AUSTRALIAN PRODUCT INFORMATION – MINIMS PHENYLEPHRINE (PHENYLEPHRINE HYDROCHLORIDE) EYE DROPS

1 NAME OF THE MEDICINE

Phenylephrine hydrochloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Minims Phenylephrine Eye Drops containing phenylephrine hydrochloride 2.5% w/v (25 mg/mL) or 10% w/v (100 mg/mL). No preservatives are contained in the formulation.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

A single-use eye drops, solution.

Minims Phenylephrine are clear, colourless sterile solutions, reasonable free from visible particulate matter.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Phenylephrine is a directly acting sympathomimetic agent used topically in the eye as a mydriatic. Minims Phenylephrine Hydrochloride Eye Drops are indicated to dilate the pupil for diagnostic or therapeutic procedures.

4.2 DOSE AND METHOD OF ADMINISTRATION

The use of a drop of topical anaesthetic a few minutes before instillation of Minims Phenylephrine Eye Drops is recommended to prevent stinging.

Adults
Instil one drop topically to each eye. If necessary, this dose may be repeated once only, at least one hour after the first drop.

Children and the elderly
Instil one drop of the 2.5% solution topically to the eye. It is not usually necessary to exceed this dose. The use of phenylephrine 10% is contraindicated in children (see Sections 4.3 Contraindications and 4.4 Special warnings and precautions for use – Paediatric use) and the elderly because of the increased risks of systemic toxicity.

Systemic absorption of phenylephrine may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops. (This blocks the passage of

the drops via the naso-lacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa. It is especially advisable in children.)

Each Minims Phenylephrine Eye Drops unit should be discarded after a single use.

4.3 CONTRAINDICATIONS

Minims Phenylephrine Eye Drops are contraindicated in:

- Patients with hypersensitivity to any of the components of the preparation.

- Children and the elderly with Minims Phenylephrine Hydrochloride Eye Drops 10% because of the increased risk of systemic toxicity.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Identified precautions

Minims Phenylephrine Eye Drops are for topical ophthalmic use only. The solution should not be injected.

Caution must be exercised when using Minims Phenylephrine Hydrochloride Eye Drops in the following patient groups:

- Patients with cardiac disease, hypertension, aneurysms, long-standing insulin dependent diabetes mellitus and tachycardia.
- Patients on monoamine oxidase inhibitors, tricyclic antidepressants and anti- hypertensive agents (including beta blockers).
- Patients with closed angle glaucoma (unless previously treated with iridectomy) and patients with a narrow angle prone to glaucoma precipitated by mydriatics.
- The use of phenylephrine 10% solution is contraindicated in children and the elderly because of the increased risks of systemic toxicity (see also Paediatric use).
- Patients treated with:

Anti-hypertensive agents: Topical phenylephrine may reverse the action of many anti-hypertensive agents with possibly fatal consequences.

Monoamine oxidase inhibitors: There is an increased risk of adrenergic reactions when used simultaneously with, or up to three weeks after, the administration of MAOIs.

Tricyclic anti-depressants: The pressor response to adrenergic agents and the risk of cardiac arrhythmia may be potentiated in patients receiving tricyclic anti-depressants (or within several days of their discontinuation).

Halothane: Because of the increased risk of ventricular fibrillation, phenylephrine should be used with caution during general anaesthesia with anaesthetic agents which sensitise the myocardium to sympathomimetics.

Cardiac glycosides or quinidine: There is an increased risk of arrhythmias if phenylephrine is used in patient taking cardiac glycosides or quinidine.

There have been rare reports associating the use of phenylephrine hydrochloride 2.5% and 10% ophthalmic solutions with the development of serious cardiovascular reactions, including ventricular arrhythmias and myocardial infarctions. These episodes, some ending fatally, have usually occurred in elderly patients with pre- existing cardiovascular diseases.

A significant elevation in blood pressure is rare but has been reported following conjunctival instillation of recommended doses of phenylephrine hydrochloride 10% ophthalmic solutions. Caution should be exercised in children, the elderly, and patients with diabetes, hypertension, hyperthyroidism, generalised arteriosclerosis or cardiovascular disease.

Minims Phenylephrine Eye Drops should be used with caution in the presence of long standing bronchial asthma.

To reduce the risk of precipitating an attack of narrow angle glaucoma the anterior chamber angle should be evaluated before use.

Ocular hyperaemia can increase the absorption of phenylephrine given topically. Corneal clouding may occur if phenylephrine 10% is instilled when the corneal epithelium has been denuded or damaged.

Due to a strong action of the drug on the dilator muscle, older individuals may also develop transient pigment floaters in the aqueous humor 30 to 45 minutes following the administration of the eye drops. The appearances may confused with anterior uveitis or to a microscopic hyphema.

Systemic absorption of phenylephrine may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops. (This blocks the passage of the drops via the naso-lacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa).

Use in the elderly

The use of phenylephrine 10% is contraindicated in the elderly because of the increased risks of systemic toxicity. Where phenylephrine eye drops are indicated for use in this group, the 2.5% solution should be used.

Paediatric use

Use of phenylephrine 10% solution is contraindicated in children. Serious systemic adverse reactions have been reported with ophthalmic products containing phenylephrine in children below 12 years of age.

