

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

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

1. NAME OF THE MEDICINAL PRODUCT

Ebglyss 250 mg solution for injection in pre-filled syringe
Ebglyss 250 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ebglyss 250 mg solution for injection in pre-filled syringe

Each single-use pre-filled syringe contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

Ebglyss 250 mg solution for injection in pre-filled pen

Each single-use pre-filled pen contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

Lebrikizumab is produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.

Excipient with known effect

Each Ebglyss 250 mg solution for injection in pre-filled syringe contains 0.6 mg of polysorbate 20 (E 432).

Each Ebglyss 250 mg solution for injection in pre-filled pen contains 0.6 mg of polysorbate 20 (E 432).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

Clear to opalescent, colourless to slightly yellow to slightly brown solution, free of visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ebglyss is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older with a body weight of at least 40 kg who are candidates for systemic therapy.

4.2 Posology and method of administration

Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of atopic dermatitis.

Posology

The recommended dose of lebrikizumab is 500 mg (two 250 mg injections) at both week 0 and week 2, followed by 250 mg administered subcutaneously every other week up to week 16.

Consideration should be given to discontinuing treatment in patients who have shown no clinical response after 16 weeks of treatment. Some patients with initial partial response may further improve with continued treatment every other week up to week 24.

Once clinical response is achieved, the recommended maintenance dose of lebrikizumab is 250 mg every fourth week.

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

Missed dose

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

Special populations

Elderly (≥ 65 years)

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

Renal and hepatic impairment

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

Body weight

No dose adjustment for body weight is recommended (see section 5.2).

Paediatric population

The safety and efficacy of lebrikizumab in children aged 6 months to <12 years or adolescents 12 to 17 years of age and weighing less than 40 kg have not yet been established. No data are available.

Method of administration

Subcutaneous use.

Lebrikizumab is administered by subcutaneous injection into the thigh or abdomen, except for 5 cm around the navel. If somebody else administers the injection, the upper arm can also be used.

For the initial 500 mg dose, two 250 mg injections should be administered consecutively in different injection sites.

It is recommended to rotate the injection site with each injection. Lebrikizumab should not be injected into skin that is tender, damaged or has bruises or scars.

A patient may self-inject lebrikizumab or the patient's caregiver may administer lebrikizumab if their healthcare professional determines that this is appropriate. Proper training should be provided to patients and/or caregivers on the administration of lebrikizumab prior to use. Detailed instructions for use are included at the end of the package leaflet.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Traceability

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

Hypersensitivity

If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of lebrikizumab should be discontinued and appropriate therapy initiated.

Conjunctivitis

Patients treated with lebrikizumab who develop conjunctivitis that does not resolve following standard treatment should undergo ophthalmological examination (see section 4.8).

Helminth infection

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 signalling.

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

Vaccinations

Prior to initiating therapy with lebrikizumab, it is recommended that patients are brought up to date with all age-appropriate immunisations according to current immunisation guidelines. Live and live attenuated vaccines should not be given concurrently with lebrikizumab as clinical safety and efficacy has not been established. Immune responses to non-live vaccines were assessed in a combined tetanus, diphtheria and acellular pertussis vaccine (Tdap) and a meningococcal polysaccharide vaccine (see section 4.5).

Excipients

This medicine contains 0.6 mg of polysorbate 20 (E 432) in each pre-filled syringe or pre-filled pen of 250 mg, which is equivalent to 0.3 mg/mL. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Live vaccines

The safety and efficacy of concurrent use of lebrikizumab with live and live attenuated vaccines has not been studied. Live and live attenuated vaccines should not be given concurrently with lebrikizumab.

Non-live vaccines

Immune responses to non-live vaccines were assessed in a study (ADopt-VA) in which adult patients with atopic dermatitis were treated with lebrikizumab 500 mg at weeks 0 and 2 followed by lebrikizumab 250 mg every other week. After 12 weeks of lebrikizumab administration, patients were vaccinated with a combined tetanus, diphtheria, and acellular pertussis vaccine Tdap vaccine (T cell-dependent) and a meningococcal polysaccharide vaccine (T cell-independent) and immune responses were assessed 4 weeks later. Antibody responses to both non-live vaccines were not negatively impacted by the concomitant lebrikizumab treatment. No adverse interactions between the non-live vaccines and lebrikizumab were noted in the study. Therefore, patients receiving lebrikizumab may receive concurrent inactivated or non-live vaccinations. For information on live vaccines see section 4.4.

Concomitant therapies

Given that lebrikizumab is a monoclonal antibody, no pharmacokinetic interactions are expected.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breast-feeding

It is unknown whether lebrikizumab is excreted in human milk or absorbed systemically after ingestion. Maternal IgG is known to be present in human milk. 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.

Fertility

Animal studies showed no impairment of fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions are conjunctivitis (6.9%), injection site reactions (2.6%), conjunctivitis allergic (1.8%) and dry eye (1.4%).

Tabulated list of adverse reactions

Across all clinical studies in atopic dermatitis, a total of 1720 patients were administered lebrikizumab, of which, 891 patients were exposed to lebrikizumab for at least one year. Unless otherwise stated, the frequencies are based on a pool of 4 randomised, double-blind studies in patients with moderate-to-severe atopic dermatitis where 783 patients were treated with subcutaneous lebrikizumab during the placebo-controlled period (first 16 weeks of treatment).

Listed in Table 1 are adverse reactions observed from clinical trials presented by system organ class and frequency, using the following categories: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1\ 000$ to $< 1/100$); rare ($\geq 1/10\ 000$ to $< 1/1\ 000$); very rare ($< 1/10\ 000$). Within each frequency grouping the adverse reactions are presented in the order of decreasing seriousness.

Table 1. List of adverse reactions

MedDRA System Organ Class	Frequency	Adverse reaction
Infections and infestations	Common	Conjunctivitis
	Uncommon	Herpes zoster
Blood and lymphatic system disorders	Uncommon	Eosinophilia
Eye disorders	Common	Conjunctivitis allergic
	Uncommon	Dry eye Keratitis Blepharitis
General disorders and administration site conditions	Common	Injection site reaction

Description of selected adverse reactions

Conjunctivitis and related events

During the first 16 weeks of treatment conjunctivitis, conjunctivitis allergic, blepharitis and keratitis were reported more frequently in patients treated with lebrikizumab (6.9%, 1.8%, 0.8% and 0.6% respectively) compared to placebo (1.8%, 0.7%, 0.2% and 0.3%).

During maintenance treatment period (16-52 weeks) the incidence of conjunctivitis and conjunctivitis allergic with lebrikizumab was 5.0% and 5.9% respectively.

Across all clinical studies, among lebrikizumab-treated patients treatment discontinuation due to conjunctivitis and conjunctivitis allergic occurred in 0.7% and 0.3% of cases, respectively. Severe cases of conjunctivitis and conjunctivitis allergic occurred in 0.1% and 0.2% of cases, respectively. 72% of patients recovered, of those 57% recovered within 90 days.

Eosinophilia

Lebrikizumab-treated patients had a greater mean increase from baseline in eosinophil count compared to patients treated with placebo. In lebrikizumab treated patients 20.3% had any increase in eosinophil count compared to 11.7% with placebo. In general, the increase in the lebrikizumab-treated patients was mild or moderate and transient. Eosinophilia ≥ 5000 cells/mcL was observed in 0.4% lebrikizumab-treated patients and none of the placebo-treated patients. Adverse reactions of eosinophilia were reported in 0.6% of patients treated with lebrikizumab and with a similar rate in patients treated with placebo during the initial treatment period. Eosinophilia did not result in treatment discontinuation and no eosinophil-related disorders were reported.

Injection site reactions

Injection site reactions (including pain and erythema) were reported more frequently in patients who received lebrikizumab (2.6%) compared to placebo (1.5%). The majority (95 %) of injection site reactions were mild or moderate in severity, and few patients ($< 0.5\%$) discontinued lebrikizumab treatment.

Herpes zoster

Herpes zoster was reported in 0.6% of the patients-treated with lebrikizumab and none of the patients in the placebo group. All herpes zoster events reported were mild or moderate in severity and none led to permanent discontinuation of treatment.

Long term safety

The safety of lebrikizumab was assessed in adults and adolescents with up to 3 years of continuous treatment. A total of 1153 patients were enrolled in the ADjoin extension study, either directly or from studies ADvocate-1, ADvocate-2, and ADore, with up to 1 year of exposure, or from studies ADhere and Adopt-VA, with up to 16 weeks of exposure, and 771 patients completed 2 years of additional lebrikizumab treatment in ADjoin. The safety profile remained consistent with longer exposure to lebrikizumab, and no new safety concerns were observed.

