Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Drynol 6 mg/mL eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL solution contains 6 mg of bilastine.
Each drop contains 0.2 mg of bilastine.

For thefull list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution.
Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of ocular signs and symptoms of seasonal and perennial allergic conjunctivitis.

Drynol is indicated in adults and paediatric population aged 2 years and older.

4.2 Posology and method of administration

Posology
The recommended daily dosage in adults and paediatric population aged 2 years and older is: one drop in the affected eye(s) once daily.

Duration of treatment
Improvements in signs and symptoms in response to Drynol therapy are usually evident within a few days, but longer treatment for up to 8 weeks is sometimes required. Once symptomatic improvement has been established, therapy should be continued for as long as needed to sustain improvement. Therapy should not be used for more than 8 weeks without seeking medical advice.

Special populations

Elderly
No dosage adjustments are required in elderlypatients (see sections5.1 and 5.2).

Hepatic and renal impairment
Bilastine in the form of eye drops has not been studied in patients with renal or hepatic impairment. However, no dosage adjustment is expected to be necessary in hepatic or renal impairment (see section 5.2).

Paediatric population
The safety and efficacy of bilastine eye drops in children under 2 years have not been established. No data are available.

Method of administration
Ocular use.
The tip of the nozzle should be wiped with a clean tissue after use to remove any residual liquid.

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

Bilastine is an antiallergic/antihistaminic active substance and, although administered topically, it is absorbed systemically. If signs of serious reactions or hypersensitivity occur, treatment should be discontinued.
After dropping Drynol antiallergic eye drops into the conjunctival sac of the eye, the visual acuity can deteriorate for a few minutes due to the formation of streaks.

Reactions at administration site:
If adverse events at the administration site, such as eye irritation, pain, redness or change in vision occur or if the patient´s condition is worsened, discontinuation of the treatment should be considered.

Paediatric population
Efficacy and safety of bilastine eye drops in children under 2 years of age have not been established, therefore this medicinal product should not be used in these age group (see section 5.1).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. Considering the low systemic exposure to bilastine after ocular administration no clinically relevant interaction with other medicinal products is expected.
In case of concomitant therapy with other topical ocular medicinal products, an interval of 5 minutes should be allowed between successive applications. Eye ointments should be administered last.

Contact lenses:
Physical compatibility with contact lenses has been demonstrated *in vitro*. Patients can continue using contact lenses during treatment with this medicinal product.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited data from the oral or ocular use of bilastine in pregnant women.
Reproductive toxicity in animals was only observed at oral exposures more than 1000-fold higher than human levels after ocular dosing (see section 5.3).
No effects during pregnancy are therefore anticipated since systemic exposure to bilastine after ocular administration is negligible. Drynol can be used during pregnancy.

Breast-feeding
The excretion of bilastine in milk has not been studied in humans. Considering the low systemic absorption of bilastine after ocular administration (see section 5.2), no effects on the breastfed newborn/infant are anticipated after ocular administration in humans. Drynol can be used during breast-feeding.

Fertility
No impairments of fertility have been observed in rats (see section 5.3). Regarding human fertility, no effects are anticipated since systemic exposure to bilastine after ocular administration is negligible (see section 5.2).

4.7 Effects on ability to drive and use machines

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs after instillation, the patient should be advised to wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

Summary of safety profile in adult patients
In clinical studies involving bilastine 6 mg/mL eye drops, solution, 682 patients received one dose per day up to 8 weeks. Approximately 9.7% of patients can be expected to experience adverse reactions associated with the use of bilastine 6 mg/ml eye drops, solution. No serious or severe adverse event was reported.

Tabulated list of adverse reactions in adults
The following adverse reactions have been reported during clinical studies and are classified according to the following convention:

Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1,000 to < 1/100)
Rare (≥ 1/10,000 to < 1/1,000)
Very rare (< 1/10,000)
Not known (cannot be estimated from the available data)
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

	Uncommon
Nervous system disorders	Dysgeusia, Headache
Eye disorders	Dry eye Eye discharge Eye irritation Lacrimation increased Ocular discomfort

During post-marketing experience with oral bilastine formulations hypersensitivity reactions have been observed with frequency not known.

