Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pred Mild Sterile Ophthalmic Suspension, 0.12% w/v, Eye Drops, Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains prednisolone acetate 0.12% w/v.
Excipient(s) with known effect: benzalkonium chloride 0.004% w/v.
boric acid 1% w/v.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops suspension.
Off-white microfine suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Mild to moderate non-infectious allergic and inflammatory disorders of the lid, conjunctiva, cornea and sclera (including chemical and thermal burns) in adults.

4.2 Posology and method of administration

Posology

One to two 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 two drops every hour.
Care should be taken not to discontinue therapy prematurely.

Paediatric population
The safety and efficacy of Pred Mild in paediatric patients have not been established. No posology can be recommended.

Method of administration

To reduce possible systemic absorption, it may be recommended that the lacrimal sac be compressed at the medial canthus (punctal occlusion) for 1 minute. This should be performed immediately following the instillation of each drop.

Shake well before use.

4.3 Contraindications

Acute untreated purulent ocular infections, such as superficial (or epithelial) herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, fungal infections of the ocular structures, mycobacterial infection such as tuberculosis of the eye.

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Eye drops containing corticosteroids, should not be used for more than one week except under strict ophthalmic supervision with regular checks for intraocular pressure.

Use of intraocular steroids may prolong the course and may exacerbate the severity of many viral infections on the eye (including herpes simplex). Employment of a corticosteroid medication in the treatment of the patients with a history of herpes simplex requires great caution; frequent slit lamp microscopy is recommended.

Corticosteroids are not effective in mustard gas keratitis and Sjogren's keratoconjunctivitis.

Since Pred Mild contains no antimicrobial, if infection is present appropriate measures must be taken to counteract the organism involved.

Prolonged use may increase intraocular pressure in susceptible individuals, resulting in glaucoma, with damage to the optic nerve, defects in visual acuity and fields of vision and posterior subcapsular cataract formation. Steroids should be used with caution in the presence of glaucoma; intraocular pressure should be checked frequently. Prolonged use may also result in the establishment of secondary ocular infections from fungi or viruses liberated from ocular tissue, or by suppression of the host immune response.

Various ocular diseases and long-term use of topical corticosteroids have been known to cause corneal and scleral thinning. Use of topical corticosteroids in the presence of thin corneal or scleral tissue may lead to perforation.

Acute purulent untreated infection of the eye may be masked or activity enhanced by presence of steroid medication. As fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid applications, 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.

If this product is used for 10 days or longer, intraocular pressure should be routinely monitored though it may be difficult in children and uncooperative patients.

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

Systemic adverse events may occur with extensive use of topical steroids; punctal occlusion may be recommended (see Section 4.2).

Pred Mild contains benzalkonium chloride, which is irritant to the eye and may be absorbed by and cause discoloration of soft (hydrophilic) contact lenses. The patient should avoid contact with contact lenses and therefore be instructed to remove them before Pred Mild is used and then wait for at least 15 minutes before reinsertion.

Pred Mild contains boron and should not be used in children less than 12 years old because of safety concerns over impairment of fertility.

Pred Mild contains sodium metabisulphite, a sulphite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes. Sulphite sensitivity is seen more frequently in asthmatic patients.

To prevent eye injury or contamination, care should be taken to avoid touching the bottle or tube tip to the eye or to any other surface.

<u>Visual disturbance</u>
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, the patient should be considered for referral to an ophthalmologist for evaluation of 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.

4.5 Interaction with other medicinal products and other forms of interactions

None known.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate and well controlled studies in pregnant women. Administration of corticosteroids to pregnant animals has been associated with abnormalities of foetal development therefore this product should be used with caution during pregnancy only if the potential benefit outweighs the potential risk to the foetus.

Breast-feeding
It is not known whether topical administration of Pred Mild 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

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.

4.8 Undesirable effects

The following events have been reported since the product was marketed:

Frequency categories: 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 available data).

Immune system disorders
Not known: Hypersensitivity
Urticaria

Nervous system disorders
Not known: Headache

Eye disorders
Not known: Intraocular pressure increased*
Cataract (including subcapsular)*
Eye penetration (scleral or corneal perforation) *
Foreign body sensation
Ocular hyperemia
Ocular infection (including bacterial*, fungal*, and viral* infections)
Eye irritation
Eye pain
Vision blurred*/Visual impairment
Mydriasis

Gastrointestinal disorders
Not known: Dysgeusia

Skin and subcutaneous tissue disorders
Not known: Pruritus
Rash

Systemic side effects may occur rarely with extensive use of topical steroids.*

* See Section 4.4 for further information.

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:

HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
E-mail: medsafety@hpra.ie

4.9 Overdose

Overdosage will not ordinarily cause acute problems. If accidentally ingested, drink fluids to dilute.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: corticosteroids,
ATC code: S01BA04

Prednisolone acetate is a glucocorticoid that, on the basis of weight, has 3-5 times the antiinflammatory potency of hydrocortisone. Glucocorticoids inhibit the edema, fibrin deposition, capillary dilatation and phagocytic migration of the acute inflammatory response as well as capillary proliferation, deposition of collagen and scar formation.

5.2 Pharmacokinetic properties

After absorption, prednisolone acetate hydrolyses to the active metabolite prednisolone.
After application of 50 microL of a 0.125 % prednisolone acetate preparation, the following corticoid concentrations were measured:

Time (min)	Cornea (ng/g)	Aqueous humour (ng/ml)
15	3240	120
30	2850	180
60	1910	450
90	3050	290
120	2170	280

In rabbits, the half life of prednisolone acetate (0.125% preparation) was found to be 89 minutes in the cornea and 136 minutes in the aqueous humour.
Due to the highly lipophilic properties, prednisolone acetate penetrates to a higher extent through the intact corneal epithelium compared with other more hydrophilic prednisolone derivates. Based on the relatively small particle size (100% ≤ 5 micrograms, 99% ≤ 2 micrograms), a relatively high bioavailability is achieved with Pred Mild 0.12%.
Removal of the corneal epithelium results in higher steroid concentrations in both cornea and aqueous humour.

5.3 Preclinical safety data

In rabbit eyes, no toxic effects were observed after application of approx. 6 mg prednisolone acetate per day over 20 days as a 1% suspension. Also, no toxic effects were observed after a single oral administration of 500 mg/kg in rats.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Polysorbate 80
Boric acid
Sodium citrate
Sodium metabisulphite
Sodium chloride
Disodium edetate
Hypromellose
Purified water
Hydrochloric acid for pH adjustment
Sodium hydroxide for pH adjustment

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Unopened: 3 years.
Discard 1 month after opening.

6.4 Special precautions for storage

Do not refrigerate or freeze.
Do not store above 25°C.

6.5 Nature and contents of container

Low density, opaque, effectively sealed, polyethylene bottle with polyethylene controlled delivery dropper plug and cap.
5ml and 10ml bottles in packs containing 1 bottle each.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

AbbVie Limited
Citywest Business Campus
Co Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1824/009/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st April 1977

Date of last renewal: 1st April 2007

10 DATE OF REVISION OF THE TEXT

April 2022