1. Generic Name

Neomycin, Beclomethasone, Clotrimazole

2. Qualitative and Quantitative composition

Neomycin	0.5% w/v
Beclomethasone	0.025%
Clotrimazole	1%w/v

3. Dosage form and strength

Topical Ear Drops of Neomycin 0.5%, Beclomethasone 0.025%, Clotrimazole 1%,

4. Clinical particulars

4.1 Therapeutic indication

Indication Otiflox new ear drops are indicated for treatment:

- Mixed Ear Infections
- Otitis Externa
- Chronic suppurative otitis media

4.2 Posology and method of administration

Instil two drops of Otiflox new Ear Drops in affected ear 2-3 times a day.

4.3 Contraindication

Otiflox ear drops are contraindicated in patients with:

- Hypersensitivity to any of the ingredients
- Psychiatric illnesses and in patients with epilepsy or other seizure disorders.
- Severe systemic infections

4.4 Special warnings and precautions for use

None.

4.5 Drug interactions

No specific drug interactions noted.

4.6 Use in special population

- Pediatric: Not recommended in children.
- Geriatric: Safety and effectiveness of Otiflox ear drops in geriatric patients have not been established.
- Liver impairment: Use with caution.
- Renal failure: Use with caution.
- Pregnancy and lactation: Use with caution.

4.7 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 new Ear Drops is known.

4.8 Undesirable effects

Otiflox new ear drops can give mild irritation, burning or stinging sensation in the ear after application.

4.9 Overdose

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

5. Pharmacological properties

5.1 Mechanism of action

Aminoglycosides like neomycin "irreversibly" bind to specific 30S-subunit proteins and 16S rRNA. Specifically neomycin binds to four nucleotides of 16S rRNA and a single amino acid of protein S12. This interferes with decoding site in the vicinity of nucleotide 1400 in 16S rRNA of 30S subunit. This region interacts with the wobble base in the anticodon of tRNA. This leads to interference with the initiation complex, misreading of mRNA so incorrect amino acids are inserted into the polypeptide leading to non-functional or toxic peptides and the breakup of polysomes into non-functional monosomes.

Beclomethasone is a steroid which promptly blocks inflammation & allergy.

Clotrimazole works to kill individual Candida or fungal cells by altering the permeability of the fungal cell wall. It binds to phospholipids in the cell membrane and inhibits the biosynthesis of ergosterol and other sterols required for cell membrane production. This leads to the cell's death via loss of intracellular elements.

5.2 Pharmacodynamic properties

Neomycin is an aminoglycoside antibiotic. Aminoglycosides are useful primarily in infections involving aerobic, Gram-negative bacteria, such as Pseudomonas, Acinetobacter, and Enterobacter. In addition, some mycobacteria, including the bacteria that cause tuberculosis, are susceptible to aminoglycosides. Infections caused by Gram-positive bacteria can also be treated with aminoglycosides, but other types of antibiotics are more potent and less damaging to the host. In the past the aminoglycosides have been used in conjunction with penicillin-related antibiotics in streptococcal infections for their synergistic effects, particularly in endocarditis. Aminoglycosides are mostly ineffective against anaerobic bacteria, fungi and viruses.

Beclomethasone dipropionate works by attenuating the inflammatory responses associated with asthma, allergic rhinitis, nasal polyps, and corticosteroid-responsive dermatoses. It suppresses the actions of inflammatory cells, such as mast cells, eosinophils, basophils, lymphocytes, macrophages, and neutrophils. It also inhibits the release of inflammatory mediators, such as histamine, eicosanoids, leukotrienes, and cytokines. Beclomethasone dipropionate is reported to exhibit potent topical activity while possessing low systemic effects. Beclomethasone dipropionate is a corticosteroid drug with anti-inflammatory and vasoconstrictive effects used to treat chronic inflammatory processes such as asthma, allergic rhinitis, and corticosteroid-responsive dermatoses. When inhaled, it improves lung function, decreases airway hyper-reactivity, and reduces the severity of asthmatic symptoms. Although inhaled corticosteroids, including beclomethasone dipropionate, are reported to mainly act locally in the lungs, systemic effects such as disruption of hypothalamic-pituitary-adrenal (HPA) axis function, bone turnover, osteoporosis, and growth suppression may still be observed with chronic use or high dose administration. There were varying findings from clinical studies examining the effect of Beclomethasone dipropionate on growth suppression in pediatric patients. It was shown to suppress the hypothalamo-pituitary-adrenal (HPA) axis in a dosedependent manner. HPA axis is a central hormonal response system to stress and activation of HPA axis leads to the production of endogenous steroid hormone production. Long-term use of high-dose systemic corticosteroids, including those inhaled, was often associated with signs and symptoms of adrenal insufficiency when exposed to stress conditions, such as trauma, surgery, or infections. As corticosteroids work by suppressing the immune system, there may be an increased risk for developing infections. Cases of *Candida albicans* infection of the mouth and throat have been reported with inhaled Beclomethasone dipropionate therapy.

