Summary of Product Characteristics

CYCLONAL

(Cyclopentolate Hydrochloride 1% w/v Eye Drops, Solution)

1 Name of the medicinal product

CYCLONAL – Cyclopentolate Hydrochloride 1% w/v Eye Drops, Solution

2 Qualitative and quantitative composition

Each ml of solution contains cyclopentolate hydrochloride 10 mg (1% w/v).

Excipient(s) with known effect
This medicinal product contains benzalkonium chloride and boric acid.

For the full list of excipients, see section 6.1.

3 Pharmaceutical form

Eye drops, solution.

A clear, colourless to pale yellow solution.

4 Clinical particulars

4.1 Therapeutic indications

CYCLONAL contains cyclopentolate hydrochloride, an anticholinergic (antimuscarinic) agent, and is used to produce mydriasis and cycloplegia. It is indicated:

- for diagnostic purposes, in fundoscopy and cycloplegic refraction;
- for dilating the pupil in inflammatory conditions of the iris and uveal tract.

4.2 Posology and method of administration

Posology

Adults (including the elderly)
Instil 1 or 2 drops into the eye, which may be repeated in 5 to 10 minutes if necessary. Maximal cycloplegia occurs within 25 to 75 minutes after instillation. Complete recovery of accommodation usually takes 6 to 24 hours, and complete recovery from mydriasis in some individuals may require several days.

Children
Instil 1 or 2 drops into the eye, which may be repeated in 5 to 10 minutes if necessary. Deeply pigmented irides may require more doses than lightly pigmented irides.

Infants and neonates
CYCLONAL 1% should not be used in small infants, as concentrations greater than 0.5% are not recommended in this population owing to the risk of serious systemic adverse reactions. Cyclopentolate should not be used during the first three months of life, because of the possible association between the cycloplegia produced and the development of amblyopia, and because of the increased risk of systemic toxicity in neonates.

Patients with hepatic or renal impairment

The safety and efficacy of CYCLONAL in patients with hepatic or renal impairment have not been established.

Method of administration

For ocular use only.

After the cap is removed, if the tamper-evident snap collar is loose, it should be removed before using the product.

To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip. The bottle should be kept tightly closed when not in use.

Nasolacrimal occlusion, or gently closing the eyelid, for 2 to 3 minutes after administration is recommended. This may reduce the systemic absorption of medicinal products administered via the ocular route and result in a decrease in systemic adverse reactions. If more than one topical ophthalmic product is being used, the products must be administered at least 5 minutes apart. Eye ointments should be administered last.

4.3 Contraindications

- Hypersensitivity to the active substance, to benzalkonium chloride, or to any of the excipients listed in section 6.1.
- Known, suspected or untreated angle-closure glaucoma, or untreated anatomically narrow angles, including patients with a shallow anterior chamber or a tendency towards glaucoma.
- Use whilst soft contact lenses are being worn, as this preparation contains benzalkonium chloride.
- Patients with paralytic ileus.
- Use in children with organic brain syndromes, including congenital or neurodevelopmental abnormalities, particularly those predisposing to epileptic seizures.

4.4 Special warnings and precautions for use

For topical ocular use only. Not for injection.

Systemic anticholinergic effects

Use with caution in patients, especially children, who have previously had a severe systemic reaction to atropine. Extreme caution is advised for use in children and in individuals susceptible to belladonna alkaloids, because of the increased risk of systemic toxicity.

Caution should be observed when medicinal products of this group are administered to patients with prostatic enlargement, coronary insufficiency or cardiac failure, or ataxia. Atropine-like effects have been reported as adverse reactions.

Intraocular pressure and glaucoma

CYCLONAL may cause increased intraocular pressure. The possibility of undiagnosed glaucoma should be considered in some patients, such as elderly patients. Because of the risk of precipitating angle-closure glaucoma in the elderly and others prone to raised intraocular pressure, the intraocular pressure should be determined and an estimate made of the depth of the angle of the anterior chamber prior to initiation of therapy, particularly if therapy is likely to be intense or protracted, in order to avoid glaucoma attacks.

Central nervous system effects

Cyclopentolate-induced psychotic reactions, behavioural disturbances and other central nervous system disturbances may occur in patients with increased susceptibility to anticholinergic medicinal

products. Use with caution in children and in elderly patients, although reactions may occur at any age.

Systemic absorption
Use with caution in an inflamed eye, as the hyperaemia greatly increases the rate of systemic absorption through the conjunctiva. To reduce systemic absorption, the lacrimal sac should be compressed at the medial canthus by digital pressure for at least two minutes after instillation of the drops.

