SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Otosporin Ear Drops.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Polymyxin B Sulphate 10,000 units per ml
Neomycin Sulphate 3,400 units per ml
Hydrocortisone 1.0% w/v

Excipient(s) with known effect:
Also contains cetostearyl alcohol and methyl hydroxybenzoate E218

For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Liquid for topical application to humans.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Otosporin Ear Drops are indicated for the treatment of otitis externa due to, or complicated by, bacterial infection.

Route of Administration

Topical

In Vitro Activity

Otosporin 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

Otosporin Ear Drops are not expected to be active against streptococci, including *Streptococcus pyogenes*.

Hydrocortisone possesses anti-inflammatory, anti-allergic and antipruritic activity.

4.2 Posology and method of administration

Otosporin ear drops are for topical administration into the ear only.

Adults

Following cleansing and drying of the external auditory meatus and canal as appropriate, three drops should be instilled into the affected ear three or four times daily. Alternatively, a gauze wick may be introduced into the external auditory canal and kept saturated with the solution; the wick may be left in place for 24 to 48 hours.

Treatment should not be continued for more than 7 days without medical supervision.

Soap should not be used for cleansing of the external auditory meatus and canal as it may inactivate the antibiotics.

Children

Otosporin Ear Drops are suitable for use in children (3 years and over) at the same dose as adults. A possibility of increased absorption exists in very young children, thus Otosporin Ear Drops are not recommended 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

The use of Otosporin 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 Otosporin 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 Otosporin Ear Drops is contra-indicated in patients who have demonstrated allergic hypersensitivity to any of the components of the preparation or to cross-sensitising substances such as framycetin, kanamycin, gentamicin and other related antibiotics.

The use of Otosporin 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 Otosporin Ear Drops are not recommended 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 hydrocortisone component of Otosporin 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.

Hydrocortisone may mask the allergic effects produced by any components of Otosporin ear drops.

Accidental maladministration, prescription and dispensing errors have been reported. Otosporin 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.
Otosporin 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.

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.

4.6 Fertility, Pregnancy and lactation

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 use of Otosporin Ear Drops is not recommended in pregnancy or lactation.

4.7 Effects on ability to drive and use machines

None known.

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 hydrocortisone 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 Otosporin Ear Drops gained access to the middle ear.

Postmarketing Data

<u>Immune System Disorders</u>

Rare: Application site hypersensitivity

<u>General Disorders and Administration Site Conditions</u>

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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

4.9 Overdose

Possible symptoms or signs associated with excessive use of Otosporin 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

Otosporin 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

Cetostearyl Alcohol
Sorbitan Monolaurate
Polysorbate 20
Methyl Hydroxybenzoate, E218
Dilute Sulphuric Acid
Purified Water

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 25°C
Protect from light

6.5 Nature and contents of container

Polypropylene bottles with integral nozzles and pilfer proof caps
5ml or l0ml pack sizes
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Otosporin ear drops should be shaken gently prior to use.

7 MARKETING AUTHORISATION HOLDER

Phoenix Labs

Suite 12, Bunkilla Plaza, Bracetown Business Park

Clonee, Co. Meath, Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 35104/0015

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

MAA: 27.12.90

10 DATE OF REVISION OF THE TEXT

16/11/2020