There is inadequate clinical experience in children aged 12 to 18 years. Where phenylephrine eye drops are indicated for use in this group, the 2.5% solution should be used.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Although negligible phenylephrine passes into the bloodstream after ocular instillation, drug interactions are nevertheless possible. The interactions observed with phenylephrine administered by any route should therefore be taken into account (see Section 4.4 Special Warnings and Precautions for Use).

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Studies have not been performed in either animals or humans to evaluate the potential for phenylephrine to impair fertility.

Use in pregnancy – Category B2

Safety for use in pregnancy has not been established. Minims Phenylephrine Eye Drops should only be used during pregnancy if it is considered by the physician to be essential.

Use in lactation.

Safety for use in lactation has not been established. Minims Phenylephrine Eye Drops should only be used during lactation if it is considered by the physician to be essential.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Minims Phenylephrine Eye Drops may cause stinging and transient blurring of vision. Patients should be advised not to drive or operate hazardous machinery until vision is clear.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

Local

Eye pain and stinging on instillation, temporary blurred vision, photophobia, conjunctival allergy, reactive hyperaemia and transient punctuate keratitis may occur. Other local adverse effects reported include: lacrimation, corneal oedema, pigmented aqueous floaters, rebound miosis, and rebound conjunctival vasoconstriction.

Systemic

Palpitations, tachycardia, extrasystoles, cardiac arrhythmias and hypertension, headache, subarachnoid haemorrhage, reflex bradycardia, blanching of the skin, trembling or tremors, and increased perspiration.

Serious cardiovascular reactions including significant hypertension, aneurisms, coronary artery spasm, ventricular arrhythmias and myocardial infarctions have occurred following topical use of 2.5% and 10% phenylephrine. These sometimes fatal reactions have usually occurred in patients with pre-existing cardiovascular disease.

Undesirable effects

Paediatric population

Phenylephrine 2.5% Eye Drops: Periorbital pallor in preterm patients – Frequency not known (cannot be estimated from the available data).

Phenylephrine 10% Eye Drops: Respiratory, thoracic and mediastinal disorders – Pulmonary oedema – Frequency not known (cannot be estimated from the available data).

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

Because severe toxic reaction to phenylephrine is of rapid onset and short duration, treatment is primarily supportive. Prompt injection of a rapidly acting alpha- adrenergic blocking agent such as phentolamine (dose 2 to 5 mg IV) has been recommended.

Reversal of mydriasis is possible with 0.1% thymoxamine.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Phenylephrine is a direct acting sympathomimetic agent. It causes mydriasis via the stimulation of alpha-adrenergic receptors. There is almost no cycloplegic effect.

Phenylephrine is an alpha agonist, with both alpha-1A and alpha –1B effects.

Alpha adrenergic receptors are unimportant in the aqueous humour outflow response, hence there is no effect on intraocular pressure in open angle glaucoma.

The Phenylephrine molecule differs from adrenalin only by the substitution of a hydrogen atom for a hydroxyl group on position 4 of the benzene ring

Maximal mydriasis occurs in 10 – 90 minutes with recovery after 5 – 7 hours.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Phenylephrine is a weak base at physiological pH. The extent of ocular penetration is determined by the condition of the cornea. A healthy cornea presents a physical barrier, in addition to which, some metabolic activity may occur. Where the corneal epithelium is damaged, the effect of the barrier and the extent of metabolism are reduced, leading to greater absorption.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Phenylephrine was negative in tests for bacterial mutagenicity and did not cause chromosomal aberrations in Chinese hamster ovary cells.

Carcinogenicity

There are no studies on the carcinogenicity of phenylephrine by the topical ocular route. No carcinogenic activity was noted in mice or rats receiving oral doses of up to 270 and 50 mg/kg/day, respectively, for 2 years.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium metabisulphite, disodium edetate and purified water.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C to 8°C. (Refrigerate. Do not freeze.). Do not expose to strong light.

6.5 NATURE AND CONTENTS OF CONTAINER

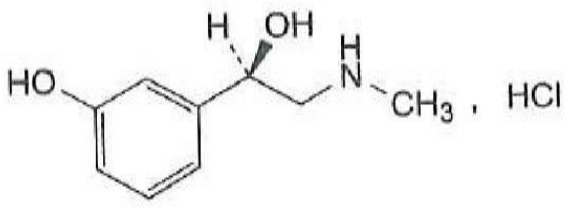
Minims Phenylephrine Eye Drops are supplied in a single use polypropylene tube (unit) overwrapped in a polyester/paper blister. The blisters are packed in cartons of 20 units. Each unit contains approximately 0.5 mL solution.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



Chemical name: (1*R*)-1-(3-Hydroxyphenyl)-2-(methylamino)ethanol hydrochloride

Molecular formula: $C_9H_{13}NO_2.HCl$

Molecular weight: 203.7

CAS number

61-76-7

7 MEDICINE SCHEDULE (POISONS STANDARD)

Minims Phenylephrine Eye Drops 2.5% - S2 – Pharmacy Medicine

Minims Phenylephrine Eye Drops 10% - S4 – Prescription Only Medicine

8 SPONSOR

Bausch & Lomb (Australia) Pty Ltd

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9 DATE OF FIRST APPROVAL

17 June 2009

10 DATE OF REVISION

27 January 2021

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2	Clarification of use of Phenylephrine 10% solution in children
4.4	Clarification of use of Phenylephrine 10% in children