PRESCRIBING INFORMATION

1 NAME OF THE MEDICINAL PRODUCT

DESOREN EAR DROPS

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml solution contains:
Polymyxin B Sulfate 10,000 IU
Neomycin (as Sulfate) 5 mg
Dexamethasone (as Sodium Phosphate) 1 mg

Excipient(s) with known effect: Propylene glycol
1 ml solution contains 250 mg of propylene glycol.

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Ear drops, solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Desoren Ear Drops are indicated for the treatment of superficial bacterial infections of the external auditory canal, caused by organisms susceptible to the action of the antibiotics.

Route of Administration

Topical

In Vitro Activity
Desoren Ear Drops are active against a wide range of bacterial pathogens.
The range of activity includes:
Gram-Positive Organisms:
Staphylococcus epidermis and *Staphylococcus aureus*:
Gram-Negative Organisms:
Enterobacter Spp.
Escherichia Spp.
Haemophilus Spp.
Klebsiella Spp.
Proteus Spp.
Pseudomonas aeruginosa

Desoren Ear Drops are not expected to be active against streptococci, including *Streptococcus pyogenes*.
Dexamethasone Sodium Phosphate possesses anti-inflammatory, anti-allergic and antipruritic activity.

4.2 Posology and method of administration

Desoren ear drops are for topical administration into the ear only. The medicine should not be swallowed.
The usual dosage is generally:
In adults: 2-3 drops into the ear, 3-4 times a day.
In children: 1-2 drops into the ear, 3-4 times a day.
Treatment should not be continued for more than 7 days without medical supervision.

Children
A possibility of increased absorption exists in very young children, thus Desoren Ear Drops shall not be used in neonates and infants (<3 years). (See 4.3 Contra-indications, 4.4 Special Warnings and Precautions for Use).

Use in the Elderly
As for adults. Caution should be exercised in cases where a decrease in renal function exists and significant systemic absorption of neomycin sulphate may occur (see 4.4 Special Warnings and Precautions for Use).

Use in Renal Impairment
Dosage should be reduced in patients with reduced renal function (see 4.4 Special Warnings and Precautions for Use).

4.3 Contraindications

Hypersensitivity to the active substances Dexamethasone Sodium Phosphate and/or Neomycin Sulphate and/or Polymyxin B Sulphate, or to any of the excipients listed in section 6.1.

The use of Desoren Ear Drops is contra-indicated in patients in whom perforation of the tympanic membrane is known or suspected.

Due to the known ototoxic and nephrotoxic potential of neomycin sulphate, the use of Desoren Ear Drops in large quantities or on large areas for prolonged periods of time is not recommended in circumstances where significant systemic absorption may occur.

The use of Desoren Ear Drops is contra-indicated in patients who have demonstrated allergic hypersensitivity to cross-sensitising substances such as framycetin, kanamycin, gentamicin and other related aminoglycoside antibiotics.
The use of Desoren Ear Drops is contra-indicated in the presence of untreated viral, fungal and tubercular infections.

A possibility of increased absorption exists in very young children, thus Desoren Ear Drops shall not be used in neonates and infants (up to 3years). In neonates and infants, absorption by immature skin may be enhanced and renal function may be immature.

4.4 Special warnings and precautions for use

Occasionally, delayed hypersensitivity to corticosteriods may occur.

Treatment with topical steroid antibiotic combinations should not be continued for more than seven days in the absence of any clinical improvement, since prolonged use may lead to occult extension of infection due to the masking effect of the steroid. Prolonged use may also lead to skin sensitisation and the emergence of resistant organisms.

Following significant systemic absorption, aminoglycosides such as neomycin can cause irreversible ototoxicity; neomycin and polymyxin B sulphate have nephrotoxic potential and polymyxin B sulphate has neurotoxic potential.

All topically active corticosteroids possess the potential to suppress the pituitary-adrenal axis following systemic absorption. Development of adverse systemic effects due to the Dexamethasone~~h~~ component of Desoren Ear Drops is considered to be unlikely, although the recommended dosage should not be exceeded, particularly in infants.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is unlikely to occur with topically applied antibiotics, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Dexamethasone may mask the allergic effects produced by any components of Desoren ear drops.

Accidental maladministration, prescription and dispensing errors have been reported. Desoren ear drops should only be used in the ear and are not suitable for use in the eye. Particular care should be taken to ensure that the correct formulation has been provided and administered. If ear drops are accidentally introduced into the eye, the eye should be rinsed thoroughly with water.
Desoren ear drops should be kept out of the reach of children.

Prolonged, unsupervised, use should be avoided as it may lead to irreversible partial or total deafness, especially in the elderly and in patients with impaired renal function. In renal impairment the plasma clearance of neomycin is reduced (see Dosage in Renal Impairment).

Use in the immediate pre- and post- operative period is not advised as neomycin may rarely cause neuro-muscular block; because it potentiates skeletal muscle relaxant drugs, it may cause respiratory depression and arrest.

