# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Elymbus 0.1 mg/g eye gel in single-dose container

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One g of eye gel contains 0.1 mg bimatoprost.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Eye gel.
Colourless opalescent gel.
pH: 6.9 – 7.9.
Osmolality: 250 – 350 mosmol/kg.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension in adults (as monotherapy or as adjunctive therapy to beta-blockers).

### 4.2 Posology and method of administration

Posology
The recommended dose is one drop in the affected eye(s) once daily, administered in the evening. The dose should not exceed once daily, as more frequent administration may lessen the intraocular pressure lowering effect.

***Special populations***
*Patients with hepatic impairment*
Elymbus has not been studied in patients with moderate to severe hepatic impairment and should therefore be used with caution in such patients. In patients with a history of mild liver disease or abnormal alanine aminotransferase (ALT), aspartate aminotransferase (AST) and/or bilirubin at baseline, bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation) had no adverse effect on liver function over 24 months.

*Patients with renal impairment*
Elymbus has not been studied in patients with renal impairment and should therefore be used with caution in such patients.

*Paediatric population*
The safety and efficacy of Elymbus in children aged 0 to 18 years has not yet been established.

Method of administration
Ocular use.
The use of bimatoprost in contact lens wearers has not been studied. Therefore, contact lenses should be removed before instillation of the eye gel and may be reinserted after 15 minutes.
If more than one topical ophthalmic medicinal product is being used, they should be administered at least 15 minutes before Elymbus. Elymbus should be instilled last.
A single-dose container contains enough eye gel to treat both eyes.
For single-use only.
This medicinal product is a sterile eye gel that does not contain a preservative. The eye gel from one individual single-dose container is to be used immediately after opening for administration to the affected eye(s). Since sterility cannot be maintained after the individual single-dose container is opened, any remaining contents must be discarded immediately after administration.

*Patients should be instructed:*

- to avoid contact between the dropper tip and the eye or eyelids.
- to use the eye gel immediately after first opening the single-dose container and to discard the single-dose container after use.
- to store the unopened single-dose containers in the sachet.

**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**

Ocular
Before treatment is initiated, patients should be informed of the possibility of prostaglandin analogue periorbitopathy (PAP) and increased iris pigmentation, since these have been observed during treatment with bimatoprost 0.1 mg/ml eye drops, solution (preserved formulation). Some of these changes may be permanent, and may lead to impaired field of vision and differences in appearance between the eyes when only one eye is treated (see section 4.8).

Cystoid macular oedema has been uncommonly reported (≥1/1,000 to <1/100) following treatment with bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation). Therefore, Elymbus should be used with caution in patients with known risk factors for macular oedema (e.g. aphakic patients, pseudophakic patients with a torn posterior lens capsule).

There have been rare spontaneous reports of reactivation of previous corneal infiltrates or ocular infections with bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation). Elymbus should be used with caution in patients with a prior history of significant ocular viral infections (e.g. herpes simplex) or uveitis/iritis.

Elymbus has not been studied in patients with inflammatory ocular conditions, neovascular, inflammatory, angle-closure glaucoma, congenital glaucoma or narrow-angle glaucoma.

Skin
There is a potential for hair growth to occur in areas where Elymbus comes repeatedly in contact with the skin surface (see section 4.8). Thus, it is important to apply Elymbus as instructed and avoid it running onto the cheek or other skin areas.

Respiratory
Elymbus has not been studied in patients with compromised respiratory function. While there is limited information available on patients with a history of asthma or COPD, there have been reports of exacerbation of asthma, dyspnoea and COPD, as well as reports of asthma, in post marketing experience (see section 4.8). The frequency of these symptoms is not known. Patients with COPD, asthma or compromised respiratory function due to other conditions should be treated with caution.

Cardiovascular
Elymbus has not been studied in patients with heart block more severe than first degree or uncontrolled congestive heart failure. There have been a limited number of spontaneous reports of bradycardia or hypotension with bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation) (see section 4.8). Elymbus should be used with caution in patients predisposed to low heart rate or low blood pressure.