Paediatric population

Adolescents 12 to 17 years of age

The safety of lebrikizumab was assessed in 372 patients 12 to 17 years of age with moderate-to-severe atopic dermatitis, including 270 patients exposed for at least one year. The safety profile of lebrikizumab in these patients was similar to the safety profile in adults with atopic dermatitis.

Reporting of suspected adverse reactions

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

4.9 Overdose

Single intravenous doses up to 10 mg per kg of body weight and multiple subcutaneous doses up to 500 mg have been administered to humans in clinical trials without dose-limiting toxicity. There is no specific treatment for lebrikizumab overdose. In the event of overdose, the patient should be monitored for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other dermatological preparations, agents for dermatitis, excluding corticosteroids, ATC code: D11AH10

Mechanism of action

Lebrikizumab is an immunoglobulin (IgG4) monoclonal antibody that binds with high affinity to interleukin (IL)-13 and selectively inhibits IL-13 signalling through the IL-4 receptor alpha (IL-4R α)/IL-13 receptor alpha 1 (IL-13R α 1) heterodimer, thereby inhibiting the downstream effects of IL-13. Inhibition of IL-13 signalling is expected to be of benefit in diseases in which IL-13 is a key contributor to the disease pathogenesis. Lebrikizumab does not prevent the binding of IL-13 to the IL-13 receptor alpha 2 (IL-13R α 2 or decoy receptor), which allows the internalisation of IL-13 into the cell.

Pharmacodynamic effects

In lebrikizumab clinical studies, lebrikizumab reduced the levels of serum periostin, total immunoglobulin E (IgE), CC chemokine ligand (CCL)17 [thymus and activation-regulated chemokine (TARC)], CCL18 [pulmonary and activation-regulated chemokine (PARC)], and CCL13 [monocyte chemotactic protein-4 (MCP-4)]. The decreases in the type 2 inflammation mediators provide indirect evidence of inhibition of the IL-13 pathway by lebrikizumab.

Immunogenicity

Anti-drug antibodies (ADA) were commonly detected. No evidence of ADA impact on pharmacokinetics, efficacy or safety was observed.

Clinical efficacy and safety

Adults and adolescents with atopic dermatitis

The efficacy and safety of lebrikizumab as monotherapy (ADvocate-1, ADvocate-2) and with concomitant TCS (ADhere) were evaluated in three randomised, double-blind, placebo-controlled pivotal studies in 1062 adults and adolescents (aged 12 to 17 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) ≥ 3 , and a body surface area (BSA) involvement of $\geq 10\%$. Patients enrolled into the three studies previously had an inadequate response to topical medication or determination that topical treatments are otherwise medically inadvisable.

In all three studies, patients received an initial dose of 500 mg of lebrikizumab (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-mid potency TCS or TCI on active lesions. 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.

Patients achieving IGA 0 or 1 or at least a 75% reduction in EASI (EASI 75) without having received any rescue therapy were re-randomised in a blinded manner to (i) lebrikizumab 250 mg Q2W; (ii) lebrikizumab 250 mg every 4 weeks (Q4W); or (iii) matching placebo up to 52 weeks.

In ADvocate-1 and 2, patients not achieving IGA 0 or 1 or EASI 75 at week 16, or who received rescue medication prior to week 16, were entered into an Escape Arm and treated with open-label lebrikizumab 250 mg Q2W through Week 52.

In ADvocate-1 and ADvocate-2, after completing the 52-week study, and in ADhere, after completing the 16-week study, patients were offered the option to continue treatment in a separate long-term extension study (ADjoin).

Endpoints

In all three studies, the co-primary endpoints were the percentage of patients with IGA 0 or 1 ("clear" or "almost clear"), with a ≥ 2 -point reduction from baseline, and the percentage of patients achieving EASI 75 from baseline to week 16. Key secondary endpoints (adjusted for multiplicity) included the percentage of patients who achieved at least a 90% reduction in EASI (EASI 90), percentage of patients with at least 4-point improvement from baseline in Pruritus Numerical Rating Scale (Pruritus NRS), percentage of patients with at least 4-point improvement from baseline in Dermatology Life Quality Index (DLQI) and interference of itch on sleep (Sleep-Loss Scale), which is a patient-reported, single-item, daily scale measuring the extent of interference of itch on sleep over the last night on a 5-point Likert scale. An additional secondary endpoint (not adjusted for multiplicity) included the change from baseline in Patient Oriented Eczema Measure (POEM).

Patients

Baseline characteristics

The monotherapy studies ADvocate-1 and ADvocate-2 enrolled 424 and 427 patients, respectively, and across studies the mean age was 35.8, the mean weight was 77.1 kg, 49.9% were female, 63.7% were white, 22.6% were Asian, and 9.9% were black, 12.0% were adolescents (12 to 17 years). Overall, 61.5% of patients had a baseline IGA of 3 (moderate atopic dermatitis), 38.5% of patients had a baseline IGA of 4 (severe atopic dermatitis), and 54.8% of patients had received prior systemic treatment. The mean baseline EASI was 29.6, the mean baseline Pruritus NRS was 7.2 and the mean baseline DLQI was 15.5.

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

Clinical response

Monotherapy studies (ADvocate-1 and ADvocate-2) – induction period, weeks 0-16

In ADvocate-1 and ADvocate-2, a significantly greater proportion of patients randomised to lebrikizumab 250 mg Q2W achieved IGA 0 or 1 with a ≥ 2 -point improvement from baseline, EASI 75, EASI 90, and an improvement of ≥ 4 points in Pruritus NRS and DLQI compared to placebo at week 16 (see Table 2).

In both monotherapy studies, lebrikizumab reduced daily worst itch severity compared to placebo, as measured by the percent change from baseline in Pruritus NRS, already at week 1 of treatment. The improvement in Pruritus NRS occurred in conjunction with improvements in skin inflammation related to atopic dermatitis and quality of life.

Table 2. Efficacy results of lebrikizumab monotherapy at week 16 in ADvocate-1 and Advocate-2

	ADvocate-1		ADvocate-2	
	Week 16			
	Placebo N=141	LEB 250 mg Q2W N=283	Placebo N=146	LEB 250 mg Q2W N=281
IGA 0 or 1, % ^a	12.7	43.1***	10.8	33.2***
EASI 75, % ^b	16.2	58.8***	18.1	52.1***
EASI 90, % ^b	9.0	38.3***	9.5	30.7***
Pruritus NRS (≥ 4-point improvement), % ^c	13.0	45.9***	11.5	39.8***
DLQI (Adults) (≥ 4-point improvement), % ^d	33.8	75.6***	33.6	66.3***

LEB = lebrikizumab; N = number of patients.

^a Patients with IGA 0 or 1 (“clear” or “almost clear”) with a reduction of ≥ 2 points from baseline on a 0-4 IGA scale.

^b Patients with a 75% or 90% reduction in EASI from Baseline to Week 16, respectively.

^c The percentage is calculated relative to the number of patients with a baseline Pruritus NRS ≥ 4 .

^d The percentage is calculated relative to the number of patients with a baseline DLQI ≥ 4 .

*** p<0.001 versus placebo.

In the two studies, fewer patients randomised to lebrikizumab needed rescue treatment (topical corticosteroids, systemic corticosteroids, immunosuppressants) as compared to patients randomised to placebo (14.7% versus 36.6%, respectively, across both studies).

Monotherapy Studies (ADvocate-1 and ADvocate-2) – maintenance period, weeks 16-52

To evaluate maintenance of response, 157 patients from ADvocate-1 and 134 patients from ADvocate-2 treated with lebrikizumab 250 mg Q2W, who achieved IGA 0 or 1 or EASI 75 at week 16 without topical or systemic rescue treatment, were re-randomised in a blinded manner 2:2:1 to an additional 36-week treatment of (i) lebrikizumab 250 mg Q2W, or (ii) lebrikizumab 250 mg Q4W, or (iii) matching placebo for a cumulative 52-week study treatment (see Table 3).

Table 3. Efficacy results of lebrikizumab monotherapy at week 52 in patients responding to treatment at week 16 in ADvocate-1 and ADvocate-2 (pooled analysis)

	ADvocate-1 and ADvocate-2 (pooled)	
	Week 52	
	Placebo ^d (LEB Withdrawal) N=60	LEB 250 mg Q4W N=118
IGA 0 or 1, %^a	47.9	76.9**
EASI 75, %^b	66.4	81.7*
EASI 90, %^b	41.9	66.4**
Pruritus NRS (≥ 4-point improvement), %^c	66.3	84.7

^a Patients with IGA 0/1 with a ≥2-point improvement from baseline at week 16 who continued to exhibit IGA 0/1 with a ≥2-point improvement at week 52.

^b Patients who achieved EASI 75 at week 16 and continued to exhibit EASI 75 at week 52, or patients who achieved EASI 75 at Week 16 and exhibited EASI 90 at week 52, respectively.

