NEW ZEALAND DATA SHEET

1 PRODUCT NAME

Sofradex, Ear/Eye Drops

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of drops contains framycetin sulfate 5mg, gramicidin 0.05mg and dexamethasone 0.5mg.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ear/Eye Drops

Sterile, clear, colourless drops

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

In the eye: For the short term treatment of steroid responsive conditions of the eye when prophylactic antibiotic treatment is also required, after excluding the presence of fungal or viral disease.

In the ear: Otitis externa.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage

Adults, Elderly and Children

In the eye: 1 or 2 drops applied to each affected eye up to six times daily or more frequently if required.

In the ear: 2 or 3 drops instilled into the ear three or four times daily.

(No dosage adjustment is necessary for the Elderly and Children).

Administration

Auricular and Ocular use.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance (see Section 2) or to any of the excipients listed in Section 6.1
- Acute purulent, untreated infections of the eye, which, like other diseases caused by micro-organisms, may be masked or enhanced by the presence of the steroid
- Tuberculosis and fungal diseases of the eye
- Glaucoma
- If herpetic keratitis (eg dendritic ulcer) is considered a possibility
- Herpes simplex and other viral diseases of the cornea and conjunctiva, use of topical steroids in this condition can lead to extension of the ulcer and marked visual deterioration
- Trachoma
- Eardrum perforation because of the risk of ototoxicity
- Viral and fungal infections of the ear
- Acute purulent, untreated infections of the ear

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Although it is unlikely that infants will be treated with Sofradex for prolonged periods, there is a risk of adrenal suppression, even without occlusive dressings, after prolonged treatment of these patients with topical steroids.

Sofradex should be discontinued if there are signs of sensitivity to any of its ingredients.

Topical corticosteroids should never be given for an undiagnosed red eye as inappropriate use is potentially blinding.

Treatment with corticosteroid/antibiotic combinations should not be continued in the absence of clinical improvement, since prolonged use may lead to occult extension of infection due to the masking effect of the steroid. Prolonged use may lead to skin sensitisation and the emergence of resistant organisms.

Prolonged use may lead to the risk of adrenal suppression in infants.

Treatment with corticosteroid preparations should not be repeated or prolonged without regular review to exclude raised intraocular pressure, cataract formation or unsuspected infections.

In patients known to be allergic to other aminoglycoside antibiotics (neomycin, kanamycin) cross sensitisation to framycetin sulfate may occur, but not invariably so.

Aminoglycoside antibiotics may cause irreversible, partial or total deafness when applied topically to open wounds or damaged skin. This effect is aggravated by renal or hepatic impairment and prolonged by duration of treatment. The treatment should not be continued after resolution of symptoms.

There have been reported cases of ototoxicity with aminoglycosides administered to patients with mitochondrial mutations, particularly the m.1555A>G mutation, which suggests an increased risk of ototoxicity in these patients, including cases where the patient's aminoglycoside serum levels were within the recommended range. Some cases were associated with a maternal history of deafness and/or mitochondrial mutation. Mitochondrial mutations are rare, and the penetrance of this observed effect is unknown.

Although no cases were identified with topical preparations of neomycin, framycetin or gentamicin, the potential for a similar effect with neomycin and other aminoglycosides administered topically cannot be ruled out.

Visual disturbance may be associated 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) (Section 4.8).

Pheochromocytoma crisis, which can be fatal, has been reported after administration of corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

During therapy with Sofradex, a possible increased need for insulin or antidiabetics should be considered in patients with diabetes. The hypoglycaemic reactions can be reduced.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

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 such side-effects, in which case patients should be monitored.

4.6 FERTILITY, PREGNANCY AND LACTATION

Safety for use in pregnancy and lactation has not been established. There is inadequate evidence of safety in human pregnancy.

Sofradex should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the foetus.

Topical administration of corticosteroids in pregnant animals can cause abnormalities of foetal development including cleft palate and intrauterine growth retardation. There may therefore be a very small risk of such effects in the human foetus.