Other Information
In studies of bimatoprost 0.3 mg/ml in patients with glaucoma or ocular hypertension, it has been shown that the more frequent exposure of the eye to more than one dose of bimatoprost daily may decrease the IOP-lowering effect (see section 4.5). Patients using Elymbus with other prostaglandin analogues should be monitored for changes to their intraocular pressure.

**4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed.

No interactions are anticipated in humans, since systemic concentrations of bimatoprost are extremely low (less than 0.2 ng/ml) following ocular dosing with bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation).
Bimatoprost is biotransformed by any of multiple enzymes and pathways (see section 5.2), and no effects on hepatic drug metabolising enzymes were observed in preclinical studies.

In clinical studies, bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation) was used concomitantly with a number of different ophthalmic beta-blocking agents without evidence of interactions.

Concomitant use of bimatoprost and antiglaucomatous agents other than topical beta-blockers has not been evaluated during adjunctive glaucoma therapy.

There is a potential for the IOP-lowering effect of prostaglandin analogues (e.g. Elymbus) to be reduced in patients with glaucoma or ocular hypertension when used with other prostaglandin analogues (see section 4.4).

**4.6 Fertility, pregnancy and lactation**

Pregnancy
There are no adequate data from the use of bimatoprost in pregnant women. Animal studies have shown reproductive toxicity at high maternotoxic doses (see section 5.3).
Elymbus should not be used during pregnancy unless clearly necessary.

Breast-feeding
It is unknown whether bimatoprost is excreted in human breast milk. Animal studies have shown excretion of bimatoprost in breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue from Elymbus therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
There are no data on the effects of bimatoprost on human fertility.

**4.7 Effects on ability to drive and use machines**

Elymbus has minor influence on the ability to drive and use machines. As with any ocular treatment, if transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.

**4.8 Undesirable effects**

In a 3-month phase III clinical study comparing the efficacy and safety of preservative-free Elymbus versus preserved bimatoprost 0.1 mg/ml eye drops solution reference product, 236 patients were exposed to Elymbus. The most frequently reported adverse reactions with Elymbus were conjunctival hyperaemia (6.8%), eye irritation (5.1%), foreign body sensation in eye (2.5%), dry eye (2.5%) and transient blurred vision (2.1%). Table 1 lists adverse reactions identified with Elymbus in the phase III trial. Most were ocular, mild and none was serious.

Adverse reactions associated with Elymbus are listed by system organ class and frequency. Frequency categories are defined as: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000); not known (cannot be estimated from available data) adverse reactions are presented according to System Organ Class in Table 1 in order of decreased seriousness within each frequency grouping.

**Table 1.**

| System Organ Class | Frequency | Adverse reaction |
|---|---|---|
| Eye disorders | common | conjunctival hyperaemia, eye pain, eye irritation, noninfective conjunctivitis, foreign body sensation in eyes, dry eye, eye pruritus, transient blurred vision* |
| | uncommon | punctate keratitis, eye paraesthesia, blepharitis, madarosis, growth of eyelashes, photophobia, lacrimation increased, eyelash darkening, blepharal pigmentation, eyelid oedema, eyelid eczema |
| Nervous system disorders | uncommon | dizziness |

* transient blurred vision after ocular administration of the eye gel (see section 4.7).

In a 12-month Phase III clinical study approximately 38% of patients treated with bimatoprost 0.1 mg/ml eye drops, solution (preserved formulation) experienced adverse reactions. The most frequently reported adverse reaction was conjunctival hyperaemia (mostly trace to mild and of a non-inflammatory nature) occurring in 29% of patients. Approximately 4% of patients discontinued due to any adverse event in the 12-month study.

The following adverse reactions were reported during clinical trials with bimatoprost 0.1 mg/ml eye drops, solution (preserved formulation) or in the post-marketing period. Most were ocular, mild and none was serious.

