AUSTRALIAN PRODUCT INFORMATION - PREDNEFRIN® FORTE (PREDNISOLONE ACETATE AND PHENYLEPHRINE HYDROCHLORIDE)

1 NAME OF THE MEDICINE

Phenylephrine hydrochloride and prednisolone acetate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

PREDNEFRIN® FORTE eye drops contains prednisolone acetate (microfine suspension) 10 mg (1%) and phenylephrine hydrochloride 1.2 mg (0.12%).

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

3 PHARMACEUTICAL FORM

PREDNEFRIN® FORTE eye drops is a sterile ophthalmic suspension.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Severe inflammation (non-infectious) of the eye, such as acute iritis, iridocyclitis, scleritis, episcleritis, uveitis, resistant ocular allergy and inflammation following surgery (where no infectious aetiology is suspected), particularly where unusually rapid control of the inflammation is desired.

4.2 DOSE AND METHOD OF ADMINISTRATION

1 to 2 drops instilled into the conjunctival sac two to four times daily. During the initial 24 to 48 hours the dosage may be safely increased to 2 drops every hour. The physician may choose the dosage which affords optimal therapeutic effect in each case.

In order to minimise systemic absorption of PREDNEFRIN® FORTE eye drops, apply pressure to the tear duct immediately following administration of the drug.

Care should be taken not to discontinue therapy prematurely.

4.3 CONTRAINDICATIONS

PREDNEFRIN® FORTE eye drops is contraindicated in:

- Acute untreated purulent infections, such as superficial (or epithelial) Herpes simplex keratitis (dendritic keratitis), vaccinia, varicella and most other viral diseases of the cornea and conjunctiva
- Ocular tuberculosis and fungal infections of the ocular structures of the eye

- Mycobacterial infection of the eye
- Narrow angle glaucoma
- Hypersensitivity to prednisolone acetate, phenylephrine hydrochloride, benzalkonium chloride or any of the other constituents.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

In diseases due to microorganisms, acute untreated infection may be masked, enhanced or activated by the steroid. Since PREDNEFRIN® FORTE eye drops is not an anti-infective, if infection is present, appropriate measures must be taken to counteract the organisms involved. Prolonged use may also suppress the host immune response and thus increase the hazard of secondary ocular infections. As fungal infections of the cornea are particularly prone to develop with long-term local steroid application, fungal invasion must be suspected in any persistent corneal ulceration where a steroid has been used, or is in use. Fungal cultures should be taken when appropriate. Use of intraocular steroid medication in the presence of stromal Herpes simplex may prolong the course and may exacerbate the severity of many viral infections of the eye. Use of corticosteroid mediciation in the treatment of patients with a history of Herpes Simplex requires caution and should be followed by frequent mandatory slit-lamp microscopy (please refer to section **4.3 Contraindications**). PREDNEFRIN® FORTE eye drops contains benzalkonium chloride as a preservative.

Eye drops containing corticosteroids should not be used for more than 10 days except under strict ophthalmic supervision with regular checks for intraocular pressure. Extended use of topical corticosteroids may cause increased intraocular pressure in susceptible individuals resulting in glaucoma, with damage to the optic nerve, defects in visual acuity and fields of vision. Prolonged use may result in posterior subcapsular cataract formation.

In diseases causing thinning of the cornea, perforation has been known to have occurred with the use of topical steroids. Reports in the literature indicate that posterior subcapsular lenticular opacities have been reported to occur after heavy or protracted use of topical ophthalmic corticosteroids.

PREDNEFRIN® FORTE eye drops contains sodium metabisulfite, a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. Sulfite sensitivity is seen more frequently in asthmatic patients.

The possibility of adrenal suppression should be considered with prolonged, frequent use of high dose topical steroids, particularly in infants and children.

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

If patient experiences eye pain, changes in vision, ocular irritation or if eye irritation and redness persist over 72 hours, discontinue use and consult a doctor.

Potential Systemic Effects
PREDNEFRIN® FORTE eye drops should be used with caution in patients with arteriosclerosis, hypertension, hyperthyroidism, prostatic enlargement, or diabetes.

