SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pilocarpine hydrochloride 2.0% w/v eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains 20 mg pilocarpine hydrochloride .

Excipient(s) with known effect
Each mL of solution contains 0.1 mg of benzalkonium chloride

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution

Clear, colourless, solution.

pH: 3.0 – 4.4

Osmolality: 120– 200 mOsmol/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of primary acute angle closure glaucoma, in conjunction with other medications / procedures to decrease intra-ocular pressure, after excluding secondary (lenticular and retrolenticular) causes of angle closure. Use only when intraocular pressure is less than 40 mm Hg

4.2 Posology and method of administration

Posology
One drop in the conjunctival sac of the affected eye, followed by one drop every 6 hours.

No dosage adjustments are required in the elderly and in patients with mild to moderate renal or hepatic impairment based on data from oral pilocarpine, the

expected very short duration of use and low systemic levels observed with ophthalmic pilocarpine.

Paediatric population:
Detailed reviews of the well-established safety profile of both topical and systemic pilocarpine did not reveal any significant differences in adverse effects in population groups. However, owing to theoretical pharmacokinetic considerations, treatment should be started with 1% pilocarpine in patients under 18 years of age. Depending on the clinical response and tolerability, the dose may be increased up to 2% pilocarpine eye drops.

Method of administration
For ocular use.

Patients should be instructed to wash their hands before use and avoid allowing the tip of the container to come into contact with the eye or surrounding structures.

Directly after administration of any dose, the lacrimal punctum should be occluded for one minute with a finger to limit systemic exposure.

4.3 Contraindications

- Hypersensitivity to the active substances(s) or to any of the excipients listed in section 6.1.
- Lenticular (phacomorphic or hypermature cataract) or Retrolenticular (drug-induced e.g. topiramate uveal effusions; viterous or subretinal haemorrhage; inflammatory effusions; tumors) causes of acute glaucoma
- Anterior uveitis
- Secondary glaucoma following trauma, ocular neovascularization or inflammation such as uveitis
- Soft contact lenses.

4.4 Special warnings and precautions for use

The use of intensive pilocarpine eye drops is not advised.

It should be used with caution in patients with darkly pigmented iris (may require a higher concentration or more frequent administration with care taken to avoid overdosage), conjunctival or corneal damage, pre-existing retinal disease since retinal detachment may occur, bronchial asthma, chronic bronchitis, chronic obstructive pulmonary disease, significant cardiovascular disease, hyperthyroidism, peptic ulceration, gastro-intestinal spasm, nephrolithiasis or urinary tract obstruction, cholelithiasis or biliary tract disease, epilepsy, Parkinson’s disease and psychiatric disturbances.

Adverse effects due to systemic absorption are rare, and more likely with higher concentrations of pilocarpine and/or more frequent dosing.

Excipients

Pilocarpine contains benzalkonium chloride which is known to discolour soft contact lenses. Contact with soft contact lenses should be avoided. Patients must be instructed to remove contact lenses prior to application of pilocarpine and wait at least 15 minutes after instillation of the dose before reinsertion.
Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

4.5 Interaction with other medicinal products and other forms of interaction

No specific drug interaction studies have been performed with ophthalmic pilocarpine.

Based on the known clinical pharmacology of pilocarpine:
- pilocarpine may enhance the pharmacologic effects of concomitant drugs with parasympathomimetic / cholinergic effects
- pilocarpine may inhibit the pharmacologic effects of concomitant drugs (e.g. atropine, ipratropium) with parasympatholytic / anticholinergic effects

Given the low systemic exposure following topical instillation, inhibition of CYP2A6 in vivo by pilocarpine is not expected. Thus, there is no in vitro basis to suspect in vivo drug-drug interactions. Also, drug-drug interactions involving protein binding are unlikely since pilocarpine does not significantly bind to plasma proteins.

4.6 Fertility, pregnancy and lactation

Pregnancy
The safety of pilocarpine for use in human pregnancy has not been established. Studies in animals report of reproductive and developmental toxicity following oral administration of pilocarpine (see section 5.3). However, given the expected short duration of use of ophthalmic pilocarpine and the low systemic levels following ocular instillation, this medicinal product can be used in pregnancy when considered essential.