**Table 2.**

| System Organ class | Frequency | Adverse reaction |
|---|---|---|
| *Immune system disorders* | not known | hypersentivity reaction including signs and symptoms of eye allergy and allergic dermatitis |
| *Nervous system disorders* | uncommon | headache |
| | not known | dizziness |
| *Eye disorders* | very common | conjunctival hyperaemia, prostaglandin analogue periorbitopathy |
| | common | punctate keratitis, eye irritation, eye pruritus, growth of eyelashes, eye pain, erythema of eyelid, eyelid pruritus |
| | uncommon | asthenopia, blurred vision, conjunctival disorder, conjunctival oedema, iris hyperpigmentation, madarosis, eyelid oedema |
| | not known | blepharal pigmentation, macular oedema, dry eye, eye discharge, eye oedema, foreign body sensation in eyes, lacrimation increased, ocular discomfort, photophobia |
| *Vascular disorders* | not known | hypertension |
| *Respiratory, thoracic and mediastinal disorders* | not known | asthma, asthma exacerbation, COPD exacerbation and dyspnoea |
| *Gastrointestinal disorders* | uncommon | nausea |
| *Skin and subcutaneous tissue disorders* | common | skin hyperpigmentation, hypertrichosis |
| | uncommon | dry skin, eyelid margin crusting, pruritus |
| | not known | skin discoloration (periocular) |
| *General disorders and administration site conditions* | common | instillation site irritation |

Description of selected adverse reactions

Prostaglandin analogue periorbitopathy (PAP)
Prostaglandin analogues including Elymbus can induce periorbital lipodystrophic changes which can lead to deepening of the eyelid sulcus, ptosis, enophthalmos, eyelid retraction, involution of dermatochalasis and inferior scleral show. Changes are typically mild, can occur as early as one month after initiation of treatment with Elymbus, and may cause impaired field of vision even in the absence of patient recognition. PAP is also associated with periocular skin hyperpigmentation or discoloration and hypertrichosis. All changes have been noted to be partially or fully reversible upon discontinuation or switch to alternative treatments.

Iris hyperpigmentation
Increased iris pigmentation is likely to be permanent. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long-term effects of increased iris pigmentation are not known. Iris colour changes seen with ophthalmic administration of bimatoprost may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts become more brownish. Neither naevi nor freckles of the iris appear to be affected by the treatment. At 12 months, the incidence of iris hyperpigmentation with bimatoprost 0.1 mg/ml eye drops, solution was 0.5%. At 12 months, the incidence with bimatoprost 0.3 mg/ml eye drops, solution was 1.5% (see section 4.8 Table 3) and did not increase following 3 years treatment.

In clinical studies, over 1800 patients have been treated with bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation). On combining the data from phase III monotherapy and adjunctive bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation) usage, the most frequently reported adverse reactions were:

- growth of eyelashes in up to 45% in the first year with the incidence of new reports decreasing to 7% at 2 years and 2% at 3 years
- conjunctival hyperaemia (mostly trace to mild and thought to be of a non-inflammatory nature) in up to 44% in the first year with the incidence of new reports decreasing to 13% at 2 years and 12% at 3 years

- ocular pruritus in up to 14% of patients in the first year with the incidence of new reports decreasing to 3% at 2 years and 0% at 3 years. Less than 9% of patients discontinued due to any adverse event in the first year with the incidence of additional patient discontinuations being 3% at both 2 and 3 years.