^c The percentage is calculated relative to the number of patients with a baseline Pruritus NRS ≥4.

^d Patients responding to lebrikizumab 250 mg Q2W at week 16 (IGA 0 or 1 or EASI 75) and re-randomised to placebo.

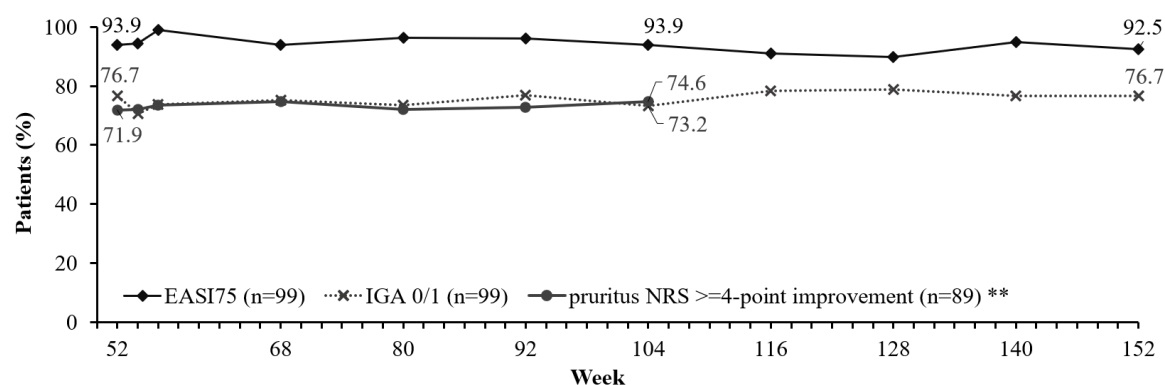
*p<0.05; ** p<0.01 versus placebo.

Among patients who received lebrikizumab during the induction period and continued lebrikizumab 250 mg Q2W open-label treatment up to week 52 in the Escape Arm, 58% achieved EASI 75 and 28% achieved IGA 0 or 1 with a ≥2-point improvement from baseline at week 52 in ADvocate-1 and ADvocate-2 (pooled).

Monotherapy Studies (ADvocate-1 and ADvocate-2) - Long-Term Extension (ADjoin), weeks 52 – 152

Maintenance of clinical response was evaluated in patients who achieved IGA 0 or 1 or EASI 75 at week 16 without topical or systemic rescue treatment, completed 52 weeks of lebrikizumab monotherapy in ADvocate-1 or ADvocate-2, and continued treatment in the 100-week extension study ADjoin. (Figure 1).

Figure 1. IGA 0 or 1, EASI 75, and Pruritus NRS in week 16 treatment responders who completed week 52 in ADvocate-1 and ADvocate-2 and were treated with lebrikizumab 250 mg Q4W in ADjoin*



*Missing data imputed using Markov Chain-Monte Carlo multiple imputation.

** Only in patients with pruritus NRS score ≥ 4 at baseline. Pruritus was evaluated only for the first year of ADjoin.

Concomitant TCS Study (ADhere), weeks 0 - 16

In ADhere, from baseline to week 16, a significantly greater proportion of patients randomised to and dosed with lebrikizumab 250 mg Q2W + TCS achieved IGA 0 or 1, EASI 75, and improvements of ≥ 4 points in the Pruritus NRS and DLQI compared to placebo + TCS (see Table 4).

Table 4. Efficacy results of lebrikizumab combination therapy with TCS at week 16 in ADhere

	ADhere	
	Week 16	
	Placebo + TCS N=66	LEB 250 mg Q2W + TCS N=145
IGA 0 or 1, %^a	22.1	41.2*
EASI 75, %^b	42.2	69.5***
EASI 90, %^b	21.7	41.2**
Pruritus NRS (≥ 4-point improvement), %^c	31.9	50.6*
DLQI (Adults) (≥ 4-point improvement), %^d	58.7	77.4*

^a Patients with IGA 0 or 1 ("clear" or "almost clear") with a reduction of ≥ 2 points from baseline on a 0-4 IGA scale.

^b Patients with a 75% or 90% reduction in EASI from Baseline to week 16, respectively.

^c The percentage is calculated relative to the number of patients with a baseline Pruritus NRS ≥ 4 .

^d The percentage is calculated relative to the number of patients with a baseline DLQI ≥ 4 .

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ versus placebo.

In ADhere, patients who received lebrikizumab 250 mg Q2W+TCS from week 0 to 16 used high potency TCS as rescue medication less often as compared to patients who received placebo + TCS (1.4% and 4.5%, respectively).

Concomitant TCS Study (ADhere) - Long-Term Extension (ADjoin), weeks 16 to 116

Clinical response was maintained among patients who achieved IGA 0 or 1 or EASI 75 at week 16 in ADhere and continued treatment with lebrikizumab 250 mg Q4W in the 100-week extension study ADjoin.

Clinical response in patients not adequately controlled with, intolerant to, or for whom ciclosporin is not medical advisable (ADvantage)

The ADvantage study evaluated the efficacy of lebrikizumab compared to placebo in adults and adolescents (aged ≥ 12 to < 18 years and weighing ≥ 40 kg) with moderate-to-severe atopic dermatitis treated concomitantly with TCS who were not adequately controlled with ciclosporin or for whom ciclosporin was not medically advisable.

A total of 331 patients were enrolled and the mean age was 33.8 years, 52.9% were male, 93.7% identified as white, and adolescents comprised 11.8% of the patient population. At baseline, mean EASI was 28.1, mean Pruritus NRS score was 6.9, and 38.7% of patients had IGA of 4. Overall, 53.2% were previously exposed to ciclosporin (see Table 5).

Table 5. Efficacy results of lebrikizumab combination therapy with TCS at week 16 in ADvantage

	ADvantage	
	Week 16	
	Placebo + TCS N=111	LEB 250 mg Q2W + TCS N=220
EASI 75, %^a	40.8	68.4***
IGA 0 or 1, %^b	24.5	42.0**
EASI 90, %^c	20.8	42.9***
Pruritus NRS (≥ 4-point improvement), %^d	29.7	49.9*
DLQI (Adults) (≥ 4-point improvement), %^e	69.6	78.0

^a Patients with a 75% reduction in EASI from baseline to week 16, respectively.

^b Patients with IGA 0 or 1 ("clear" or "almost clear") with a reduction of ≥ 2 points from baseline on a 0-4 IGA scale.

^c Patients with a 90% reduction in EASI from baseline to week 16, respectively.

^d The percentage is calculated relative to the number of patients with a baseline Pruritus NRS ≥ 4 .

^e The percentage is calculated relative to the number of patients with a baseline DLQI ≥ 4 .

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ versus placebo. p-values for IGA 0 or 1, EASI 90, Pruritus NRS, and DLQI are nominal.

Other patient-reported outcomes

In both monotherapy studies (ADvocate-1 and ADvocate-2) and in the concomitant TCS studies (ADhere and ADvantage) lebrikizumab 250 mg Q2W significantly improved POEM and interference of itch on sleep (Sleep-Loss Scale) at week 16 compared to placebo.

Adolescents (12 to 17 years of age)

In the monotherapy studies ADvocate 1 and ADvocate 2, the mean age of adolescent patients 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 patients 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.

The efficacy results at week 16 in adolescent patients are presented in Table 6.

Table 6. Efficacy results of lebrikizumab monotherapy in ADvocate-1, ADvocate-2 and lebrikizumab combination therapy with TCS in ADhere at week 16 in adolescent patients

	ADvocate-1		ADvocate-2		ADhere	
	Week 16					
	Placebo	LEB 250 mg Q2W	Placebo	LEB 250 mg Q2W	Placebo + TCS	LEB 250 mg Q2W + TCS
	N=18	N=37	N=17	N=30	N=14	N=32
IGA 0 or 1, % ^a	22.2	48.6	5.9	44.1**	28.6	57.3
EASI 75, % ^a	22.2	62.2**	12.0	61.7**	57.1	88.0*
EASI 90, % ^a	16.7	45.9*	6.1	34.3*	28.6	55.1
Pruritus NRS (≥ 4-point improvement). % ^b	22.8	54.3*	0.3	42.1	13.8	45.8

^a At Week 16, patients with IGA 0 or 1 ("clear" or "almost clear") with a reduction of ≥ 2 points from baseline on a 0-4 IGA scale, or a 75% or 90% reduction in EASI from baseline to week 16, respectively.

^b The percentage is calculated relative to the number of patients with a baseline Pruritus NRS ≥ 4 .

* $p < 0.05$; ** $p < 0.01$ versus placebo.

Adolescent patients treated with lebrikizumab and lebrikizumab + TCS achieved clinically meaningful improvements in disease severity and maintained response up to week 52. Additional data from the single-arm ADore study with lebrikizumab in 206 adolescents support the efficacy of lebrikizumab in adolescent patients up to 52 weeks of treatment.