Summary of safety profile in paediatric population
In a paediatric clinical safety study involving bilastine 6 mg/mL eye drops, solution, 59 (42 bilastine and 17 placebo) patients aged from 2 to less than 18 years of age received one dose per day up to 8 weeks. The percentage of patients reporting adverse events during the 8-week treatment period with bilastine 6 mg/mL eye drops, solution was comparable with patients receiving placebo (23,8% vs 23,5%, respectively), also in terms of ocular adverse events (16.7% vs 17.6%, respectively).
The percentage of patients treated with bilastine 6 mg/mL eye drops, solution related adverse events was 0%. No serious or severe adverse events were reported.
Safety of bilastine eye drops in children below 2 years of age has not been established.

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 specific reactions after ocular overdose are known and with ocular use, overdose reactions are not anticipated as excessive fluid will flow out of the eye quickly.

In phase I clinical trials with oral formulations, doses up to 11 times (single dose) and up to 10 times (multiple dose), the human recommended oral dose have been tested, without any safety problems.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ophthalmologicals; decongestant and antiallergics.
ATC code: S01GX13

Mechanism of action
Bilastine is a non-sedating, long-acting second-generation histamine antagonist with selective peripheral H_1 receptor affinity and no apparent affinity for muscarinic receptors. Bilastine antagonises histamine, stabilizes mast cells and prevents histamine induced inflammatory cytokine production by human conjunctival epithelial cells, and thus prevents itching, vasodilation and vascular leak leading to ocular redness, chemosis and blepharitis.

Clinical efficacy and safety
The efficacy and safety of bilastine 6 mg/mL eye drops, solution was demonstrated in a Phase III multi-center, double-blind, randomized, parallel, placebo and active drug controlled study in 228 subjects using the Conjunctival Allergen Challenge (CAC) Model. The primary endpoint was defined as ocular itching evaluated by the subject at 3, 5 and 7 minutes after CAC performed 16 hours post-treatment (Day 1) and 15 minutes post-treatment (Day 8). Treatment differences for bilastine 6 mg/mL eye

drops, solution were statistically significant ($p < 0.05$) at both treatment visits (Day 1 and Day 8) for ocular itching compared to vehicle. LSMean treatment differences on a 5-point ocular itch scale across all time points were -1.167 (15 minutes post treatment) and -0.710 (16 hours post treatment).

For the key secondary efficacy endpoint of conjunctival redness, treatment differences were statistically significant ($p< 0.05$) for bilastine 6 mg/mL eye drops, solution compared to vehicle for all time points following CAC performed on Day 8 (15 minutes post treatment).

Subsequently, in a multi-centre, randomised, double blind, placebo-controlled, parallel, phase III study conducted to assess the safety, tolerability and efficacy of bilastine 6 mg/mL eye drops, solution, the product was found to be well tolerated and effective when used for up to 8 weeks in 218 adult patients. In this study, the number of ocular adverse events considered as related to treatment was low, with 7 adverse events in 6 patients (0.6%) for the bilastine group, and 5 adverse events in 5 patients (4.3%) in the placebo group.

Additionally, the safety, tolerability, both as primary endpoints, and efficacy, among the secondary endpoints, of bilastine 6 mg/mL eye drops, solution was studied in a double-blind, randomised, placebo-controlled, parallel-group, phase III clinical trial in 59 patients from 2 to less than 18 years of age with seasonal (SAC) or perennial allergic conjunctivitis (PAC) over a 8-week treatment period. In this study, bilastine 6 mg/mL eye drops, solution demonstrated a safety profile similar to placebo and consistent with that observed in adults, without any new safety concerns arising from its use.

Paediatric population
The European Medicines Agency has waived the obligation to submit the results of studies with this medicinal product in the paediatric population from birth to less than 2 years of age in the treatment of allergic conjunctivitis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Bilastine pharmacokinetic properties have been extensively studied with the oral formulation. In order to assess the PK properties of bilastine 6 mg/mL eye drops, solution, in a phase I study twelve healthy subjects received one drop into each eye per day (0.42 mg/day) for 5 days.