There have been observed cases of an increased risk of ototoxicity with aminoglycosides administered to patients with mitochondrial mutations, particularly the m.1555A>G mutation, 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. While no cases were identified with neomycin, based on a shared mechanism of action there is the potential for a similar effect with neomycin.
These mitochondrial mutations are rare, and the penetrance of this observed effect is unknown.

Desoren Ear Drops contains excipient with known effect: 250 mg of propylene glycol in each 1 ml, which is equivalent to 250 mg/ml.

4.5 Interaction with other medicinal products and other forms of interaction

Following significant systemic absorption, both neomycin sulphate and polymixin b sulphate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents.

Using Desoren Ear Drops at the same time with antibiotics such as framycetin, kanamycin or gentamicin, or other aminoglycosides, may increase the risk of hearing, nerve and kidney damage (see section 4.3 above)

4.6 Pregnancy, lactation and fertility

There is little information to demonstrate the possible effect of topically applied neomycin in pregnancy and lactation. However, neomycin present in maternal blood can cross the placenta and may give rise to a theoretical risk of foetal toxicity thus Desoren Ear Drops shall not be used in pregnancy or lactation.

4.7 Effects on ability to drive and use machines

Desoren Ear Drops is not expected to affect the ability to drive or use machines.

4.8 Undesirable effects

The incidence of allergic hypersensitivity reactions to neomycin sulphate in the general population is low. There is, however, an increased incidence of hypersensitivity to neomycin in certain selected groups of patients in dermatological practice, particularly those with venous stasis eczema and ulceration, and chronic otitis externa.

Allergic hypersensitivity reactions following topical application of polymyxin B sulphate and Dexamethasone are rare.

Allergic hypersensitivity to neomycin following topical use may manifest itself as an eczematous exacerbation with reddening, scaling, swelling and itching or as a failure of the lesion to heal.

Stinging and burning have occasionally been reported when Desoren Ear Drops gained access to the middle ear.

Postmarketing Data
Immune System Disorders
Rare: Application site hypersensitivity

General Disorders and Administration Site Conditions
Rare: Headache, application site reaction including: pain, irritation, oedema, burning sensation, rash

Skin and Subcutaneous Tissue Disorders

Rare: Local exfoliative dermatitis, skin atrophy, telangiectasia, striae, exacerbation of underlying skin conditions, including eczema.

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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

4.9 Overdose

Possible symptoms or signs associated with excessive use of Desoren Ear Drops are those due to significant systemic absorption (see 4.4 Special Warnings and Precautions for Use).

Management:
Use of the product should be stopped and the patient's general status, hearing acuity, renal and neuromuscular functions should be monitored.

In overdose, blood concentrations of neomycin sulphate, and polymyxin b sulphate should be determined. Haemodialysis may reduce the serum level of neomycin sulphate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Desoren solution is a bactericidal preparation active against all the pathogens commonly found in bacterial infections of the ear. Polymixin B is bactericidal against a wide range of gram negative bacilli including *Pseudomonas* Spp., *Escherichia coli*, *Enterobacter* Spp., *Klebsiella* Spp., and *Haemophilus influenzae*. It exerts a bactericidal effect by binding to acid phospholipids in the cell wall and membranes of the bacterium, thereby rendering ineffective the osmotic barrier normally provided by the cell membrane. This leads to escape of the cell contents and the death of the organism.

Neomycin sulphate is bactericidal against a wide range of gram positive and negative bacterial pathogens including *Staphylococci, Streptococci, Escherichia, Enterobacter*, *Klebsiella, Haemophilus, Proteus, Salmonella and Shigella* species. It is also active against some strains of the *Pseudomonas aeruginosa* and against *Mycobacterium tuberculosis* and *Neisseria gonorrhoea*. Neomycin exerts its bactericidal effect by interfering with the protein synthesis of susceptible organisms.

5.2 Pharmacokinetic properties

No data are available regarding the pharmacokinetics of this product.
However since this is a topical preparation and significant systemic absorption is unlikely to occur, the data are irrelevant.

Systemically absorbed neomycin is predominantly excreted by the kidney and the total amount excreted in the urine varies between 30% and 50%. The pharmacokinetics of systemically absorbed polymixin B has been described.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene Glycol, Sodium Citrate, Methylparaben Sodium, Sodium Metabisulfite, Propylparaben Sodium, HCl dilute
Purified Water

6.2 Incompatibilities

None known

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25°C
The medicine can be used for up to 6 months after the bottle is first opened and not later than the expiry date, that appears on the package.

6.5 Nature and contents of container

A bottle containing a clear colorless to straw color (yellowish) solution.
Approved package size: 5 ml

7 REGISTRATION HOLDER AND MANUFACTURER

Vitamed Pharmaceutical Industries Ltd., 6 Hatahana St., P.O.B. 114, Binyamina 3055002, Israel.

8. DRUG REGISTRATION NUMBER AT THE NATIONAL DRUG REGISTRY OF THE MINISTRY OF HEALTH:

060-83-27506-00

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