Paediatric population

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

5.2 Pharmacokinetic properties

Absorption

After a subcutaneous dose of 250 mg lebrikizumab, peak serum concentrations were achieved approximately 7 to 8 days post dose.

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.

Based on a population pharmacokinetic (PK) analysis, the predicted steady-state trough concentrations ($C_{trough,ss}$) following lebrikizumab 250 mg Q2W and Q4W subcutaneous dosing in patients with atopic dermatitis (median and 5th - 95th percentile) were 87 (46-159) $\mu\text{g/mL}$ and 36 (18-68) $\mu\text{g/mL}$, respectively.

The absolute bioavailability was estimated at 86% based on a population PK analysis. Injection site location did not significantly influence the absorption of lebrikizumab.

Distribution

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

Biotransformation

Specific metabolism studies were not conducted because lebrikizumab is a protein. Lebrikizumab is expected to degrade to small peptides and individual 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 approximately 24.5 days.

Linearity/non-linearity

Lebrikizumab exhibited linear pharmacokinetics with dose-proportional increase in exposure over a dose range of 37.5 to 500 mg given as a subcutaneous injection in patients with AD or in healthy volunteers.

Special populations

Gender, age, and race

Gender, age (range 12 to 93 years), and race did not have a significant effect on the pharmacokinetics of lebrikizumab.

Renal and hepatic impairment

Specific clinical pharmacology studies to evaluate the effects of renal or hepatic impairment on the pharmacokinetics of lebrikizumab have not been conducted. Lebrikizumab, as a monoclonal antibody, is not expected to undergo significant renal or hepatic elimination. Population PK analyses show that markers of renal or hepatic function did not affect the pharmacokinetics of lebrikizumab.

Body weight

Exposure to lebrikizumab was lower in patients with higher body weight but this had no meaningful impact on clinical efficacy.

Paediatric population

Based on population PK analysis adolescents 12 to 17 years of age with atopic dermatitis had slightly higher lebrikizumab serum trough concentrations compared to adults, which was related to their lower body weight distribution.

5.3 Preclinical safety data

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

The mutagenic potential of lebrikizumab has not been evaluated; however monoclonal antibodies are not expected to alter DNA or chromosomes.

Carcinogenicity studies have not been conducted with lebrikizumab. Evaluation of the available evidence related to IL-13 inhibition and animal toxicology data with lebrikizumab does not suggest carcinogenic potential for lebrikizumab.

No effects on fertility parameters were observed in sexually mature monkeys after a long-term intravenous (females) or subcutaneous (males) treatment with lebrikizumab. Lebrikizumab had no effects on embryo-fetal or postnatal development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Histidine
Glacial acetic acid (E 260)
Sucrose
Polysorbate 20 (E 432)
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years

After removal from the refrigerator, Ebglyss must be used within 7 days (up to 30°C) or discarded. Once stored out of refrigeration, do not place back in the refrigerator.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

Do not freeze.

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

6.5 Nature and contents of container

Ebglyss 250 mg solution for injection in pre-filled syringe

2 mL solution in a 2.25 mL Type-1 clear glass pre-filled syringe with small round flange, with a 27 gauge special thin wall x 12.7 mm stacked stainless steel needle, closed with a laminated bromobutyl elastomeric plunger and a rigid needle shield and assembled in a passive safety device.

Pack sizes:

1 pre-filled syringe

2 pre-filled syringes

3 pre-filled syringes

multipack containing 4 (2 packs of 2) single-dose pre-filled syringes

multipack containing 5 (5 packs of 1) single-dose pre-filled syringes

multipack containing 6 (3 packs of 2) single-dose pre-filled syringes

Ebglyss 250 mg solution for injection in pre-filled pen

2 mL solution in a 2.25 mL Type-1 clear glass syringe in a pre-filled pen with extra-small round flange, with a 27 gauge special thin wall x 8 mm stacked stainless steel needle, and closed with a laminated bromobutyl elastomeric plunger and a rigid needle shield.

Pack sizes:

1 pre-filled pen

2 pre-filled pens

3 pre-filled pens

multipack containing 4 (2 packs of 2) single-dose pre-filled pens

multipack containing 5 (5 packs of 1) single-dose pre-filled pens

multipack containing 6 (3 packs of 2) single-dose pre-filled pens

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Detailed instructions for administration of Ebglyss in a pre-filled syringe or in a pre-filled pen are given at the end of the package leaflet.

The solution should be clear to opalescent, colourless to slightly yellow to slightly brown solution and free from visible particulates. If the solution is cloudy, discoloured or contains visible particulate matter, the solution should not be used.

The pre-filled syringe or the pre-filled pen should not be exposed to heat or direct sunlight and should not be shaken.

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

7. MARKETING AUTHORISATION HOLDER

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1765/001
EU/1/23/1765/002
EU/1/23/1765/003
EU/1/23/1765/004
EU/1/23/1765/005
EU/1/23/1765/006
EU/1/23/1765/007
EU/1/23/1765/008
EU/1/23/1765/009
EU/1/23/1765/010
EU/1/23/1765/011
EU/1/23/1765/012

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 November 2023

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

- A. MANUFACTURER OF THE BIOLOGICAL ACTIVE
SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR
BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY
AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE
MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO
THE SAFE AND EFFECTIVE USE OF THE MEDICINAL
PRODUCT**

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

Name and address of the manufacturer of the biological active substance

Samsung Biologics
300 Songdo bio-daero
Yeonsu-gu
Republic of Korea

Name and address of the manufacturer responsible for batch release

Industrias Farmacéuticas Almirall, S.A.
Ctra. Martorell 41-61
08740 Sant Andreu de la Barca
Barcelona, Spain

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

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

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING
AUTHORISATION**

- **Periodic safety update reports (PSURs)**

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

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

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

- **Risk management plan (RMP)**

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

An updated RMP should be submitted:

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

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**OUTER CARTON - Pre-filled syringe 250 mg****1. NAME OF THE MEDICINAL PRODUCT**

Ebglyss 250 mg solution for injection in pre-filled syringe
lebrikizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe
2 pre-filled syringes
3 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP
Removal from refrigerator date: ____/____/____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

After removal from the refrigerator, store below 30°C and use within 7 days or discard.

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

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1765/001	1 pre-filled syringe
EU/1/23/1765/002	2 pre-filled syringes
EU/1/23/1765/003	3 pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ebglyss 250 mg syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**OUTER CARTON FOR MULTIPACK (WITH BLUE BOX)****1. NAME OF THE MEDICINAL PRODUCT**

Ebglyss 250 mg solution for injection in pre-filled syringe
lebrikizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 4 (2 packs of 2) pre-filled syringes

Multipack: 5 (5 packs of 1) pre-filled syringes

Multipack: 6 (3 packs of 2) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only

Read the package leaflet before use.

Subcutaneous use

Do not shake

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

Removal from refrigerator date: ____/____/____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

After removal from the refrigerator, store below 30°C and use within 7 days or discard.

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

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1765/004 4 pre-filled syringes (2 packs of 2)

EU/1/23/1765/005 5 pre-filled syringes (5 packs of 1)

EU/1/23/1765/006 6 pre-filled syringes (3 packs of 2)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ebglyss 250 mg syringe

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Ebglyss 250 mg solution for injection in pre-filled syringe
lebrikizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe

2 pre-filled syringes

Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only

Read the package leaflet before use.

Subcutaneous use

Do not shake

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Removal from refrigerator date: ____/____/____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

After removal from the refrigerator, store below 30°C and use within 7 days or discard.

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

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1765/004 4 pre-filled syringes (2 packs of 2)

EU/1/23/1765/005 5 pre-filled syringes (5 packs of 1)

EU/1/23/1765/006 6 pre-filled syringes (3 packs of 2)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ebglyss 250 mg syringe

17. UNIQUE IDENTIFIER – 2D BARCODE**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL - Pre-filled syringe 250 mg
--

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

Ebglyss 250 mg injection
lebrikizumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

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

2 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**OUTER CARTON - Pre-filled pen 250 mg****1. NAME OF THE MEDICINAL PRODUCT**

Ebglyss 250 mg solution for injection in pre-filled pen
lebrikizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled pen
2 pre-filled pens
3 pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP
Removal from refrigerator date: ____/____/____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

After removal from the refrigerator, store below 30°C and use within 7 days or discard.

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

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1765/007	1 pre-filled pen
EU/1/23/1765/008	2 pre-filled pens
EU/1/23/1765/009	3 pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ebglyss 250 mg pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**OUTER CARTON FOR MULTIPACK (WITH BLUE BOX)****1. NAME OF THE MEDICINAL PRODUCT**

Ebglyss 250 mg solution for injection in pre-filled pen
lebrikizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 4 (2 packs of 2) pre-filled pens

Multipack: 5 (5 packs of 1) pre-filled pens

Multipack: 6 (3 packs of 2) pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only

Read the package leaflet before use.

