1. NAME OF THE MEDICINAL PRODUCT

TERRAMYCIN w/Polymyxin B

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ophthalmic Ointment with Polymyxin B contains 0.5% oxytetracycline and 10,000 units of Polymyxin B per gram of sterile petrolatum base.

A 1% solution in water is acidic (pH about 2.5). Its potency is reduced in solutions more acidic than pH 2 and it is rapidly destroyed by alkali hydroxides.

Oxytetracycline is chemically designated as 4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-2-naphthacenacarboxamide and has a molecular formula of $C_{22}H_{24}N_2O_9$.

The molecular weight of oxytetracycline hydrochloride is 496.90. It is an odorless, bitter, yellow crystalline powder soluble in water. It forms a cloudy or turbid solution in water due to liberation of oxytetracycline base.

Polymyxin B Sulfate is a white or buff-coloured, hygroscopic powder, odorless or with a slight odor. It is very soluble in water with a 2% solution producing a pH of 5 to 7.

3. PHARMACEUTICAL FORM

Oxytetracycline Ophthalmic Ointment with Polymyxin B

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxytetracycline with Polymyxin B Ophthalmic preparations are indicated in the treatment of superficial ocular infections involving the conjunctiva and/or cornea due to susceptible microorganisms.

4.2 Posology and method of administration

Oxytetracycline with Polymyxin B ophthalmic preparations are administered as a small quantity (approximately 1 cm) of the ointment. The preparation should be instilled or applied into the conjunctival sac of the lower lid 4 to 6 times daily until the infection is cleared and healing is complete. This may take from one day to several weeks depending on the nature and severity of the infection. In blepharitis, scales and crusts should be removed before applying medication. For prophylaxis, the same procedure is followed on the day before the operation and subsequently for several days following it.

The patient should be instructed to avoid contamination of the tip of the tube when applying the ointment.

4.3 Contraindications

This product is contraindicated in persons who have shown hypersensitivity to any of their components.

4.4 Special warnings and precautions for use

As with other antibiotic preparations, Oxytetracycline may result in overgrowth of nonsusceptible organisms, including fungi. Constant observation of the patient for this possibility is essential. If new infections due to nonsusceptible bacteria or fungi appear during therapy, appropriate measures should be taken.

Topical application of Oxytetracycline with Polymyxin B should be supplemented with systemic administration when infections are severe or do not respond to topical therapy alone.

Usage in Children
Systemic administration of tetracyclines during tooth development (last half of pregnancy, infancy, and childhood to the age of 8 years) may cause permanent discoloration of the teeth as well as retardation in the development of the skeleton. Enamel hypoplasia has also been reported. Although these effects are unlikely following topical application of tetracyclines because of the low doses used, the possibility that these effects could occur should be considered.

4.5 Interaction with other medicinal products and other forms of interaction

No known interactions with Oxytetracycline Ophthalmic preparations.

4.6 Pregnancy and lactation

Pregnancy
There are no controlled studies to date using topical tetracyclines in pregnant women. The use of systemic tetracyclines in pregnant women has resulted in retardation of skeletal development and bone growth in the fetus. None the less, topical tetracyclines should be used during pregnancy only when the possible benefits outweigh the potential risks.

Lactation
It is not known whether topically applied tetracyclines are distributed into breast milk. Tetracyclines are distributed into milk following systemic administration. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Oxytetracycline topical preparations are not expected to have an influence on the ability to drive and to operate machinery. However, directly following the application of the ophthalmic dosage form, a short period of less acute vision may occur.

4.8 Undesirable effects

Immune System Disorders: Hypersensitivity

Nervous System Disorders: Burning sensation

Eye Disorders: Lacrimation increased

Skin & Subcutaneous Tissue Disorders: Dermatitis contact

General Disorders and Administration Site Conditions: Pain, Sensation of foreign body

4.9 Overdose

No cases of overdosage with topical use of oxytetracycline have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Oxytetracycline is a product of the metabolism of *Streptomyces rimosus* and is one of the family of tetracycline antibiotics. Oxytetracycline is primarily bacteriostatic and is thought to exert its antimicrobial effect by the inhibition of protein synthesis. Oxytetracycline is a broad-spectrum antibiotic which is useful topically for prevention or treatment of superficial infections due to a variety of pyogenic bacteria, both gram-positive and gram-negative.

The drugs in the tetracycline class have similar antimicrobial spectra, and cross resistance among them is common.

Polymyxin B Sulfate, one of a group of basic polypeptide antibiotics derived from *B. polymyxa*, is bacteriocidal. It is thought to act by altering the structure of the bacterial membrane resulting in leakage of essential intracellular components. Polymyxin B has antimicrobial activity against a wide variety of gram-negative microorganisms. It is particularly effective against infections caused by *Pseudomonas aeruginosa* and *Haemophilus aegyptius*, frequently found in local infections of the eye.

Thus the combination of Oxytetracycline and Polymyxin B sulfate is a particularly effective antimicrobial combination against primarily causative or secondarily infecting organisms.

One mg of pure Polymyxin B is equivalent to 10,000 units.

5.2 Pharmacokinetic properties

Oxytetracycline
In one study in rabbits with abraded corneas, oxytetracycline hydrochloride concentrations of 28 mcg/ml were detected in the aqueous humor 30 minutes after 5-minute bathing of the eye with a solution containing 5 mg/ml.

Polymyxin B
In one study in rabbits, 0.1 mcg/ml concentrations of polymyxin B were detected in the aqueous humor and vitreous humor following six topical applications of 0.25% polymyxin B, one every 10 minutes.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mineral oil, white petrolatum

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

Observe "Expiry Date" (month/year) on outer pack.

6.4 Special storage precautions

Store below 30°C.

6.5 Nature and contents of container

Aluminium tube of 3.5g in a carton

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Not applicable.

7. MANUFACTURER

PT Pfizer Indonesia
Jakarta, Indonesia

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