SCHEDULING STATUS

Schedule 4

PROPRIETARY NAME AND DOSAGE FORM

FML-NEO Liquifilm Ophthalmic Suspension

COMPOSITION

FML-NEO Liquifilm Ophthalmic Suspension contains per ml:

Fluorometholone 1,0 mg

Neomycin sulfate (equivalent to 3,5 mg neomycin base) 5,0 mg

Excipients: Benzalkonium chloride 0,004 % m/v (as a preservative), Liquifilm® (polyvinyl alcohol), disodium edetate, sodium phosphate, dibasic, heptahydrate, sodium chloride, sodium thiosulfate, pentahydrate, polysorbate 80 (10% solution), purified water

PHARMACOLOGICAL CLASSIFICATION

A. 15.2 Ophthalmic preparation with corticosteroids

PHARMACOLOGICAL ACTION

Fluorometholone is a glucocorticoid and has anti-inflammatory properties. It inhibits the inflammatory response (oedema, fibrin deposition, capillary dilation, and phagocytic migration) as well as capillary proliferation, deposition of collagen and scar formation.

Glucocorticosteroids such as fluorometholone may increase intraocular pressure, in normal eyes and in subjects with ocular hypertension.

Neomycin is a broad spectrum bactericidal aminoglycoside antibiotic with activity against gram-positive and gram-negative organisms. Due to extensive topical use, neomycin resistance has been reported among *Pseudomonas aeruginosa*, *Staphylococci*, and some *Salmonella*, *Shigella*, and *Escherichia coli* strains. Cross-resistance with kanamycin, framycetin and paromomycin occurs. The primary mechanism of action is through inhibition of protein synthesis by irreversibly binding with 30S ribosomal subunits. Pus, exudates, and bacteria growth products do not inactivate the antibiotic.

INDICATIONS

FML-NEO is indicated in the treatment of infectious conjunctivitis due to organisms sensitive to neomycin.

FML-NEO may be used for the treatment of anterior segment inflammatory disorders complicated by bacteria sensitive to neomycin.

FML-NEO may be used following removal of foreign bodies as well as before and after surgery, where there is a possibility of infection with susceptible organisms.

CONTRA-INDICATIONS

Hypersensitivity to fluorometholone or neomycin sulfate or to any of the excipients.
Acute untreated purulent ocular infections caused by micro-organisms not sensitive to neomycin.
Acute superficial keratitis and conjunctivitis due to herpes simplex (dendritic keratitis).
Fungal diseases of ocular structures.
Vaccinia, varicella, and most other viral diseases of the conjunctiva and cornea.
Ocular tuberculosis.
Mycobacterial ocular infections.
Glaucoma.
Pregnancy and lactation.

WARNINGS AND SPECIAL PRECAUTIONS

Eye drops containing corticosteroids such as in FML-NEO, should not be used for more than one week except under strict medical supervision with regular checks for intraocular pressure.

Prolonged use of FML-NEO may increase intraocular pressure (IOP) with possible development of glaucoma and damage to the optic nerve, defects in visual acuity and fields of vision, and delayed wound healing.

Reports in the literature indicate that posterior subcapsular lenticular opacities have occurred after heavy or protracted use of topical ophthalmic corticosteroids such as contained in FML-NEO.

Acute ocular infection with secretion may be masked, or its activity enhanced by the presence

of fluorometholone as in FML-NEO®.

There have been occurrences of systemic hypercorticoidism after use of topical corticosteroids, as in FML-NEO.

Prolonged use may also suppress the host immune response and thus increase the risk of secondary ocular infections. In these cases, it may cause corneal ulceration or thinning of the cornea, with risk of keratic perforation.

Use of FML-NEO in the treatment of patients with a history of herpes simplex requires great caution; frequent slit-lamp microscopy is required.

As fungal infections of the cornea have been reported coincidentally with long-term local steroid applications, fungal invasion may be suspected in any persistent corneal ulceration where FML-NEO® has been used, or is in use, over a prolonged period of time.

Because of the possibility of inducing corneal abscess, fungal keratopathy or glaucoma, the patient should be referred to an ophthalmologist if the eye has not responded within 48 hours.