Oral toxicity
Patients should be warned of the oral toxicity of this preparation and advised to wash their hands after use. If the product is accidentally swallowed, patients should be advised to seek medical attention.

Paediatric population
Use of mydriatic agents has been associated in preterm infants with feed intolerance, abdominal distension, increased gastric aspirate and rare cases of necrotising enterocolitis. Convulsions in children have also been reported in association with the use of cyclopentolate (see section 4.8).

Excipients
This medicinal product contains benzalkonium chloride, which may cause eye irritation and is known to discolour soft contact lenses. Contact with soft contact lenses must be avoided (see section 4.3).

This medicinal product contains boric acid, which may impair fertility.

4.5 Interaction with other medicinal products and other forms of interaction

The effects of CYCLONAL may be enhanced by concomitant use of other medicinal products having antimuscarinic properties, such as amantadine, some antihistamines, butyrophenones, phenothiazine antipsychotics and tricyclic antidepressants.

CYCLONAL may interfere with the ocular antihypertensive action of carbachol, pilocarpine or ophthalmic cholinesterase inhibitors.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no, or a limited amount of, data from the use of cyclopentolate eye drops in pregnant women. Animal reproduction studies have not been conducted with cyclopentolate. CYCLONAL is not recommended during pregnancy.

Breast-feeding
It is not known whether cyclopentolate or its metabolites are excreted into human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from CYCLONAL therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
Studies have not been performed to evaluate the effects of topical ocular administration of cyclopentolate on fertility.

4.7 Effects on ability to drive and use machines

CYCLONAL has a major influence on the ability to drive and use machines. It may cause drowsiness, blurred vision, difficulty in focusing and sensitivity to light. Patients receiving CYCLONAL should be advised not to drive or engage in other hazardous activities (including

climbing ladders and scaffolding) while the pupils are dilated and unless their vision is clear. Complete recovery from the effects may take up to 24 hours.

4.8 Undesirable effects

Tabulated list of adverse reactions

The following adverse reactions have been identified from post-marketing surveillance following administration of cyclopentolate eye drops. The frequency cannot be estimated from the available data. Within each System Organ Class, adverse reactions are presented in order of decreasing seriousness. Frequencies 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) and not known (cannot be estimated from the available data).

System Organ Class	Adverse reaction	Frequency
Psychiatric disorders	Abnormal behaviour[a], psychotic disorders[a]	Not known
Nervous system disorders	Dizziness, convulsions[b], partial seizures[b]	Not known
Eye disorders	Eye pain, increased intraocular pressure, eye oedema[1], eye irritation (stinging)[1], ocular hyperaemia[1], conjunctivitis[1], photophobia[2]	Not known
Cardiac disorders	Bradycardia, tachycardia, palpitations, arrhythmia, cardiopulmonary failure[a]	Not known
Vascular disorders	Flushing	Not known
Gastrointestinal disorders	Dry mouth, vomiting, gastrointestinal hypomotility and constipation, abdominal distension[c], necrotising enterocolitis[d]	Not known
Skin and subcutaneous tissue disorders	Dry skin, skin rash[a]	Not known
Renal and urinary disorders	Urinary urgency, urinary retention, dysuria	Not known
General disorders and administration site conditions	Gait disturbance	Not known

[1] Following prolonged administration. [2] Secondary to pupillary dilation.

[a] Abnormal behaviour, psychotic disorders, cardiopulmonary failure and skin rashes have been reported in the paediatric population. [b] Convulsions and partial seizures have been reported in children, although the cases reported to date have been low in number or isolated. [c] Cases of abdominal distension have been reported in infants. [d] Necrotising enterocolitis has been reported in preterm infants.

Description of selected adverse reactions

This medicinal product produces reactions similar to those of other anticholinergic medicinal products, but the central nervous system manifestations are more common. These may include ataxia, incoherent speech, restlessness, hallucinations, hyperactivity, seizures, disorientation as to time and place, and failure to recognise people. Other toxic manifestations of anticholinergic medicinal products are skin rash, abdominal distension in infants, unusual drowsiness, tachycardia, hyperpyrexia, vasodilation, urinary retention, diminished gastrointestinal motility, and decreased secretion in the salivary and sweat glands, pharynx, bronchi and nasal passages. Severe reactions are manifested by hypotension with rapid progressive respiratory depression, coma, medullary paralysis and death.