Subcutaneous use

Do not shake

Open here

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

Removal from refrigerator date: ____/____/____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

After removal from the refrigerator, store below 30°C and use within 7 days or discard.

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

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1765/010 4 pre-filled pens (2 packs of 2)
EU/1/23/1765/011 5 pre-filled pens (5 packs of 1)
EU/1/23/1765/012 6 pre-filled pens (3 packs of 2)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ebglyss 250 mg pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Ebglyss 250 mg solution for injection in pre-filled pen
lebrikizumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 250 mg of lebrikizumab in 2 mL solution (125 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled pen

2 pre-filled pens

Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For single use only

Read the package leaflet before use.

Subcutaneous use

Do not shake

Open here

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Removal from refrigerator date: ____/____/____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.

After removal from the refrigerator, store below 30°C and use within 7 days or discard.

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

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1765/010 4 pre-filled pens (2 packs of 2)
EU/1/23/1765/011 5 pre-filled pens (5 packs of 1)
EU/1/23/1765/012 6 pre-filled pens (3 packs of 2)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ebglyss 250 mg pen

17. UNIQUE IDENTIFIER – 2D BARCODE**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL - Pre-filled pen 250 mg

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

Ebglyss 250 mg injection
lebrikizumab
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

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

2 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Ebglyss 250 mg solution for injection in pre-filled syringe lebrikizumab

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

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

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

What is in this leaflet

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

Instructions for use

1. What Ebglyss is and what it is used for

Ebglyss contains the active substance lebrikizumab.

Ebglyss is used to treat adults and adolescents 12 years and older with a body weight of at least 40 kg with moderate-to-severe atopic dermatitis, also known as atopic eczema, who can be treated with systemic treatments (a medicine given by mouth or injection).

Ebglyss may be used with eczema medicines that you apply to the skin or it may be used on its own.

Lebrikizumab is a monoclonal antibody (a type of protein) that blocks the action of another protein called interleukin-13. Interleukin-13 plays a major role in causing the symptoms of atopic dermatitis. By blocking interleukin-13, Ebglyss can improve your atopic dermatitis and reduce the related itching and skin pain.

2. What you need to know before you use Ebglyss

Do not use Ebglyss

- if you are allergic to lebrikizumab or any of the other ingredients of this medicine (listed in section 6).

If you think you may be allergic, or you are not sure, ask your doctor, pharmacist or nurse for advice before using Ebglyss.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Ebglyss.

Every time you get a new pack of Ebglyss, it is important that you note down the date and the batch number (which is on the packaging after “Lot”) and keep this information in a safe place.

Allergic reactions

Very rarely, this medicine can cause allergic (hypersensitivity) reactions. These reactions can occur shortly after you take Ebglyss, but also may happen later. If you notice symptoms of an allergic reaction, you should stop using this medicine and contact your doctor or get medical help immediately. Signs of an allergic reaction include:

- breathing problems
- swelling of the face, mouth and tongue
- fainting
- dizziness
- feeling lightheaded (because of low blood pressure)
- hives, itching and skin rash

Eye problems

Talk to your doctor if you have any new or worsening eye problems, including redness and discomfort in the eye, eye pain or changes in vision.

Vaccination

Talk to your doctor regarding your current vaccinations plan. See section “Other medicines and Ebglyss”.

Children and adolescents

This medicine should not be used in children with atopic dermatitis below the age of 12 or adolescents 12 to 17 years of age and weighing less than 40 kg because it has not been tested in this age group.

Other medicines and Ebglyss

Tell your doctor or pharmacist:

- if you are using, have recently used or might use any other medicines.
- if you have recently had a vaccination or plan to have one. You should not be given certain types of vaccines (live vaccines) while using Ebglyss.

Pregnancy, breast-feeding and fertility

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

The effects of this medicine in pregnant women are not known. It is better to avoid the use of Ebglyss during pregnancy unless your doctor advises you to use it.

It is not known whether lebrikizumab can pass into breast milk. If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine. You and your doctor should decide if you will breast-feed or use Ebglyss. You should not do both.

Driving and using machines

Ebglyss is unlikely to influence your ability to drive and use machines.

Ebglyss contains polysorbates

This medicine contains 0.6 mg of polysorbate 20 (E 432) in each pre-filled syringe, which is equivalent to 0.3 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Ebglyss

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

How much Ebglyss is given and for how long

Your doctor will decide how much Ebglyss you need and how long you will use it for.

The recommended dose is:

- Two initial injections of 250 mg lebrikizumab each (500 mg in total) at week 0 and week 2.
- One injection with 250 mg once every two weeks from week 4 up to week 16.
Based on how you respond to the medicine, your doctor may decide to stop giving the medicine or to keep giving you one 250 mg injection every other week up to week 24.
- One injection with 250 mg every four weeks from week 16 onwards (maintenance dosing).

Ebglyss is given as an injection under your skin (subcutaneous injection) into the thigh or abdomen, except for 5 cm around the navel. If somebody else gives the injection, it can also be given into the upper arm. You and your doctor or nurse will decide if you can inject Ebglyss yourself.

It is recommended that you change the injection site with each injection. Ebglyss should not be injected into skin that is tender, damaged or has bruises or scars, or in an area of skin that is affected by atopic dermatitis or other skin lesions. For the initial 500 mg dose, administer two 250 mg injections consecutively in different injection sites.

It is important not to try to inject yourself until you have been trained by your doctor or nurse. A caregiver may also give you your Ebglyss injection after proper training. In adolescents 12 years of age and older, it is recommended that Ebglyss is administered by or under the supervision of an adult.

The pre-filled syringe must not be shaken.

Read the “Instructions for use” for the pre-filled syringe carefully before using Ebglyss.

If you use more Ebglyss than you should

If you took more Ebglyss than your doctor prescribed or you took the dose before it was scheduled, talk to your doctor, pharmacist or nurse.

If you forget to use Ebglyss

If you have forgotten to inject a dose of Ebglyss, talk to your doctor, pharmacist or nurse.

If you forgot to inject Ebglyss when you usually have planned to do it, take it as soon as you remember. The next dose should be injected on the regular scheduled day.

If you stop using Ebglyss

Do not stop using Ebglyss without speaking to your doctor first.

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

4. Possible side effects

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

Common (may affect up to 1 in 10 people)

- Redness and discomfort in the eye (conjunctivitis)

- Inflammation of the eye due to an allergic reaction (conjunctivitis allergic)
- Eye dryness
- Injection site reactions

Uncommon (may affect up to 1 in 100 people)

- Shingles, a painful, blistering rash in one part of the body (herpes zoster)
- Increase in eosinophils (a type of white blood cell; eosinophilia)
- Inflammation of the cornea (the transparent layer that covers the front of the eye; keratitis)
- Eyelid itching, redness and swelling (blepharitis)

Reporting of side effects

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

5. How to store Ebglyss

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

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

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

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

Do not use this medicine if you notice that the solution is cloudy or discoloured or if it contains visible particles. After removal from the refrigerator, Ebglyss must be stored below 30°C and used within 7 days or discarded. Once stored out of refrigeration, do not place back in the refrigerator. The date of removal from the refrigerator may be recorded on the carton.

This medicine is for single use only.

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

6. Contents of the pack and other information

What Ebglyss contains

- The active substance is lebrikizumab. Each pre-filled syringe contains 250 mg of lebrikizumab in a 2 mL solution (125 mg/mL).
- The other ingredients are histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432) and water for injections.

What Ebglyss looks like and contents of the pack

Ebglyss is a clear to opalescent, colourless to slightly yellow to slightly brown sterile solution for injection, free of visible particles. It is supplied as carton packs containing one single-dose, glass, pre-filled syringe, 2 single-dose pre-filled syringes or 3 single-dose pre-filled syringes, and as multipacks of 4 single-dose pre-filled syringes (2 packs of 2), 5 single-dose pre-filled syringes (5 packs of 1) or 6 single-dose pre-filled syringes (3 packs of 2).

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

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

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This leaflet was last revised in .

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

Instructions for use

Read these “Instructions for use” before you use this medicine and carefully follow all the step-by-step instructions.