Gentamicin and other aminoglycosides cross the placenta. There is evidence of selective uptake of gentamicin by the foetal kidney resulting in cellular damage (probably reversible) to immature nephrons. Eighth cranial nerve damage has also been reported following *in utero* exposure to some of the aminoglycosides. Because of their chemical similarity, all aminoglycosides must be considered potentially nephrotoxic and ototoxic to the foetus. It should also be noted that therapeutic blood levels in the mother do not equate with safety for the foetus.

There are no available data on the presence of Sofradex in human milk, milk production, or the effects on the breastfed infant. No conclusions can be drawn regarding whether or not Sofradex is safe for use during breastfeeding. Sofradex should be used during breastfeeding only if the potential benefits to the mother outweigh the potential risks, including those to the breastfed child.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Use in the eye will cause blurring of vision on application. Patients should be warned not to drive or operate hazardous machinery unless vision is clear.

4.8 UNDESIRABLE EFFECTS

The following CIOMS frequency rating is used, when applicable:

Very common ≥ 10%; Common ≥ 1 and < 10%; Uncommon ≥ 0.1 and < 1%; Rare ≥ 0.01 and < 0.1%; Very rare < 0.01%; Not known (cannot be estimated from available data).

Immune system disorders:

Hypersensitivity reactions, usually of the delayed type may occur, leading to irritation, burning, stinging, itching and dermatitis.

Eye disorders:

Frequency not known: Cataracts, corneal perforation, glaucoma, blurred vision, chorioretinopathy.

Topical steroid use may result in increased intraocular pressure leading to optic nerve damage, reduced visual acuity and visual field defects.

Intensive or prolonged use of topical corticosteroids may lead to formation of posterior subcapsular cataracts. In those diseases causing thinning of the cornea or sclera, corticosteroid therapy may result in thinning of the globe leading to perforation.

Endocrine disorders:

Frequency not known: Iatrogenic Cushing's syndrome, Adrenal atrophy

Metabolism and nutrition disorders:

Frequency not known: Diabetes mellitus, Glucose tolerance decreased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 OVERDOSE

Long term intensive topical use may lead to systemic effects.

Oral ingestion of the contents of the bottle (up to 8mL) is unlikely to lead to any serious adverse effects.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Framycetin sulfate is an aminoglycoside bactericidal antibiotic active against a wide variety of Gram-positive and Gram-negative bacteria commonly found in superficial eye infections: *staphylococci* (including strains resistant to other antibiotics), *Pseudomonas aeruginosa*, *coliform* bacteria and *pneumococci*.

Gramicidin reinforces the action of framycetin sulfate against *streptococci*.

Dexamethasone is a highly potent topical corticosteroid. Its topical superiority is particularly apparent in cases in which other corticosteroids have failed.

5.2 PHARMACOKINETIC PROPERTIES

Not relevant to topical use.

5.3 PRECLINICAL SAFETY DATA

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Phenethyl alcohol

Methylated spirit - industrial

Citric acid monohydrate

Sodium citrate dihydrate

Lithium chloride

Polysorbate 80

Sodium hydroxide (for pH-adjustment)

Hydrochloric acid (for pH-adjustment)

Water - purified.

6.2 INCOMPATIBILITIES

Not applicable

6.3 SHELF LIFE

24 months from date of manufacture

Discard 4 weeks after opening

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25^{o}C.

6.5 NATURE AND CONTENTS OF CONTAINER

Glass bottle fitted with dropper attachment – Pack size 8ml

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Pharmaco (NZ) Ltd
4 Fisher Crescent
Mt Wellington
Auckland 1060
Telephone: 0800 804 079

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9 DATE OF FIRST APPROVAL

31 December 1969

10 DATE OF REVISION OF THE TEXT

15 January 2025

SUMMARY TABLE OF CHANGES

SECTION	ADDITIONAL TEXT ADDED
4.8	Update to adverse event reporting URL
8	Change of sponsor