Absorption
Bilastine is rapidly absorbed into the blood stream after ocular application. At steady state, bilastine reached maximum blood levels of 2.7 ng/mL within 2.52 hours after administration, i.e., about 1.5% of C_{max} at steady state for bilastine 20 mg tablets.

Distribution
Bilastine is 84-90% bound to plasma proteins in humans, over the concentration range of 0.2 µg/mL to 1 µg/mL, which includes the plasma levels observed at therapeutic doses following oral administration of bilastine tablets. The apparent central distribution volume (Vc/F) was 59.2 L and the apparent peripheral distribution volume (Vp/F) was 30.2 L.

Biotransformation
Little or no metabolism was observed *in vitro* and *in vivo* for bilastine after oral administration. Bilastine did not induce or inhibit activity on CYP 450 isoenzymes in *in vitro* studies. No hepatic enzyme inhibition or induction by bilastine was detected.

Elimination
In a mass balance study performed in healthy adult volunteers, after administration of a single oral dose of 20 mg ^{14}C-bilastine, almost 95% of the administered dose was recovered in urine (28.3%) and faeces (66.5%) as unchanged bilastine, confirming that bilastine is not significantly metabolized in humans. The mean elimination half-life calculated in healthy volunteers was 14.5 h, while after ocular administration was 7.88 h.

Linearity
Bilastine presents linear pharmacokinetics in the dose range studied (5 to 220 mg oral application), with a low interindividual variability.

Renal impairment
A study was performed to determine the pharmacokinetics of bilastine (oral administration, 20 mg tablets) in renally-impaired subjects and to assess whether dose-adjustment may be necessary in patients with renal impairment. Based on results of this study, it can be concluded that the same dose and dosing interval of oral bilastine can be administered to subjects independently of the GFR in a safe and efficacious manner. Therefore, a need for dose adjustment or safety concerns in

patients with renal impairment taking bilastine is not expected for the 20 mg tablets and even less so for the ophthalmic solution as plasma concentrations are much lower.

Hepatic impairment
There are no pharmacokinetic data in subjects with hepatic impairment. Bilastine is not metabolized in humans. Since the results of the renal impairment study indicate renal elimination to be a major contributor in the elimination, biliary excretion is expected to be only marginally involved in the elimination of bilastine. Changes in liver function are not expected to have a clinically relevant influence on bilastine pharmacokinetics.

Elderly
Only limited pharmacokinetic data are available from phase II and phase III studies for oral dosage form of bilastine (20 mg tablets) in subjects older than 65 years. No statistically significant differences have been observed with regard to PK of bilastine in elderly aged over 65 years compared to adult population aged between 18 and 35 years.

5.3 Preclinical safety data

Non-clinical data with bilastine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential**.**
In reproduction toxicity studies, no effect on male and female fertility or pre- and postnatal development was detected at oral bilastine dose up to 1000 mg/kg bodyweight in rats. In embryo-foetal development studies with oral bilastine administration, slightly increased pre- and post-implantation losses in rats as well as delayed ossification and growth retardation in rabbits were only observed at more than 1000-fold in excess of the human exposure at the recommended ocular dose.
In a lactation study, bilastine was identified in the milk of nursing rats administered a single oral dose (20 mg/kg). Concentrations of bilastine in milk were about half of those in maternal plasma. Considering the low systemic absorption of bilastine after ocular administration (see section 5.2), lower levels of bilastine in human breast milk may therefore be expected.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxypropyl β-cyclodextrin
Methyl cellulose
Sodium hyaluronate
Glycerol (E 422)
Sodium hydroxide 1 N (for pH-adjustment)
Water for injections

6.2 Incompatibilities

Not known.

6.3 Shelf life

3 years.
After first opening of the bottle: 2 months without any special storage conditions.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Multi-dose white LDPE bottle (5 mL preservative free solution fill in a 7.6 mL container) and white HDPE nozzle with tamper evident system cap.

Pack sizes: 1 x 5 mL bottle.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Menarini International Operations Luxembourg S.A.
1, Avenue de la Gare
1611 Luxembourg
Luxembourg

8 MARKETING AUTHORISATION NUMBER

PA0865/018/005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd July 2022

10 DATE OF REVISION OF THE TEXT

October 2025