Important information for the Ebglyss pre-filled syringe with needle safety device:

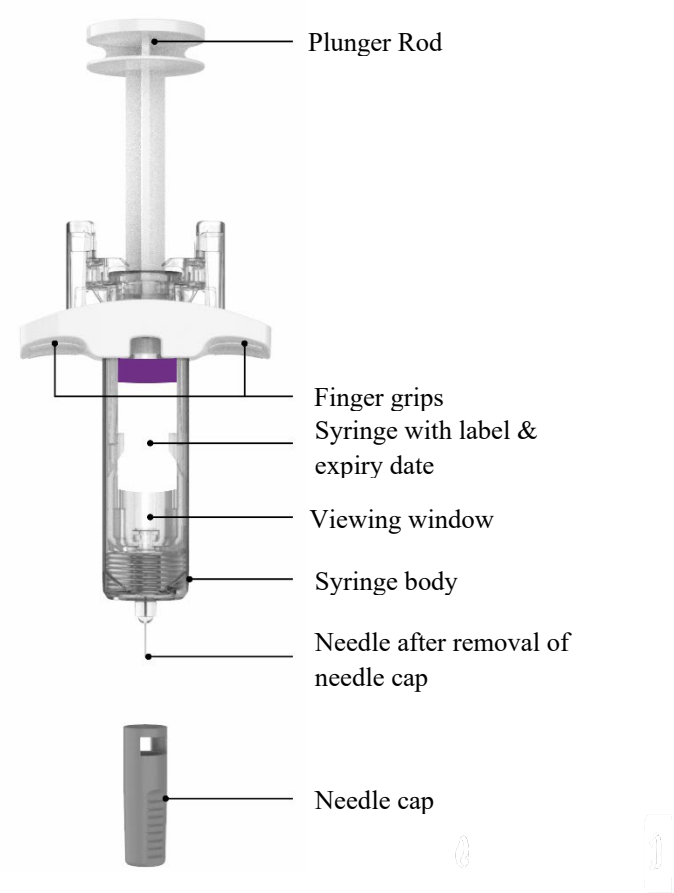
Do not inject yourself or someone else until you have been shown by your healthcare professional how to inject Ebglyss. Call your healthcare provider if you have any questions.

When using the Ebglyss pre-filled syringe

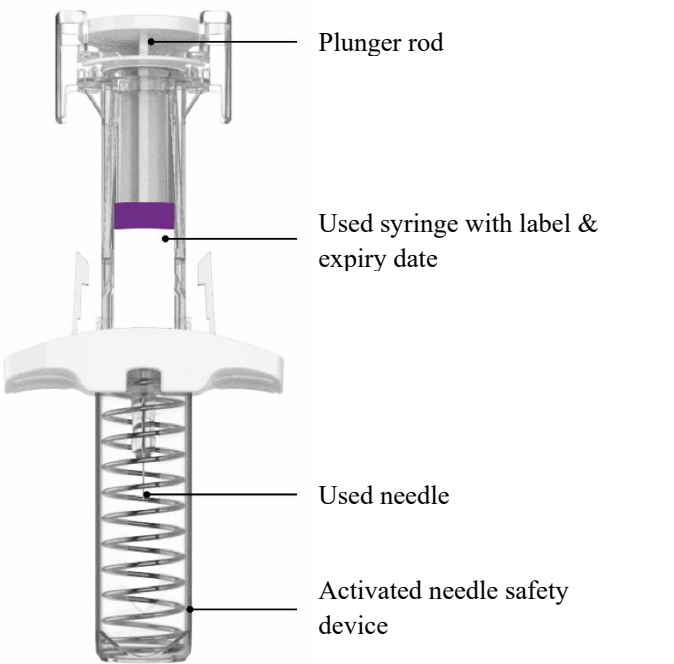
- Talk to your healthcare provider about how often you will need to inject the medicine.
- If you have vision problems, do not use Ebglyss pre-filled syringe without help from a caregiver.
- To reduce the risk of accidental needle sticks, each pre-filled syringe has a needle safety device that is automatically activated to cover the needle after your injection.
- Throw away (dispose of) your used Ebglyss single-dose pre-filled syringe immediately after use.
- **Do not** use Ebglyss pre-filled syringe if it has been dropped on a hard surface or damaged.
- **Do not** use Ebglyss pre-filled 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 bubbles in the Ebglyss pre-filled 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-dose pre-filled syringe.**

Parts of the Ebglyss pre-filled syringe with needle safety device

Before use



After Use



Preparing to inject Ebglyss

Prepare supplies

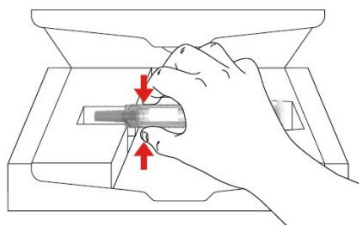


Make sure you have the following:

- 1 Ebglyss pre-filled syringe with needle safety device from the refrigerator
- 1 alcohol wipe*
- 1 cotton ball or gauze*
- 1 sharps disposal container*

*Items not included with the product.

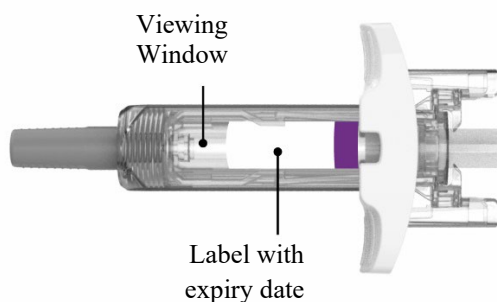
Remove pre-filled syringe from carton



Remove the Ebglyss pre-filled syringe from the carton by holding the middle of the syringe body.

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

Inspect pre-filled syringe



When you receive your Ebglyss pre-filled syringes, **always check to see that you have the correct medicine and dose and visually inspect the pre-filled syringe.**

Note: You may gently rotate the plunger rod to view the syringe label.

The label should read “Ebglyss”.

Do not use the Ebglyss pre-filled syringe if the expiry date has passed.

Do not use the Ebglyss pre-filled syringe if it has been damaged.

Look at the medicine through the viewing window on the Ebglyss pre-filled syringe. The liquid should be clear, colourless to slightly yellow to slightly brown.

Note: some air bubbles are normal.

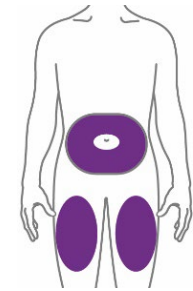
Do not use the Ebglyss pre-filled syringe if the liquid is discoloured or cloudy, or it contains visible flakes or particles, or the syringe shows signs of damage, or the

syringe has been dropped, or the medicine is frozen.

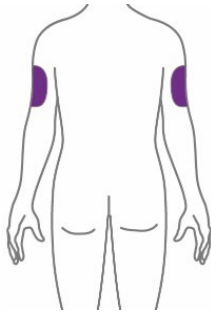
Do not heat the Ebglyss pre-filled syringe with a microwave or hot water.

Do not put the Ebglyss pre-filled syringe into direct sunlight.

Choose your injection site



You or another person may inject into these areas.



Another person should inject into this area.

- You can inject into your thigh or stomach area (abdomen), except for 5 cm (2 inches) around your belly button (navel).
- If you chose the front of your thigh, you should inject at least 5 cm (2 inches) above the knee and 5 cm (2 inches) 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 scarred, or in an area of skin that is affected by atopic dermatitis or other skin lesions.

Prepare your skin

Wash your hands with soap and water. 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

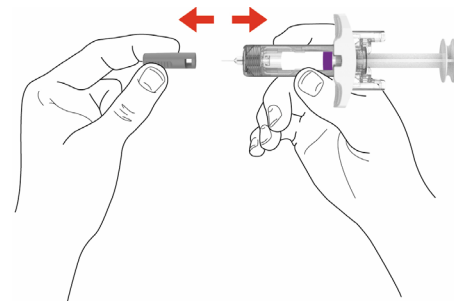
Remove needle cap

Hold the Ebglyss pre-filled 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.

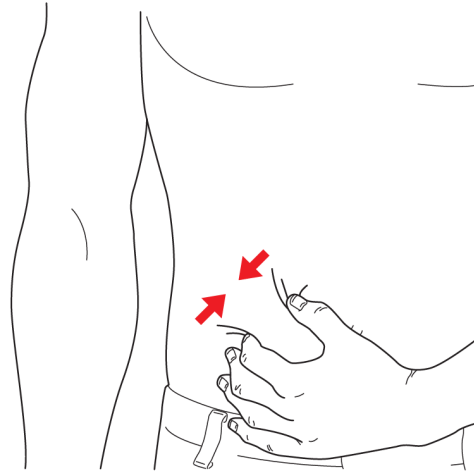
Do not touch the needle.

Inject your medicine immediately after removing the needle cap.