In diseases due to micro-organisms resistant to neomycin, infection may be masked, enhanced or activated by the steroid in FML-NEO®. Prolonged use may result in overgrowth of nonsusceptible organisms.

Recent information indicates an increase in the prevalence of persons hypersensitive to neomycin. The possibility of such a reaction should be considered. If sensitivity or other untoward reactions occur, discontinue use of FML-NEO.

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

Effects on ability to drive and use machines

FML-NEO may influence the ability to drive and use machines. If blurred vision occurs, the

patient should wait until the vision clears before driving or using machines.

Excipients

FML-NEO contains the preservative benzalkonium chloride, which may be absorbed by soft contact lenses. Eye irritation and discolouration of the soft contact lenses may also occur due to the presence of benzalkonium chloride. Contact lenses should be removed prior to instillation of FML-NEO and may be reinserted 15 minutes following administration.

As the possibility of adverse effects on the corneal permeability and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmologic preparations cannot be excluded, regular ophthalmologic examination is required.

Caution should be exercised in the use of benzalkonium chloride preserved topical medication over an extended period in patients with extensive ocular surface disease.

FML-NEO also contains sodium phosphate. Cases of corneal calcification have been reported in association with the use of phosphate-containing eye drops in patients with damaged corneas.

INTERACTIONS

Interactions studies for FML-NEO with other medicines were not conducted. In the case of simultaneous treatment with other eye drops, a period of 15 minutes between installations should be allowed.

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

PREGNANCY AND LACTATION

FML-NEO is contraindicated in pregnancy and lactation.

Pregnancy

Studies in animals have shown reproductive toxicity. FML-NEO should not be used in pregnant women.

Lactation

It is unknown whether FML-NEO is excreted in human breast milk. FML-NEO is not recommended for women breastfeeding their infants.

DOSAGE AND DIRECTIONS FOR USE

1 to 2 drops of FML-NEO® in the conjunctival sac two to four times daily. During the initial 24-48 hours, the dosage may be safely increased to 1 drop every hour. Shake well before using. Do not freeze.

To reduce possible systemic absorption, it may be recommended that the lacrimal sac be compressed at the medial canthus (punctal occlusion) for a few minutes immediately after instillation of each drop.

Patients should be advised to complete the course of treatment. To prevent contamination, care should be taken to avoid touching the bottle tip to the eye or to any other surface. The use of the bottle by more than one person may spread infection.
The safety and efficacy in children aged 2 years or younger has not been established.

SIDE-EFFECTS

Post-marketing experience

The following side-effects were reported during the post-marketing period with FML-NEO. Because post-marketing reporting is voluntary and from a population of unknown size, it is not possible to reliably estimate the frequency of these reactions:

Eye disorders

Increased intraocular pressure, eye irritation, conjunctival/ocular hyperaemia, eye pain, visual disturbance, foreign body sensation , eyelid oedema, blurred vision, eye discharge, eye pruritus, increased lacrimation, eye oedema, eye swelling, mydriasis, cataract (including subcapsular), ulcerative keratitis or conjunctival ulcer, corneal ulcer specially if there is a concomitant bacterial, fungal or viral infection, ocular infection (including bacterial, fungal and viral infections) visual field defects, punctate keratitis

Skin and subcutaneous tissue disorders

Rash

Immune system disorders

Hypersensitivity

Gastro-intestinal disorders

Dysgeusia

Reporting of side effects

If you get side effects, talk to your doctor. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

By reporting side effects, you can help provide more information on the safety of FML-NEO Liquifilm Ophthalmic Suspension.

In case of a side effect, please contact MEAPV@abbvie.com

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

If accidental overdosage occurs in the eye, flush the eye with water or normal saline. If accidentally ingested, drink fluids to dilute.

IDENTIFICATION

A milky white to slightly straw coloured, microfine suspension.

PRESENTATION

FML-NEO Liquifilm Ophthalmic Suspension is supplied in sterile dropper bottles containing 5 ml suspension. The bottle and tip are made up of low density polyethylene and the cap is made up of polystyrene. A safety seal is placed around the bottle cap to insure integrity of the product.

STORAGE INSTRUCTIONS

Store at or below 25 °C. Do not freeze. Do not use for more than 30 days after first opening. Keep bottle tightly closed when not in use. Store in an upright position. KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

J/15.2/335

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