Additional adverse reactions reported with bimatoprost 0.3 mg/ml eye drops, solution are presented in Table 3. The table also includes those adverse reactions which occurred with both formulations but at a different frequency. Most were ocular, mild to moderate, and none was serious: With each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

**Table 3.**

| System Organ class | Frequency | Adverse reaction |
|---|---|---|
| *Nervous system disorders* | common | headache |
| | uncommon | dizziness |
| *Eye disorders* | very common | ocular pruritus, growth of eyelashes |
| | common | corneal erosion, ocular burning, allergic conjunctivitis, blepharitis, worsening of visual acuity, asthenopia, conjunctival oedema, foreign body sensation, ocular dryness, eye pain, photophobia, tearing, eye discharge, visual disturbance/blurred vision, increased iris pigmentation, eyelash darkening |
| | uncommon | retinal haemorrhage, uveitis, cystoid macular oedema, iritis, blepharospasm, eyelid retraction, periorbital erythema |
| *Vascular disorders* | common | hypertension |
| *Skin and subcutaneous tissue disorders* | uncommon | hirsutism |
| *General disorders and administration site conditions* | uncommon | asthenia |
| *Investigations* | common | liver function test abnormal |

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 HPRA Pharmacovigilance, Website: www.hpra.ie

**4.9 Overdose**

No case of overdose has been reported, and is unlikely to occur after ocular administration.

If overdose occurs, treatment should be symptomatic and supportive. If Elymbus is accidentally ingested, the following information may be useful: in short-term oral (by gavage) mouse and rat studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose is at least 1100 times higher than the accidental dose of the entire content of a pack of Elymbus (30 x 0.3 g single-dose containers; 9 g) in a 10 kg child.

**5 PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Ophthalmologicals, prostaglandin analogues, ATC code: S01EE03.

Mechanism of action
The mechanism of action by which bimatoprost reduces intraocular pressure in humans is by increasing aqueous humour outflow through the trabecular meshwork and enhancing uveoscleral outflow. Reduction of the intraocular pressure starts approximately 4 hours after the first administration and maximum effect is reached within approximately 8 to 12 hours. The duration of effect is maintained for at least 24 hours.

Bimatoprost is a potent ocular hypotensive agent. It is a synthetic prostamide, structurally related to prostaglandin F2α (PGF2α), that does not act through any known prostaglandin receptors. Bimatoprost selectively mimics the effects of biosynthesised substances called prostamides. The prostamide receptor, however, has not yet been structurally identified.

Clinical efficacy and safety

A randomised, investigator masked, multicentre, 3-month, Phase III clinical trial compared the efficacy and safety of preservative-free Elymbus versus preserved bimatoprost 0.1 mg/ml eye drops solution reference product in reducing IOP in 485 patients with glaucoma or ocular hypertension. Patients attended two post-randomisation visits (Week 6 and Week 12) during the study. The mean age of study participant was 63.4 years (range 30 to 91 years).

The study was designed to show non-inferiority of Elymbus to the bimatoprost 0.1 mg/ml reference product, both dosed once daily in the evening. The primary efficacy endpoint was mean IOP change from baseline at 3 timepoints (08:00, 10:00 and 16:00) at Week 12. The non-inferiority margin applied was a difference in mean IOP ≤1.5 mmHg for all timepoints.

Elymbus demonstrated clinically significant reductions in IOP at all timepoints and was non-inferior to bimatoprost 0.1 mg/ml reference product (**Table 1**).

**Table 1.** Mean IOP (mmHg) by visit and timepoint and adjusted mean difference (Elymbus-bimatoprost 0.1 mg/ml reference product) for the worse eye (mITT set)

| **Study visits and timepoints** | | **Elymbus** | | **Bimatoprost 0.1 mg/ml (reference product)** | | **Difference mmHg±SE (95% CI) Elymbus–Bimatoprost 0.1 mg/ml (reference product)** |
|---|---|---|---|---|---|---|
| | | **N** | **mmHg±SD** | **N** | **mmHg±SD** | |
| Baseline (D1) | 08:00 | 229 | 24.66±2.18 | 240 | 24.59±2.05 | |
| | 10:00 | 229 | 24.21±2.43 | 240 | 24.13±2.36 | |
| | 16:00 | 229 | 23.81±2.66 | 240 | 23.50±2.84 | |
| Week 12 | 08:00 | 221 | 14.98±2.60 | 228 | 15.15±2.46 | -0.17±0.23 (-0.62; 0.28) |
| | 10:00 | 218 | 14.82±2.50 | 227 | 14.93±2.37 | -0.15±0.22 (-0.58; 0.27) |
| | 16:00 | 219 | 14.82±2.44 | 227 | 14.95±2.30 | -0.19±0.22 (-0.61; 0.23) |