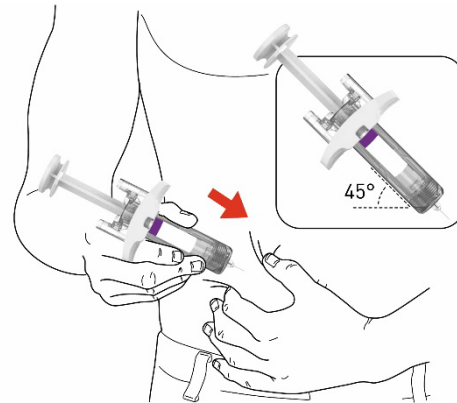
2 Pinch the injection site

Gently pinch a fold of skin at the injection site (thigh or stomach, except for 5 cm (2 inches) around your belly button, or outer area of the upper arm if injected by your caregiver).



3 Insert the needle

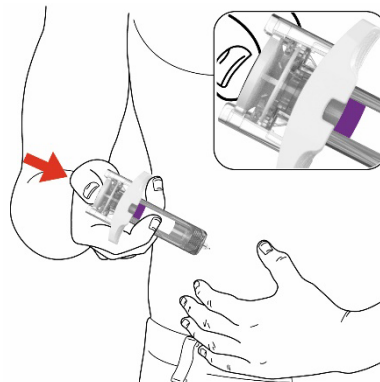
Insert the needle completely into the fold of skin at about a 45° angle.



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 pre-filled syringe is empty.

Note: It is normal to feel some resistance.



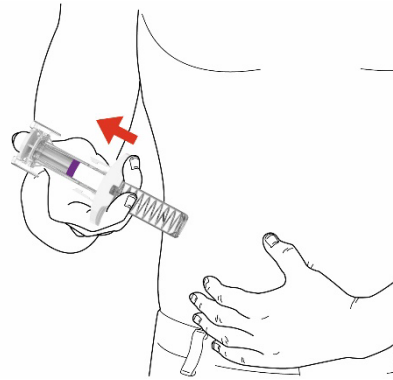
5 Release and remove

Lift your thumb to release the plunger rod until the needle is covered by the needle safety device, and then remove the pre-filled 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.



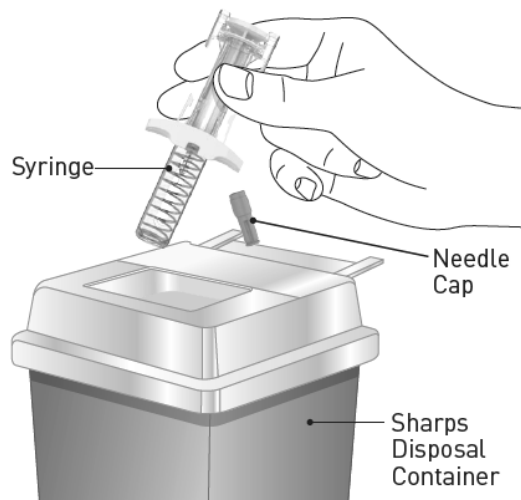
Dispose of the pre-filled syringe safely

Put your used Ebglyss pre-filled syringe and needle cap in a sharps disposal container immediately after use.

Do not dispose of (throw away) Ebglyss pre-filled syringes and needle caps in your household waste.

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

- made of a heavy-duty plastic,
- 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 labelled 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 local laws regarding the disposal of used needles and syringes.

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

Do not recycle your used sharps disposal container.

Read the full package leaflet for the pre-filled syringe before using Ebglyss.

Package leaflet: Information for the user

Ebglyss 250 mg solution for injection in pre-filled pen lebrikizumab

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

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

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

What is in this leaflet

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

Instructions for use

1. What Ebglyss is and what it is used for

Ebglyss contains the active substance lebrikizumab.

Ebglyss is used to treat adults and adolescents 12 years and older with a body weight of at least 40 kg with moderate-to-severe atopic dermatitis, also known as atopic eczema, who can be treated with systemic treatments (a medicine given by mouth or injection).

Ebglyss may be used with eczema medicines that you apply to the skin or it may be used on its own.

Lebrikizumab is a monoclonal antibody (a type of protein) that blocks the action of another protein called interleukin-13. Interleukin-13 plays a major role in causing the symptoms of atopic dermatitis. By blocking interleukin-13, Ebglyss can improve your atopic dermatitis and reduce the related itching and skin pain.

2. What you need to know before you use Ebglyss

Do not use Ebglyss

- if you are allergic to lebrikizumab or any of the other ingredients of this medicine (listed in section 6).

If you think you may be allergic, or you are not sure, ask your doctor, pharmacist or nurse for advice before using Ebglyss.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Ebglyss.

Every time you get a new pack of Ebglyss, it is important that you note down the date and the batch number (which is on the packaging after “Lot”) and keep this information in a safe place.

Allergic reactions

Very rarely, this medicine can cause allergic (hypersensitivity) reactions. These reactions can occur shortly after you take Ebglyss, but also may happen later. If you notice symptoms of an allergic reaction, you should stop using this medicine and contact your doctor or get medical help immediately. Signs of an allergic reaction include:

- breathing problems
- swelling of the face, mouth, and tongue
- fainting
- dizziness
- feeling lightheaded (because of low blood pressure)
- hives, itching and skin rash

Eye problems

Talk to your doctor if you have any new or worsening eye problems, including redness and discomfort in the eye, eye pain or changes in vision.

Vaccination

Talk to your doctor regarding your current vaccinations plan. See section “Other medicines and Ebglyss”.

Children and adolescents

This medicine should not be used in children with atopic dermatitis below the age of 12 or adolescents 12 to 17 years of age and weighing less than 40 kg because it has not been tested in this age group.

Other medicines and Ebglyss

Tell your doctor or pharmacist:

- if you are using, have recently used or might use any other medicines.
- if you have recently had a vaccination or plan to have one. You should not be given certain types of vaccines (live vaccines) while using Ebglyss.

Pregnancy, breast-feeding and fertility

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

The effects of this medicine in pregnant women are not known. It is better to avoid the use of Ebglyss during pregnancy unless your doctor advises you to use it.

It is not known whether lebrikizumab can pass into breast milk. If you are breast-feeding or are planning to breast-feed, talk to your doctor before using this medicine. You and your doctor should decide if you will breast-feed or use Ebglyss. You should not do both.

Driving and using machines

Ebglyss is unlikely to influence your ability to drive and use machines.

Ebglyss contains polysorbates

This medicine contains 0.6 mg of polysorbate 20 (E 432) in each pre-filled pen, which is equivalent to 0.3 mg/mL. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Ebglyss

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

How much Ebglyss is given and for how long

Your doctor will decide how much Ebglyss you need and how long you will use it for.

The recommended dose is:

- Two initial injections of 250 mg lebrikizumab each (500 mg in total) at week 0 and week 2.
- One injection with 250 mg once every two weeks from week 4 up to week 16.
Based on how you respond to the medicine, your doctor may decide to stop giving the medicine or to keep giving you one 250 mg injection every other week up to week 24.
- One injection with 250 mg every four weeks from week 16 onwards (maintenance dosing).

Ebglyss is given as an injection under your skin (subcutaneous injection) into the thigh or abdomen, except for 5 cm around the navel. If somebody else gives the injection, it can also be given into the upper arm. You and your doctor or nurse will decide if you can inject Ebglyss yourself.

It is recommended that you change the injection site with each injection. Ebglyss should not be injected into skin that is tender, damaged or has bruises or scars, or in an area of skin that is affected by atopic dermatitis or other skin lesions. For the initial 500 mg dose, administer two 250 mg injections consecutively in different injection sites.

It is important not to try to inject yourself until you have been trained by your doctor or nurse. A caregiver may also give you your Ebglyss injection after proper training. In adolescents 12 years of age and older, it is recommended that Ebglyss is administered by or under the supervision of an adult.

The pre-filled pen must not be shaken.

Read the “Instructions for use” for the pre-filled pen carefully before using Ebglyss.

If you use more Ebglyss than you should

If you took more Ebglyss than your doctor prescribed or you took the dose before it was scheduled, talk to your doctor, pharmacist or nurse.

If you forget to use Ebglyss

If you have forgotten to inject a dose of Ebglyss, talk to your doctor, pharmacist or nurse.

If you forgot to inject Ebglyss when you usually have planned to do it, take it as soon as you remember. The next dose should be injected on the regular scheduled day.

If you stop using Ebglyss

Do not stop using Ebglyss without speaking to your doctor first.

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

4. Possible side effects

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

Common (may affect up to 1 in 10 people)

- Redness and discomfort in the eye (conjunctivitis)
- Inflammation of the eye due to an allergic reaction (conjunctivitis allergic)
- Eye dryness
- Injection site reactions

Uncommon (may affect up to 1 in 100 people)

- Shingles, a painful, blistering rash in one part of the body (herpes zoster)
- Increase in eosinophils (a type of white blood cell; eosinophilia)
- Inflammation of the cornea (the transparent layer that covers the front of the eye; keratitis)
- Eyelid itching, redness and swelling (blepharitis)

Reporting of side effects

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

5. How to store Ebglyss

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

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

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

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

Do not use this medicine if you notice that the solution is cloudy or discoloured or if it contains visible particles. After removal from the refrigerator, Ebglyss must be stored below 30°C and used within 7 days or discarded. Once stored out of refrigeration, do not place back in the refrigerator. The date of removal from the refrigerator may be recorded on the carton.

