PRODUCT INFORMATION

MINIMS® PHENYLEPHRINE EYE DROPS

NAME OF THE MEDICINE
Phenylephrine Hydrochloride

Structural formula:

![Structural formula of Phenylephrine Hydrochloride](image)

Chemical name: (1R)-1-(3-Hydroxyphenyl)-2-(methylamino)ethanol hydrochloride
Molecular formula: C_{9}H_{13}NO_{2}.HCl
Molecular weight: 203.7
CAS number: 61-76-7

DESCRIPTION
Minims Phenylephrine Eye Drops are clear, colourless sterile eye drops containing phenylephrine hydrochloride 2.5% or 10% w/v as well as sodium metabisulphite, disodium edetate and purified water.

PHARMACOLOGY
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.

Pharmacokinetics
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.
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.

CONTRAINDICATION
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.

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.
- 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 sensitize 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.)

**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.

**Paediatric use**

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

**Use in the elderly**

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

**Effects on carcinogenicity and genotoxicity**

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

**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.

**INTERACTIONS WITH OTHER MEDICINES**
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 Precautions).

**ADVERSE EFFECTS**

**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).

**DOSAGE AND 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 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.

OVERDOSAGE

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.

PRESENTATION AND STORAGE CONDITIONS

Presentation: Minims Phenylephrine Eye Drops are supplied as a clear colourless sterile eye drops 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.

Minims Phenylephrine hydrochloride Eye Drops are available in two strengths: 2.5% (25 mg/mL) and 10% w/v (100 mg/mL)

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

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

NAME AND ADDRESS OF THE SPONSOR

iNova Pharmaceuticals (Australia) Pty Ltd
Level 10, 12 Help Street
Chatswood, NSW 2067

POISON SCHEDULE OF THE MEDICINE

Minims Phenylephrine Eye Drops 2.5% - S2 – Pharmacy Medicine
Minims Phenylephrine Eye Drops 10% - S4 – Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (the ARTG)

17 June 2009

DATE OF MOST RECENT AMENDMENT

22 January 2016