Breast-feeding
Animal studies have shown that pilocarpine is excreted in breast milk at concentrations similar to maternal plasma. It is not known whether pilocarpine is secreted in human milk. However, given the expected short duration of use of ophthalmic pilocarpine and the low systemic levels following ocular instillation, this medicinal product can be used during breast feeding when considered essential. If ophthalmic pilocarpine is used during breastfeeding, it is recommended to monitor the infant for signs of cholinergic excess (diarrhea, lacrimation, and excessive salivation or urination), especially in younger, exclusively breastfed infants

Fertility
The effects of pilocarpine on male and female fertility in humans are unknown. Animal studies have shown adverse effects on spermatogenesis and a possible impairment of female fertility (see section 5.3). Given the low systemic exposure following ocular instillation and the short duration of use of this medicinal product, these observations are unlikely to be clinically relevant

4.7 Effects on ability to drive and use machines

Reduced visual acuity due to miosis especially in poor illumination, in the elderly and when lens changes are present as well as blurred vision and induced myopia due to ciliary or accommodative spasm are commonly reported after ophthalmic pilocarpine. Therefore, patients should not drive or operate machinery especially in dim light or if they experience reduced or blurred vision.

4.8 Undesirable effects

Adverse drug reactions from clinical trials are listed by MedDRA system organ class. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. In addition, the corresponding frequency category for each adverse drug reaction is based on 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).

System Organ Class	Frequency	Undesirable effect
Eye disorders	Common	Smarting, burning or stinging on instillation with itching and discomfort; conjunctival and ciliary congestion; decreased visual acuity in poor illumination (frequently experienced by older individuals and in those patients with lens opacity); induced myopia that is usually transient and may be associated with blurred vision.
	Rare	Conjunctival and lid sensitization (allergy), pupillary block, lacrimation, retinal detachment.
Nervous system disorder	Common	Headache and brow ache (especially in younger patients who have recently initiated therapy).
	Rare	Sweating, increased salivation, tremor
Cardiac disorders	Rare	Changes in cardiac rhythm
Vascular disorders	Rare	Changes in blood pressure
Respiratory, thoracic and mediastinal disorders	Rare	Bronchial spasm, bronchial mucus secretion
Gastrointestinal disorders	Rare	Nausea, vomiting and diarrhoea
Genito-urinary disorders	Rare	Urination
Ear, Nose and Throat disorders	Rare	Rhinorrhea, Sneezing

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 Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

If topical pilocarpine is accidentally ingested, the patient may exhibit signs of muscarinic (nausea, vomiting, abdominal cramps, diarrhoea, involuntary defecation, sweating, salivation, lacrimation, rhinorrhea, bronchial secretions / respiratory distress, urination, bradycardia, hypotension, miosis) and nicotinic (generalized weakness, muscle tremor, involuntary twitching, ataxia, slurred speech and confusion) toxicity. It is stated that 10 – 15 mg of pilocarpine can be expected to cause significant cholinergic signs and symptoms while ophthalmic pilocarpine hydrochloride 2.0% contains 20 mg / ml of eye drops and the maximum approved oral dose is 30 mg daily.
Parenteral atropine may be used to counter-act the muscarinic effects. Supportive treatment should be given as required; artificial respiration may be required if respiratory depression is severe.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Parasympathomimetic
ATC code: S01EB01

Mechanism of action
Pilocarpine is a cholinergic parasympathomimetic agent; it acts primarily at muscarinic receptor sites with a broad spectrum of pharmacologic effects. Contraction of the sphincter pupillae causes the iris diaphragm to become taut, thus preventing both crowding of the angle of the anterior chamber by the peripheral iris and relaxation of the peripheral iris which predisposes to iris bombe. Pilocarpine increases conventional aqueous outflow, and thus decreases IOP (intraocular pressure), by binding to and activating muscarinic receptors on ciliary smooth muscle cells, stimulating contraction of the longitudinal ciliary muscles. Functional consequences of ciliary muscle contraction include expansion of the juxtacanalicular portion of the trabecular meshwork and opening of the lumen of Schlemm canal. It also has a direct effect on aqueous outflow facility that is not dependent on the presence of an intact functional ciliary muscle.

Pharmacodynamic effects
Pilocarpine can reduce visual acuity due to miosis, cause temporary myopia due to induced accommodation and reduce intraocular pressure. Onset of miosis after the application of ophthalmic pilocarpine occurs within 10 – 30 minutes, with peak in 40 to 60 minutes, and lasts 9 to 24 hours. Induced accommodation commences in about 15 minutes, peaks in about 30 minutes and persists for up to 3 hours. Reduced intra-ocular pressure is observed within 60 minutes with the maximal effect around 2 hours and persists for about 6 to 8 hours depending on the concentration used.

Pilocarpine can increase secretion by exocrine glands such as sweat, lacrimal, gastric, pancreatic, intestinal and respiratory. It can also increase the tone and motility of the smooth muscles in the intestinal tract, respiratory tract, urinary tract, gall bladder and biliary duct. The expected effect of a muscarinic agonist is vasodepression (bradycardia and hypotension) but pilocarpine may also be associated with tachycardia and hypertension.