Treatment should be used with caution in patients receiving monoamine oxidase (MAO) inhibitor therapy or within 14 days of stopping such treatment as patients may experience hypertensive crisis.

To minimise risk of potential systemic effects, the puncta should be depressed after instillation of drops to reduce drainage through the nasolacrimal duct to the oral and nasal mucosa.

Eye Inflammation
Use PREDNEFRIN® FORTE eye drops with caution on an inflamed eye, as hyperaemia greatly increases the rate of systemic absorption through the conjunctiva.

Use with contact lenses
PREDNEFRIN® FORTE eye drops contain the preservative benzalkonium chloride, which may be absorbed by and cause discoloration of soft contact lenses. Patients wearing soft (hydrophilic) contact lenses should be instructed to remove contact lenses prior to administration of PREDNEFRIN® FORTE eye drops and wait at least 15 minutes following administration before reinserting soft contact lenses.

Potential for Eye Injury or Contamination
To prevent eye injury or contamination, care should be taken to avoid touching the bottle tip to the eye or to any other surface.

Visual Disturbance
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, consider evaluating for possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Information for patients
Upon instillation, patients may experience transient blurred vision which may impair the ability to drive or use machinery. If affected, patients should not drive or use machinery until their vision has cleared.

Use in the elderly
No data available.

Paediatric Use
Safety and effectiveness have not been demonstrated with PREDNEFRIN® FORTE eye drops in paediatric patients. PREDNEFRIN® FORTE eye drops is not recommended to be used in pediatric patients.

Effects on laboratory tests
No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No interaction studies have been performed. Concurrent use of MAOI, tricyclic antidepressants, guanethidine or systemic adrenergic blockers may alter the effects of PREDNEFRIN® FORTE eye drops.

Although the systemic exposure is expected to be low with topical ophthalmic corticosteriod administration, co-treatment with CYP3A inhibitors may increase the risk of systemic corticosteroid-related adverse effects.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No data available.

Use in pregnancy
Pregnancy Category C
In animal experiments, corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations) and abortion. These findings do not seem to be relevant to humans. Reduced intrauterine growth and lower birth weight have been recorded in animals and humans after long-term or high dose treatment. Suppression of the adrenal cortex in the newborn baby may occur after long-term treatment. The short-term use of corticosteroids prior to delivery for the prevention of respiratory distress syndrome, does not seem to pose a risk to the fetus or the newborn infant.

There are no adequate and well-controlled studies in pregnant women. PREDNEFRIN® FORTE should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.
Maternal pulmonary oedema has been reported with tocolysis and fluid overload.

Use in lactation
It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Therefore, use is not recommended in women breast feeding infants.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

PREDNEFRIN® FORTE eye drops may cause pupillary dilation, transient blurring of vision, which may impair the ability to drive or operate machines. The patient should wait until their vision has cleared before driving or using machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Immune system disorders:
Hypersensitivity, urticaria

Nervous system disorders:
Headache

Eye disorders:
Adverse reactions include increased intraocular pressure, which may be associated with optic nerve damage and defects in the visual fields; posterior subcapsular cataract formation; eye penetration (sclera or corneal perforation), ocular infections from bacteria, fungi or viruses liberated from ocular tissues and perforation of the globe when used in conditions where there is thinning of the cornea or sclera, eye irritation, vision blurred/visual disturbances and mydriasis

Gastrointestinal disorders:
Dysgeusia

Skin and subcutaneous tissue disorders:
Pruritus and rash

General disorders and administration site conditions:
Systemic side effects may occur rarely with extensive use of topical steroids

Post-marketing experiences:
The following adverse reactions have been identified during post-marketing use of PREDNEFRIN® FORTE eye drops. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made.

Eye disorders:
Dry eye, eye discharge, cataract subcapsular, eye Irritation, eye pain, eye penetration (scleral or corneal perforation), foreign body sensation, intraocular pressure increased, ocular infection (including bacterial, fungal, and viral infections), eye pruritus, lacrimation increased, mydriasis, ocular hyperemia, vision blurred

Immune system disorders:
Hypersensitivity reaction including symptoms or signs of eye allergy and skin allergy

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.

