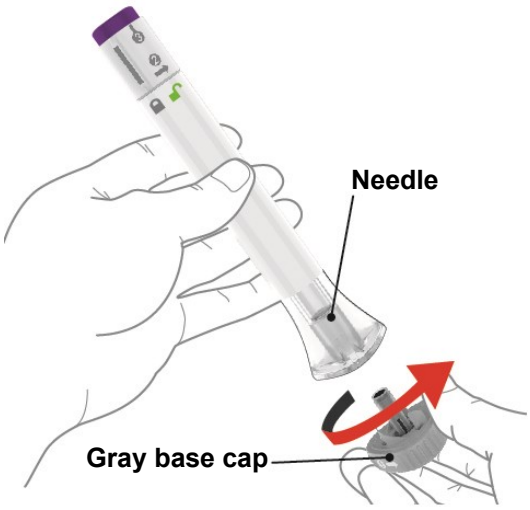
  Another person must inject into the back of your upper arm.

Do not inject in the exact same spot every time.

Do not inject into areas where the skin is tender, bruised, red, hard, or in an area of skin that is affected by atopic dermatitis or other skin lesions.

Injecting Ebglyss

1 Uncap the Pen



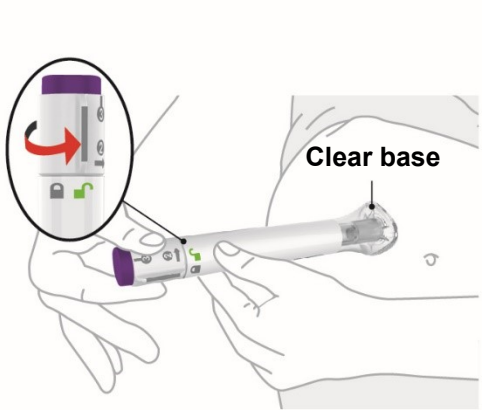
Make sure the Pen is **locked**.

When 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 inside the clear base.

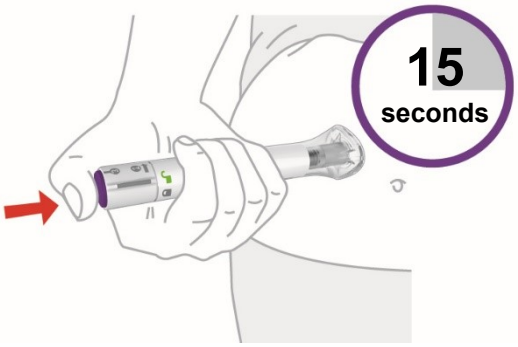
2 Place and Unlock



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 15 Seconds



Press and Hold the purple injection button and **Listen** for two loud clicks:

- first click = injection started
- second click = injection completed

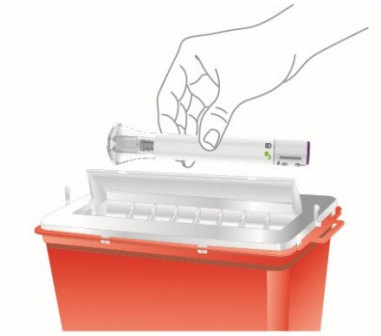
The injection may take up to 15 seconds.

You will know the injection is complete when the gray plunger is visible.

Gray Plunger

Disposing of Ebglyss

Throw away the used Pen



Put the used Ebglyss Pen in a sharps disposal container right away after use.

Do not throw away (dispose of) the Ebglyss Pen 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 provincial or local laws about how you should throw away needles and pens.

Do not recycle your used sharps disposal container.

Commonly Asked Questions

Q. What if I see bubbles in the Pen?

A. Air bubbles are normal. 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. A drop of liquid on the tip of the needle is normal. This will not harm you or affect your dose.

Q. What if I unlock the Pen and press the purple injection button before twisting off the gray base cap?

A. **Do not** remove the gray base cap. Throw away (dispose of) the Pen and use a new one.

Q. Do I need to hold the purple injection button down until the injection is complete?

A. You do not need to hold the purple 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 Lilly at 1-888-545-5979 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. How can I tell if my injection is complete?

A. After you press the purple 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. The injection may take up to 15 seconds.

Q. What if I remove the Pen before the second loud click or before the gray plunger stops moving?

A. You may not have received your full dose. **Do not** give another injection. Call your healthcare professional for help.

Q. What if I heard more than 2 clicks during my injection — 2 loud clicks and 1 soft one. Did I get my complete injection?

A. Some people 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.

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

- Call your healthcare professional
- Call 1-888-545-5972
- Visit www.lilly.ca

Storing Ebglyss

- Store your Pen in the refrigerator between 2°C to 8°C.
- Your Pen may be stored at room temperature for up to 7 days. **Do not** store above 30°C. Throw away (dispose of) Ebglyss if not used within 7 days at room temperature.
- **Do not** freeze your Pen.
- Store your Pen in the original carton to protect your Pen from light.
- **Do not** microwave your Pen, or run hot water over it, or leave it in direct sunlight.
- **Do not** shake your Pen.
- Throw away (dispose of) your Pen if any of the above conditions are not followed.
- **Keep your Pen and all medicines out of the reach and sight of children.**

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

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