CI=confidence interval; N=number of patients with evaluable data; mITT=modified intent-to-treat; SD=standard deviation; SE=standard error

During the 3-month study, no adverse events were identified for Elymbus besides those already documented with bimatoprost 0.1 mg/ml reference product. Hyperaemia (conjunctival and ocular) was the most commonly reported treatment related adverse event in either treatment group, and was less common with Elymbus (6.8% of patients) compared to the bimatoprost 0.1 mg/ml reference product (11.2%). Worsening of conjunctival hyperaemia was also less common with Elymbus group compared to bimatoprost 0.1 mg/ml at Week 6 (20.1% *vs* 29.3%, respectively) and Week 12 (18.3% *vs* 30.4%, respectively). Elymbus was associated with fewer subjective ocular symptoms throughout the day at Week 12 (irritation/burning: 12.3% *vs* 19.5% and eye dryness feeling: 16.4% *vs* 25.6%) as well as subjective symptoms upon instillation (irritation/burning: 12.8% *vs* 21.2%, itching: 5.4% *vs* 10.4% and eye dryness feeling: 7.3% *vs* 14.3%) compared to the reference product.

Limited experience is available with the use of Elymbus in patients with open-angle glaucoma with pseudoexfoliative and pigmentary glaucoma, and chronic angle-closure glaucoma with patent iridotomy.

Paediatric population

The safety and efficacy of Elymbus in children aged 0 to less than 18 years has not been established.

**5.2 Pharmacokinetic properties**

Pharmacokinetic studies in humans have not been performed with Elymbus but with bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation).

Absorption

Bimatoprost penetrates the human cornea and sclera well *in vitro*. After ocular administration in adults, the systemic exposure of bimatoprost is very low with no accumulation over time. After once daily ocular administration of one drop of 0.3 mg/ml bimatoprost (preserved formulation) to both eyes for two weeks, blood concentrations peaked within 10 minutes after dosing and declined to below the lower limit of detection (0.025 ng/ml) within 1.5 hours after dosing. Mean Cmax and AUC 0-24hrs values were similar on days 7 and 14 at approximately 0.08 ng/ml and 0.09 ng•hr/ml respectively, indicating that a steady bimatoprost concentration was reached during the first week of ocular dosing.

Distribution

Bimatoprost is moderately distributed into body tissues and the systemic volume of distribution in humans at steady-state was 0.67 l/kg. In human blood, bimatoprost resides mainly in the plasma. The plasma protein binding of bimatoprost is approximately 88%.

Biotransformation
Bimatoprost is the major circulating species in the blood once it reaches the systemic circulation following ocular dosing. Bimatoprost then undergoes oxidation, N-deethylation and glucuronidation to form a diverse variety of metabolites.

Elimination
Bimatoprost is eliminated primarily by renal excretion, up to 67% of an intravenous dose administered to healthy adult volunteers was excreted in the urine, 25% of the dose was excreted via the faeces. The elimination half-life, determined after intravenous administration, was approximately 45 minutes; the total blood clearance was 1.5 l/hr/kg.

Characteristics in elderly patients
After twice daily dosing with 0.3 mg/ml bimatoprost (preserved formulation), the mean AUC0-24hr value of 0.0634 ng•hr/ml bimatoprost in the elderly (subjects 65 years or older) were significantly higher than 0.0218 ng•hr/ml in young healthy adults. However, this finding is not clinically relevant as systemic exposure for both elderly and young subjects remained very low from ocular dosing. There was no accumulation of bimatoprost in the blood over time and the safety profile was similar in elderly and young patients.