This medicine is for single use only.

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

6. Contents of the pack and other information

What Ebglyss contains

- The active substance is lebrikizumab. Each pre-filled pen contains 250 mg of lebrikizumab in a 2 mL solution (125 mg/mL).
- The other ingredients are histidine, glacial acetic acid (E 260), sucrose, polysorbate 20 (E 432) and water for injections.

What Ebglyss looks like and contents of the pack

Ebglyss is a clear to opalescent, colourless to slightly yellow to slightly brown sterile solution for injection, free of visible particles. It is supplied as carton packs containing one single-dose pre-filled pen, 2 single-dose pre-filled pens or 3 single-dose pre-filled pens and as multipacks containing 4 single-dose pre-filled pens (2 packs of 2), 5 single-dose pre-filled pens (5 packs of 1) or 6 single-dose pre-filled pens (3 packs of 2).

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Almirall, S.A.
Ronda General Mitre, 151
08022 Barcelona
Spain

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

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This leaflet was last revised in.

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

Instructions for use

These Instructions for use contain information on how to inject Ebglyss.

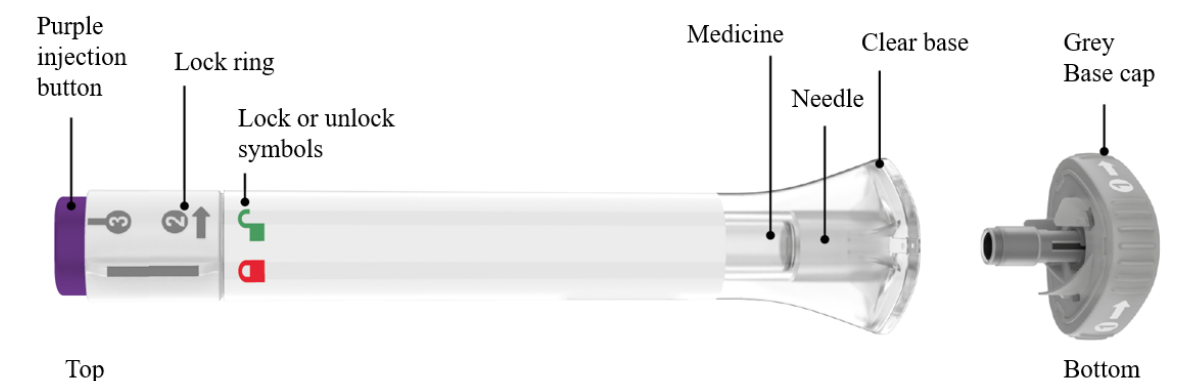
Read these “Instructions for use” before you use this medicine and carefully follow all the step-by-step instructions.



Important information you need to know before injecting Ebglyss

- Your healthcare provider should show you how to prepare and inject Ebglyss using the pre-filled pen. **Do not** inject yourself or someone else until you have been shown how to inject Ebglyss.
- Each Ebglyss pre-filled pen contains 1 dose of Ebglyss (250 mg). **The pre-filled pen is for one-time use only.**
- The Ebglyss pre-filled pen contains glass parts. Handle it carefully. If you drop it on a hard surface, **do not** use it. Use a new Ebglyss pre-filled 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 and clean your injection site** section of these instructions to help you choose which area works best for you.
- If you have vision or hearing problems, **do not** use Ebglyss pre-filled pen without help from a caregiver.

Parts of the Ebglyss pre-filled pen



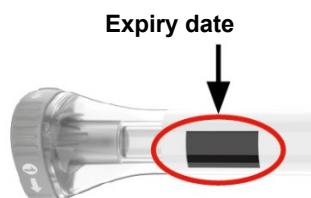
Preparing to inject Ebglyss

Prepare supplies:

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

Inspect the pre-filled pen and the medicine

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



Do not use the pre-filled pen (see **Disposing of Ebglyss pre-filled pen**) if the:

- pen looks damaged
- medicine is frozen
- medicine is cloudy, is discoloured, or contains particles
- expiry date printed on the label has passed

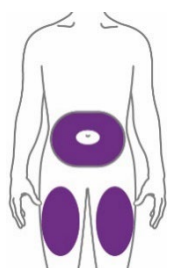
Do not warm up the pre-filled pen with a microwave, or hot water, or direct sunlight.

Wash your hands with soap and water

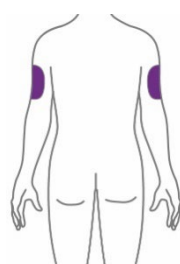
Choose and clean your injection site

Your healthcare provider 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.



Another person should inject into this area.

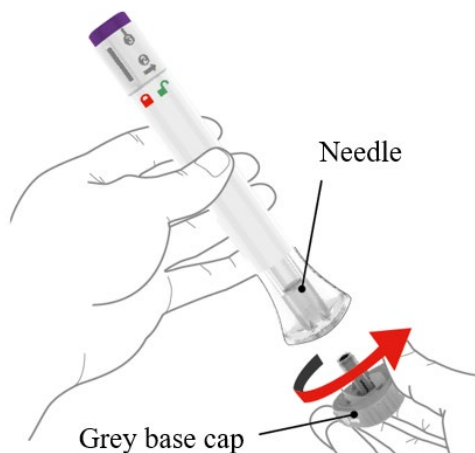
- **Stomach area (abdomen) —**
At least 5 cm (2 inches) away from the belly button (navel).
- **Front of thigh —**
At least 5 cm (2 inches) above the knee and 5 cm (2 inches) below the groin.
- **Back of upper arm —**
Another person should inject into the back of your upper arm.


Do not inject in the exact same spot every time.

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

Injecting Ebglyss

1 Uncap the pre-filled pen



 Make sure the pre-filled pen is **locked**.

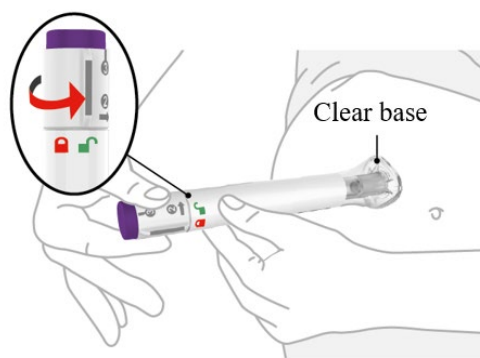


When you are ready to inject, twist off the grey base cap and throw it away in your household waste.

Do not put the grey base cap back on — this could damage the needle.

Do not touch the needle inside the clear base.

2 Place and unlock

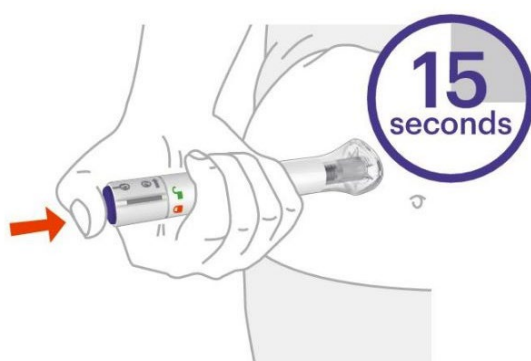


Place and hold the clear base flat and firmly against the skin.



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 grey plunger is visible. Then remove the pre-filled pen from the injection site.



Grey Plunger

Disposing of Ebglyss pre-filled pen

Throw away the used pre-filled pen



Dispose of the used Ebglyss pre-filled pen in a sharps disposal container right away after use.

Do not throw away (dispose of) the Ebglyss pre-filled pen in your household waste.

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

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

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container.

There may be local laws about how you should throw away needles and syringes.

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

Do not recycle your used sharps disposal container.

Commonly Asked Questions

Q. What if I see bubbles in the pre-filled 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 grey 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 grey base cap?

A. **Do not** remove the grey base cap. Throw away (dispose of) the pre-filled 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 pre-filled pen steady and firm against your skin.

Q. What if the needle did not retract after my injection?

A. **Do not** touch the needle or replace the grey base cap. Store the pre-filled pen in a safe place to avoid an accidental needlestick.

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 grey plunger at the top of the clear base. The injection may take up to 15 seconds.

Q. What if I remove the pre-filled pen before the second loud click or before the grey plunger stops moving?

A. You may not have received your full dose. Do not give another injection. Call your healthcare provider 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 pre-filled pen. **Do not** remove the pre-filled pen from your skin until you hear the second loud click.

Read the full package leaflet for the pre-filled pen before using Ebglyss.