Otiflox® Ear drops Neo

1. Composition

Prednisolone acetate	0.5%w/v
Chloramphenicol	5%w/v
Glacial acetic acid	2%w/v
Benzocaine	3%w/v
Benzyl alcohol	2%v/v

2. Dosage form and strength

Otiflox neo Ear Drops is available in 10 ml bottle with in-built dropper

3. Clinical particulars

3.1 Therapeutic indication

Otiflox neo ear drops is indicated in

- Otitis Externa
- Acute Suppurative Otitis Media
- Chronic Suppurative Otitis Media

3.2 Posology and method of administration

Instil 2 drops of Otiflox neo ear drops in affected era 2-3 times a day.

3.3 Contraindication

The use of Otiflox neo ear drops is contraindicated in patients with hypersensitivity to any ingredient of the formulations.

3.4 Special warnings and precautions for use

None.

3.5 Drug interactions

3.6 Use in special population

- Paediatric: Safety and efficacy has not been evaluated in children.
- Geriatric: Safety and efficacy has not been evaluated in elderly patients.

- Liver impairment: No data available.
- Renal failure: No data available.
- Pregnancy and lactation: During pregnancy, Otiflox neo ear drops should be used only when clearly needed. It is unknown if this medication passes into breast milk. Consult doctor before breast-feeding.

3.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to Otiflox neo Ear drops is known.

3.8 Undesirable effects

- Temporary stinging/burning in the ear canal
- Slight feeling of irritation

3.9 Overdose

There is limited experience of overdose with Otiflox neo Ear drops. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

4. Pharmacological properties

4.1 Mechanism of action

The short term effects of corticosteroids are decreased vasodilation and permeability of capillaries, as well as decreased leukocyte migration to sites of inflammation. Corticosteroids binding to the glucocorticoid receptor mediates changes in gene expression that lead to multiple downstream effects over hours to days. Glucocorticoids inhibit neutrophil apoptosis and demargination; they inhibit phospholipase A2, which decreases the formation of arachidonic acid derivatives; they inhibit NF-Kappa B and other inflammatory transcription factors; they promote anti-inflammatory genes like interleukin-10. Lower doses of corticosteroids provide an anti-inflammatory effect, while higher doses are immunosuppressive. High doses of glucocorticoids for an extended period bind to the mineralocorticoid receptor, raising sodium levels and decreasing potassium levels.

Chloramphenicol is lipid-soluble, allowing it to diffuse through the bacterial cell membrane. It then reversibly binds to the L16 protein of the 50S subunit of bacterial ribosomes, where transfer of amino acids to growing peptide chains is prevented (perhaps by suppression of peptidyl transferase activity), thus inhibiting peptide bond formation and subsequent protein synthesis.

Benzocaine binds to sodium channels and reversibly stabilizes the neuronal membrane which decreases its permeability to sodium ions. Depolarization of the neuronal membrane is inhibited thereby blocking the initiation and conduction of nerve impulses.

Benzyl alcohol inhibits lice from closing their respiratory spiracles, allowing the vehicle to obstruct the spiracles and causing the lice to asphyxiate.

4.2 Pharmacodynamic properties

Corticosteroids bind to the glucocorticoid receptor, inhibiting pro-inflammatory signals, and promoting anti-inflammatory signals. Prednisolone acetate has a short duration of action as the half life is 2-3 hours. Corticosteroids have a wide therapeutic window as patients make require doses that are multiples of what the body naturally produces. Patients taking corticosteroids should be counselled regarding the risk of hypothalamic-pituitary-adrenal axis suppression and increased susceptibility to infections.

Chloramphenicol is a broad-spectrum antibiotic that was derived from the bacterium Streptomyces Venezuela and is now produced synthetically. Chloramphenicol is effective against a wide variety of microorganisms, but due to serious side-effects (e.g., damage to the bone marrow, including aplastic anaemia) in humans; it is usually reserved for the treatment of serious and life-threatening infections (e.g., typhoid fever). Chloramphenicol is bacteriostatic but may be bactericidal in high concentrations or when used against highly susceptible organisms. Chloramphenicol stops bacterial growth by binding to the bacterial ribosome (blocking peptidyl transferase) and inhibiting protein synthesis.

Benzocaine is a local anesthetic commonly used as a topical pain reliever. It is the active ingredient in many over-the-counter analgesic ointments. It is also indicated for general use as a lubricant and topical anesthetic on intratracheal catheters and pharyngeal and nasal airways to obtund the pharyngeal and tracheal reflexes; on nasogastric and endoscopic tubes; urinary catheters; laryngoscopes; proctoscopes; sigmoidoscopes and vaginal specula.

4.3 Pharmacokinetic properties

- Prednisolone acetate

<u>Absorption</u>

Prednisolone acetate oral suspension given at a dose equivalent to 15mg prednisolone has a Cmax of 321.1ng/hr, a Tmax of 1-2 hours, and an AUC of 1999.4ng*hr/mL.5 The absorption pharmacokinetics of prednisolone acetate are not significantly different from a comparable dose of prednisolone

<u>Metabolism</u>

Prednisolone acetate undergoes ester hydrolysis to prednisolone.After this step, the drug undergoes the normal metabolism of prednisolone.

Prednisolone can be reversibly metabolized to prednisone which is then metabolized to 17α,21-dihydroxy-pregnan-1,4,6-trien-3,11,30-trione (M-XVII), 20α-dihydro-prednisone (M-V), 6βhydroxy-prednisone (M-XII), 6α-hydroxy-prednisone (M-XIII), or 20β-dihydro-prednisone (M-IV).2 20β-dihydro-prednisone is metabolized to 17α,20ξ,21-trihydroxy-5ξ-pregn-1-en-3,11-dione(M-XVIII).2 Prednisolone is metabolized to Δ6-prednisolone (M-XI), 20α-dihydro-prednisolone (M-III), 20β-dihydro-prednisolone (M-II), 6αhydroxy-prednisolone (M-VII), or 6βhydroxy-prednisolone(M-VI).2 6αhydroxy-prednisolone is metabolized to 6α,11β,17α,20β,21-pentahydroxypregnan-1,4-diene-3-one (M-X).2 6βhydroxy-prednisolone is metabolized to 6β,11β,17α,20β,21-pentahydroxypregnan-1,4-diene-3-one (M-VIII), 6β,11β,17α,20α,21-pentahydroxypregnan-1,4-diene-3-one (M-IX), and 6β,11β,17α,21-tetrahydroxy-5ξ-pregn-1-en-3,20-dione (M-XIV).2 MVIII is metabolized to 6β,11β,17α,20β,21-pentahydroxy-5ξ-pregn-1-en-3-one (M-XV) and then to MXIV, while MIX is metabolized to 6β,11β,17α,20α,21-pentahydroxy-5ξ-pregn-1-en-3-one (M-XVI) and then to MXIV.2 These metabolites and their glucuronide conjugates are excreted predominantly in the urine.

Excretion

Prednisolone acetate is predominantly excreted in the urine.

- Chloramphenicol

It is active when given orally and, unlike most other antibacterial, it diffuses into the CSF even when the meninges are not inflamed. The majority of a dose is inactivated in the liver, only a small proportion appearing unchanged in the urine.

5. Nonclinical properties

5.1 Animal Toxicology or Pharmacology

Not required.

6. Description

Already mentioned and covered in the above points.

7. Pharmaceutical particulars

7.1 Incompatibilities

There are no known incompatibilities.

7.2 Shelf-life

18 months.

7.3 Storage and handling instructions

Store in cool and drop place.