**5.3 Preclinical safety data**

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Monkeys administered ocular bimatoprost concentrations of ≥0.3 mg/ml daily for 1 year had an increase in iris pigmentation and reversible dose-related periocular effects characterised by a prominent upper and/or lower sulcus and widening of the palpebral fissure. The increased iris pigmentation appears to be caused by increased stimulation of melanin production in melanocytes and not by an increase in melanocyte number. No functional or microscopic changes related to the periocular effects have been observed, and the mechanism of action for the periocular changes is unknown.

Bimatoprost was not mutagenic or carcinogenic in a series of *in vitro* and *in vivo* studies.

Bimatoprost did not impair fertility in rats up to doses of 0.6 mg/kg/day (at least 103-times the intended human exposure with bimatoprost 0.3 mg/ml). In embryo/foetal developmental studies abortion, but no developmental effects were seen in mice and rats at doses that were at least 860-times or 1700-times higher than the dose in humans with bimatoprost 0.3 mg/ml, respectively. These doses resulted in systemic exposures of at least 33- or 97-times higher, respectively, than the intended human exposure with bimatoprost 0.3 mg/ml. In rat peri/postnatal studies, maternal toxicity caused reduced gestation time, foetal death, and decreased pup body weights at ≥ 0.3 mg/kg/day (at least 41-times the intended human exposure with bimatoprost 0.3 mg/ml). Neurobehavioural functions of offspring were not affected.

*Ocular absorption*
In pharmacokinetic studies conducted in animals, maximal concentrations of bimatoprost acid (main active metabolite) were reached 1 hour post-application of Elymbus and bimatoprost 0.1 mg/ml eye drops in both aqueous humour and iris ciliary body.
Based on cumulative bimatoprost and bimatoprost free acid content:

- Elymbus $C_{max}$ represented 3.3 and 4 times bimatoprost 0.1 mg/ml eye drops, solution $C_{max}$ in aqueous humor and iris ciliary body, respectively; and 0.74 and 0.78 times bimatoprost 0.3 mg/ml eye drops, solution $C_{max}$ in aqueous humor and iris ciliary body respectively
- Elymbus $AUC_{0.5\text{-}12h}$ represented 2.7 and 3.6 times bimatoprost 0.1 mg/ml eye drops, solution (preserved formulation) $AUC_{0.5\text{-}12h}$ in aqueous humor and iris ciliary body, respectively; and 0.7 and 0.6 times bimatoprost 0.3 mg/ml eye drops, solution (preserved formulation) $AUC_{0.5\text{-}12h}$ in aqueous humor and iris ciliary body respectively.

*Ocular toxicity*
Ocular administration of Elymbus to animals once a day for 28 days did not demonstrate any local or systemic toxic effect.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Sorbitol
Carbomer
Sodium acetate trihydrate
Macrogol
Sodium hydroxide (for pH-adjustment)
Water for injections

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 years.

After opening of the sachet: use the single-dose container within 1 month.
After opening of the single-dose container: use immediately and discard the single-dose container after use.

**6.4 Special precautions for storage**

This medicinal product does not require any special temperature storage conditions.
Keep the single-dose container in the sachet, in order to protect from light.
For storage after first opening of the medicinal product, see section 6.3.

**6.5 Nature and contents of container**

10 single-dose containers (LDPE) containing 0.3 g of eye gel are packed in sachet (polyethylene/aluminium/polyethylene/PET).
Pack sizes: 10 (1x10), 30 (3x10) or 90 (9x10) single-dose containers.
Not all pack sizes may be marketed.

**6.6 Special precautions for disposal**

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

**7 MARKETING AUTHORISATION HOLDER**

Laboratoires Thea
12 Rue Louis Bleriot
Clermont-Ferrand
63100
France

**8 MARKETING AUTHORISATION NUMBER**

PA1107/019/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 23rd June 2023

**10 DATE OF REVISION OF THE TEXT**