CYCLONAL may increase intraocular pressure and provoke glaucoma attacks in patients predisposed to acute angle closure, in particular geriatric patients. The onset of cyclopentolate toxicity occurs within 20 to 30 minutes of instillation and, although usually transient (subsiding in 4 to 6 hours), the symptoms can last 12 to 24 hours.

Paediatric population

An increased risk of systemic toxicity has been observed with this class of medicinal product in premature and small infants, young children, and children with Down syndrome, spastic paralysis or brain damage. Use of cyclopentolate has been associated with psychotic reactions and

behavioural changes in paediatric patients, with central nervous system reactions manifesting as described above. Seizures and acute psychosis induced by cyclopentolate are especially prominent in children. Feeding intolerance may follow ophthalmic use of the product in infants. A local or generalised allergic-type response to cyclopentolate, consisting of an urticarial rash, has been described in children.

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 to the National Regulatory Authority.

4.9 Overdose

An ocular overdose of CYCLONAL may be flushed from the eye(s) with lukewarm water. Excessive dosage may produce behavioural disturbances, tachycardia, hyperpyrexia, hypertension, elevated intraocular pressure, vasodilation, urinary retention, diminished gastrointestinal motility and decreased secretion in the salivary and sweat glands, pharynx, bronchi and nasal passages.

Systemic toxicity may occur following topical use, particularly in children. It is manifested by flushing and dryness of the skin (a rash may be present in children), blurred vision, a rapid and irregular pulse, fever, abdominal distension in infants, convulsions, hallucinations and loss of neuromuscular coordination. Severe intoxication is characterised by central nervous system depression, coma, circulatory and respiratory failure, and death.

Patients exhibiting signs of overdosage should receive symptomatic and supportive treatment and monitoring; there is no evidence that physostigmine is superior to supportive management. In infants and small children, the body surface must be kept moist.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals; mydriatics and cycloplegics, anticholinergics.

ATC code: S01FA04

Mechanism of action
This anticholinergic preparation blocks the responses of the sphincter muscle of the iris and of the accommodative muscle of the ciliary body to cholinergic stimulation, producing pupillary dilation (mydriasis) and paralysis of accommodation (cycloplegia).

Pharmacodynamic effects
Cyclopentolate acts rapidly but has a shorter duration of action than atropine. Maximal cycloplegia occurs within 25 to 75 minutes after instillation. Complete recovery of accommodation usually takes 6 to 24 hours, and complete recovery from mydriasis in some individuals may require several days. Heavily pigmented irides may require more doses than lightly pigmented irides.

5.2 Pharmacokinetic properties

Systemic absorption may take place after topical administration to the eye, occurring primarily via the lacrimal ducts. In humans, cyclopentolate is rapidly absorbed systemically, and peak plasma concentrations of 8.3 ± 4.1 ng/ml were reached 10 ± 5 minutes after a single topical ocular administration of 2 drops of a 10 mg/ml cyclopentolate solution. Systemic concentrations of cyclopentolate decreased to 3.3 ± 1.1 ng/ml at 30 minutes after dosing. The mean elimination half-

life of cyclopentolate was 111 minutes. No additional information regarding the metabolic fate of cyclopentolate, or its route and extent of elimination following systemic absorption, is available.

5.3 Preclinical safety data

No significant ocular irritation or toxicity was observed in a one-day study in rabbits employing a high dosing regimen of a 2% cyclopentolate hydrochloride solution. There are no available data regarding the reproductive toxicity or the mutagenic potential of cyclopentolate in experimental animals, and animal reproduction studies have not been conducted with cyclopentolate. Studies have not been conducted to evaluate the carcinogenic potential of cyclopentolate, and there are no indications that cyclopentolate possesses oncogenic potential in experimental animals. Preclinical data with higher doses do not give rise to the suspicion of special risks, other than enhanced pharmacological effects.

6 Pharmaceutical particulars

6.1 List of excipients

- Boric acid
- Potassium chloride
- Disodium edetate
- Benzalkonium chloride
- Sodium carbonate
- Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 30°C.

Keep out of the sight and reach of children.

6.5 Nature and contents of container

White plastic LDPE vial containing 5 ml of solution, sealed and packed in a carton with a package insert.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7 Marketing authorisation holder

National Pharmacy Ltd

Colchester Park

P.O. Box 17843-00500

Nairobi

Kenya

8 Marketing authorisation number

9 Date of first authorisation/renewal of the authorisation

10 Date of revision of the text