5.2 Pharmacokinetic properties

Absorption
In a single dose study of pilocarpine hydrochloride 2.0% in rabbits, aqueous humor levels of pilocarpine peaked at 30 minutes (mean 3.7 µg/ml) after instillation and commenced their decrease from 1 hour (mean 2.5 µg/ml), reaching negligible levels by 8 hours (mean 0.21 µg/ml).

Distribution
After ocular instillation, pilocarpine is detected at about the same concentration in the aqueous humour, iris and ciliary body indicating rapid distribution in these tissues. After oral administration, pilocarpine distributes widely and is generally eliminated in parallel with plasma. Pilocarpine is bound to tissue protein, especially pigments. Pilocarpine does not bind to plasma proteins.
Animal data indicates that pilocarpine is distributed into breast milk at concentrations similar to plasma and to the foetus of pregnant rats at half the maternal plasma concentration except for foetal liver which is the same as maternal plasma.

Metabolism
Pilocarpine is metabolized by plasma and tissue (ocular especially cornea and uvea and liver) esterases to pilocarpic acid as well as isopilocarpic acid and isopilocarpine. It is also metabolized to 3-hydroxypilocarpine by CYP2A6.

Elimination
Pilocarpine and its metabolites are mainly excreted in the urine.

Paediatric population:
Detailed reviews of the well-established safety profile of both topical and systemic pilocarpine did not reveal any significant differences in adverse effects in population groups. However, owing to theoretical pharmacokinetic considerations, treatment should be started with 1% pilocarpine in patients under 18 years of age. Depending on the clinical response and tolerability, the dose may be increased up to 2% pilocarpine eye drops.

Elderly
Based on data from oral pilocarpine, the expected very short duration of use and the low systemic levels observed with ophthalmic pilocarpine no dosage adjustment is required in the elderly.

Renal or Hepatic impairment
Based on data from oral pilocarpine, the expected very short duration of use and the low systemic levels observed with ophthalmic pilocarpine, no dosage adjustment is required in patients with mild or moderately impaired renal or hepatic function.

5.3 Preclinical safety data

Genotoxicity and Carcinogenicity
Pilocarpine did not exhibit any genotoxic potential in several in vitro and in vivo genotoxicity studies. In lifetime oral carcinogenicity studies in rodents, pilocarpine did not cause increased tumour incidence in mice. In rats increased incidences of benign pheochromocytomas were observed in males and females and increased incidences of hepatocellular adenomas were observed in females. Given the very low systemic exposure following topical instillation and expected short duration of use of this medicinal product, preclinical data revealed no special hazard for humans based on conventional studies of genotoxicity and carcinogenicity.

Reproductive toxicity
In a teratology study in rats, oral administration of 0, 7.5, 26, or 90 mg/kg/day pilocarpine hydrochloride throughout gestation resulted in a reduction in mean fetal body weight and increased incidence of skeletal variations at 90 mg/kg/day. In a teratology study in rabbits, oral administration of 0.1, 3, or 9 mg/kg/day pilocarpine hydrochloride throughout gestation resulted in no fetal toxicity.
In a peri- and postnatal development study, oral administration of pilocarpine hydrochloride to pregnant rats during gestation and lactation resulted in increased still births, decreased neonatal survival, and reduced mean fetal body weight at 18 mg/kg/day.
Impaired reproductive function was observed in male and female rats administered 18 mg/kg/day pilocarpine via oral gavage, including reduced fertility, decreased sperm motility, and morphologic evidence of abnormal sperm. It was unclear whether the impaired fertility was due to the effects on males, females, or both males and females. In dogs, evidence of impaired spermatogenesis was observed at an oral dosage of 3 mg/kg/day for 6 months.
Given the low systemic exposure following ocular instillation and the short duration of use of this medicinal product, effects on reproductive and developmental toxicity are unlikely to be clinically relevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride solution
Water for injection
Hydrochloric acid (E507) (for pH adjustment)
Sodium hydroxide (E524) (for pH adjustment)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months (unopened)
4 weeks (once opened)

6.4 Special precautions for storage

Store bottle upright, below 25°C, and in the original carton in order to protect from light.
Do not freeze.

6.5 Nature and contents of container

White Low density polyethylene (LDPE) 10ml bottle with transparent LDPE dropper tip and white HDPE (high-density polythene) tamper-evident cap. Each bottle contains 10 mL solution.

6.6 Special precautions for disposal

No special requirements

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

7 MARKETING AUTHORISATION HOLDER

Blumont Pharma Ltd
23 Moortown Close, Grantham, NG31 9GG, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 31103/0040

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/05/2025

10 DATE OF REVISION OF THE TEXT

29/05/2025