Clotrimazole is a broad-spectrum antifungal agent that inhibits the growth of pathogenic yeasts by changing the permeability of cell membranes. The action of Clotrimazole is fungistatic at concentrations of drug up to 20 mcg/mL and may be fungicidal *in vitro* against Candida albicans and other species of the genus Candida at higher concentrations. Unfortunately, resistance to Clotrimazole, which was rare in the past, is now common in various patient populations. Clotrimazole is generally considered to be a fungistatic, and not a

fungicidal drug, although this contrast is not absolute, as Clotrimazole shows fungicidal properties at higher concentrations.

Excessive blood levels of lidocaine can cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. With central neural blockade these changes may be attributable to the block of autonomic fibers, a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system, and/or the betaadrenergic receptor stimulating action of epinephrine when present. The net effect is normally a modest hypotension when the recommended dosages are not exceeded.

In particular, such cardiac effects are likely associated with the principal effect that lidocaine elicits when it binds and blocks sodium channels, inhibiting the ionic fluxes required for the initiation and conduction of electrical action potential impulses necessary to facilitate muscle contraction . Subsequently, in cardiac myocytes, lidocaine can potentially block or otherwise slow the rise of cardiac action potentials and their associated cardiac myocyte contractions, resulting in possible effects like hypotension, bradycardia, myocardial depression, cardiac arrhythmias, and perhaps cardiac arrest or circulatory collapse.

5.3 Pharmacokinetic properties

Neomycin is poorly absorbed from the gastrointestinal tract, about 97% of an oral dose being excreted unchanged in the faeces. Doses of 3 g orally produce peak plasma concentrations of up to 4 micrograms/mL and absorption is similar after an enema. Absorption may be increased in conditions which damage or inflame the mucosa. Absorption has also been reported to occur from the peritoneum, respiratory tract, bladder, wounds, and inflamed skin. Once neomycin is absorbed it is rapidly excreted by the kidneys in active form. It has been reported to have a half-life of 2 to 3 hours

Beclomethasone is stated to be readily absorbed from sites of local application, and rapidly distributed to all body tissues. It is metabolised principally in the liver, but also in other tissues including gastrointestinal tract and lung; enzymatic hydrolysis rapidly produces the monopropionate (which has some glucocorticoid activity), and, more slowly, the free alcohol, which is virtually devoid of activity. Only a small proportion of an absorbed dose is excreted in urine, the remainder being excreted in the faeces mainly as metabolites.

When applied topically Clotrimazole penetrates the epidermis but there is little if any systemic absorption. Absorption of 3 to 10% of a dose has been reported after vaginal use. Clotrimazole is metabolised in the liver to inactive compounds and excreted in the faeces and urine.

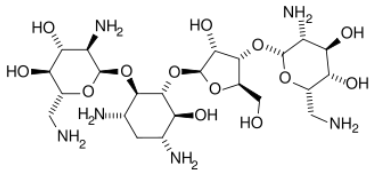
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

NA.

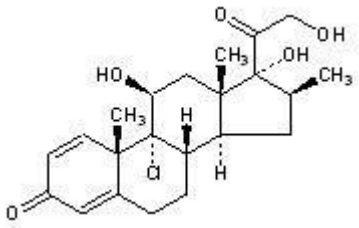
7. Description

Neomycin belongs to a class of drugs known as aminoglycoside antibiotics. Its chemical name (2*R*,3*S*,4*R*,5*R*,6*R*)-5-amino-2-(aminomethyl)-6-[(1*R*,2*R*,3*S*,4*R*,6*S*)-4,6-diamino2[(2*S*,3*R*,4*S*,5*R*)-4-[(2*R*,3*R*,4*R*,5*S*,6*R*)-3-amino-6-(aminomethyl)-4,5-dihydroxyoxan-2-yl]oxy3hydroxy-5-(hydroxymethyl)oxolan-2-yl]oxy-3-hydroxycyclohexyl]oxyoxane-3,4-diol and Its chemical structure is:



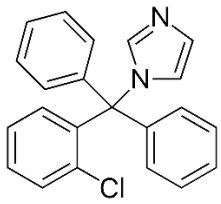
Its molecular formula is $C_{23}H_{46}N_6O_{13}$ and its molecular weight is 614.644 g/mol.

Beclomethasone belongs to a class of medications called corticosteroids. Its chemical name is (8*S*,9*R*,10*S*,11*S*,13*S*,14*S*,16*S*,17*R*)-9-chloro-11,17-dihydroxy-17-(2-hydroxyacetyl)-10,13,16trimethyl-6,7,8,11,12,14,15,16-octahydrocyclopenta[a]phenanthren-3-one and its structure is:



Its empirical formula is $C_{22}H_{29}ClO_5$ and its molecular weight is 521.042 g/mol.

Clotrimazole is in a class of antifungal medications called imidazole. It works by stopping the growth of fungi that cause infection. Its chemical name is 1-[(2-chlorophenyl)diphenylmethyl] imidazole and its chemical structure is:



Its empirical formula is $C_{22}H_{17}ClN_2$ and its molecular weight is 344.837 g/mol.

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

18 months.

8.3 Packaging Information

Otiflox new Ear Drops is available in 5 ml bottle with in-built dropper.

8.4 Storage and handling instructions

Store in a dry, well-ventilated place at a temperature not exceeding 30^oC. Do not freeze.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by

Om Sai Pharma pack.

11. Details of permission or license number with date

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12. Date of revision: April 2025