AUSTRALIAN PRODUCT INFORMATION – SOFRADEX (FRAMYCETIN SULFATE, GRAMICIDIN AND DEXAMETHASONE (AS SODIUM METASULFOBENZOATE))

1 NAME OF THE MEDICINE

Framycetin sulfate, gramicidin and dexamethasone (as sodium metasulfobenzoate)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains framycetin sulfate 5mg, gramicidin 50µg and dexamethasone (as sodium metasulfobenzoate) 500µg.

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

3 PHARMACEUTICAL FORM

Sofradex is a clear bright colourless aqueous solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Inflammatory and allergic conditions of the ear, e.g. otitis externa. Eczema of the auditory meatus is often present and causes inflammation, exudation and pruritus, which are all rapidly relieved by dexamethasone. Infection, often secondary to scratching, is generally due to staphylococci, *E. coli*, *Pseudomonas* and *Proteus spp*. which respond rapidly to framycetin sulfate.

4.2 DOSE AND METHOD OF ADMINISTRATION

2 or 3 drops should be instilled into the ear three or four times daily; alternatively, a gauze wick kept saturated with the drops may be inserted into the external auditory meatus.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substances (see Section 2 Qualitative and quantitative composition) or to any of the excipients listed in Section 6.1 List of excipients;
- viral and fungal infections;
- tubercular lesions;
- varicella, vaccinia;

- eardrum perforation;
- acute purulent, untreated infections.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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

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

In patients known to be allergic to Streptomyces-derived antibiotics (neomycin, paromomycin, 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 by prolonged 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) (see Section 4.8 Adverse effects (undesirable effects).

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.

Use in the elderly

No data available.

Paediatric 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.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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

Effects on fertility

No data available.

Use in pregnancy

Category D

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

Gentamicin and other aminoglycosides cross the placenta. There is evidence of selective uptake of aminoglycosides by the fetal kidney resulting in 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 concentrations in the mother do not equate with safety for the foetus.

Use in lactation

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

The effects of this medicine on a person's ability to drive and use machines were not accessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Immune system disorders:
Local allergic reactions of the hypersensitivity type have rarely been reported.

Frequency not known: Hypersensitivity reactions, usually of the delayed type, may occur, leading to irritation, burning, stinging, itching and dermatitis.

Eye disorders:
Not known: Glaucoma, cataracts, corneal perforation, blurred vision, chorioretinopathy

Endocrine disorders:
Frequency not known: Iatrogenic Cushing's syndrome, adrenal atrophy

Metabolism and nutrition disorders:
Frequency not known: Diabetes mellitus, glucose tolerance decreased.

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 (Australia).

4.9 OVERDOSE

Long-term intensive topical use may lead to systemic effects.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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

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

It also contains polysorbate 80, industrial methylated spirit, citric acid monohydrate, sodium citrate dihydrate, lithium chloride, sodium hydroxide, hydrochloric acid, purified water and is preserved with phenethyl alcohol.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this product.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging

Discard 4 weeks after opening.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Do not refrigerate.

6.5 NATURE AND CONTENTS OF CONTAINER

8mL bottles

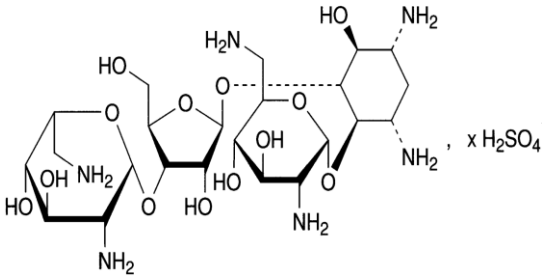
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

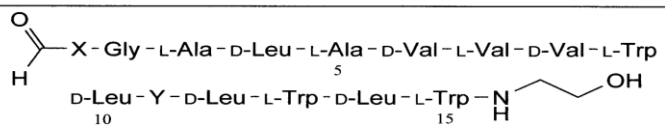
Framycetin sulfate



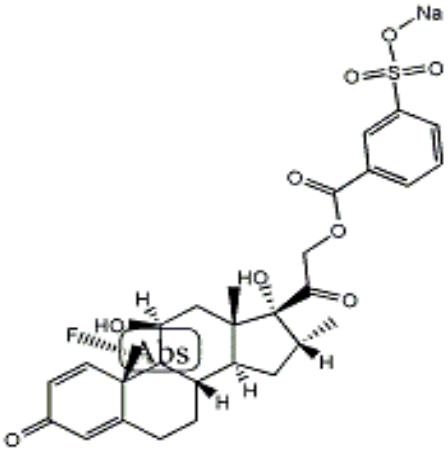
Molecular weight – 712.72

Gramicidin

Gramicidin	X	Y	Mol. formula	M_r
A1	L-Val	L-Trp	$C_{99}H_{140}N_{20}O_{17}$	1882
A2	L-Ile	L-Trp	$C_{100}H_{142}N_{20}O_{17}$	1896
B1	L-Val	L-Phe	$C_{97}H_{139}N_{19}O_{17}$	1843
C1	L-Val	L-Tyr	$C_{97}H_{139}N_{19}O_{18}$	1859
C2	L-Ile	L-Tyr	$C_{98}H_{141}N_{19}O_{18}$	1873



Dexamethasone sodium metasulfobenzoate



Molecular Weight – 598.6

CAS number

Framycetin sulphate – 4146-30-9

Gramicidin – 1405-97-6

Dexamethasone sodium metasulfobenzoate – 3936-02-5

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4

8 SPONSOR

sanofi-aventis australia pty ltd
12-24 Talavera Road
Macquarie Park NSW 2113
Tel: 1800 829 468
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

30 August 1991

10 DATE OF REVISION

02 June 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.4	New warning of Aminoglycosides produced ototoxicity in individuals with mitochondrial mutations