4.9 OVERDOSE

Although overdose by the topical ophthalmic route will not ordinarily cause acute problems, it may cause systemic sympathomimetic effects (e.g. palpitation, headache and hypertension). In case of overdose, immediately flush eyes with water or normal saline. If accidentally ingested, drink fluids to dilute.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action
Prednisolone acetate is a glucocorticoid that, on the basis of weight, has 3 to 5 times the anti-inflammatory potency of hydrocortisone. Glucocorticoids inhibit the oedema, fibrin deposition, capillary dilation and phagocytic migration of the acute inflammatory response as well as capillary proliferation, deposition of collagen and scar formation. The phenylephrine component of PREDNEFRIN® FORTE eye drops constricts the engorged vessels of the eye and lid.

Clinical trials
No data available.

5.2 PHARMACOKINETIC PROPERTIES

No data available

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
No data available.

Carcinogenicity
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Preservative: benzalkonium chloride 0.04 mg (0.004%) per 1 mL

Inactives: hypromellose, phenazone, polysorbate 80, boric acid, sodium citrate, sodium metabisulfite, sodium chloride, 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

3 years.
Contents are sterile if seal is intact.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Protect from freezing. Store upright.
Shake well before using.

6.5 NATURE AND CONTENTS OF CONTAINER

A sterile suspension in 10 mL dropper bottles.

To avoid contamination of the suspension, keep container tightly closed.
Do not touch dropper tip to any surface.

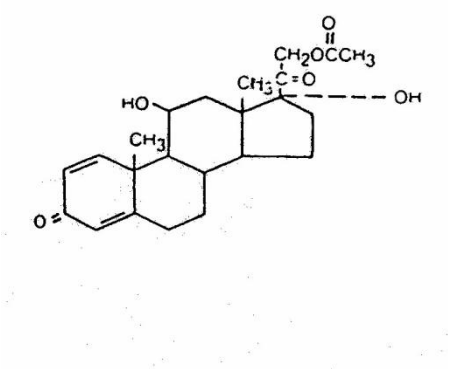
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Discard unused contents 4 weeks after opening.

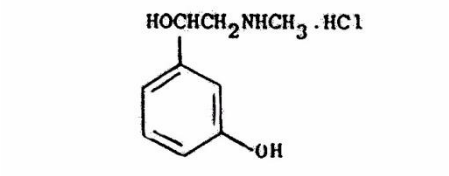
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure:



Structure of prednisolone acetate



Structure of phenylephrine hydrochloride

CAS Registry Number:

Prednisolone acetate: 52-21-1

Phenylephrine hydrochloride: 61-76-7

Prednisolone acetate is an odourless, white or almost white, crystalline powder. Practically insoluble in water, soluble 1 in 120 of alcohol; slightly soluble in acetone and chloroform.

Molecular Weight: 402.5
Chemical Name: 11ß,17α,21-trihydroxypregna-1,4-diene-3,20-dione
Empirical formula: $C_{21}H_{28}O_5$

Phenylephrine hydrochloride is white or almost white, odourless crystals or crystalline powder. Soluble 1 in 2 of water, and 1 in 4 of alcohol; practically insoluble in chloroform.
Molecular Weight: 203.7
Chemical Name: (R)-3-hydroxy- α-[(methylamino)methyl]benzenemethanol hydrochloride
Empirical formula: $C_9H_{14}ClNO_2$

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

AUST R23235

8 SPONSOR

Allergan Australia Pty Ltd
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ABN: 85 000 612 831

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9 DATE OF FIRST APPROVAL

14 October 1991

10 DATE OF REVISION

03 July 2018

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
The PI has been reformatted in line with the TGA's approved form for PIs. Additional mandatory headings and standard text have been included to the PI line with the TGA's approved form for PIs. Minor editorial changes have been made throughout the PI to improve legibility.	
3	Addition of "Pharmaceutical Form" in line with TGA Approved form for product information
4.4	Addition of safety information relating to "Visual disturbance" in line with CCDS v5.0
4.5	Addition of safety information in line with CCDS v5.0
4.8	MedDRA SOC headings added and adverse events in this section have been moved under the appropriate MedDRA SOC in line with CCDS v5.0
7	Addition of the AUST R number