SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TERRACORTRIL with Polymyxin B, eye/ear drops, suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

*1 ml drops contains:*Oxytetracycline hydrochloride, equivalent to oxytetracycline 5 mg, hydrocortisone acetate 15 mg, polymyxin B sulphate 10,000 IU,

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Eye and ear drops, suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Conditions of the Eyelid: Blepharitis--acute, chronic, nonpurulent.

Conditions of the Conjunctiva: Conjunctivitis--acute, chronic, nonpurulentphlyctenular, or nonspecific.

*Conditions of the Sclera:*Scleritis; episcleritis. It may be useful in nonspecific inflammatory conditions involving the cornea, particularly where neo-vascularization is a problem.

Conditions of the External Ear: Infections of the external ear canal caused by organisms susceptible to oxytetracycline (and Polymyxin B Sulfate for TERRA-CORTRIL Eye/Ear Suspension with Polymyxin B) especially when there is mixed bacterial etiology; for infections of undetermined etiology that are accompanied by inflammatory reactions in which hydrocortisone is indicated.

4.2 Posology and method of administration

Eye Conditions: Instill one or two drops into the affected eye three times daily.

Ear Conditions: For the treatment of infections of the external ear canal, it is recommended that 2 to 4 drops be instilled three times daily, or as prescribed by the physician.

The patient should be instructed to avoid contamination of the dropper with exudate from the infected site. The suspension should be shaken well before use. The dropper should be replaced in the bottle immediately after use.

4.3 Contraindications

Hypersensitivity to any component of the medication.

Epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella and many other viral diseases of the cornea and conjunctiva; viral otic infections.

Mycobacterial infection of the eye.

Fungal diseases of ocular or auricularstructures.

Ophthalmic use of these combinations is always contraindicated afteruncomplicated removal of a corneal foreign body.

Otic use is not recommended when there is perforation of the eardrum.

4.4 Special warnings and precautions for use

Prolonged use of ophthalmic corticosteroids may result in glaucoma, with damage to the optic nerve, defects in visual acuity and fields of vision, and posterior subcapsular cataract formation. Prolonged use may suppress the host response and thus increase the hazard of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection. If these products are used for 10 days or longer, intraocular pressure should be routinely monitored.

Employment of steroid medication in the treatment of herpes simplex requires great caution.

The initial prescription and renewal of the medication order beyond 20 ml should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

The use of oxytetracycline and other antibiotics may result in an overgrowth of resistant organisms - particularly *Candida* and staphylococci. Constant observation of the patient for this possibility is essential. If new infections of the cornea due to nonsusceptible bacteria or fungi appear during therapy, appropriate measures should be taken.

If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

If irritation develops, the product should be discontinued and appropriate therapy instituted.

The possibility of persistent fungal infections of the cornea should be considered after prolonged steroid dosing.

Supplemental therapy with oral oxytetracycline is advisable in the treatment of severe infections or those which may become systemic.

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 Terracortril with polymyxin B,eye/ear drops, suspension.

4.6 Fertility, pregnancy and lactation

Pregnancy

Although topical steroids have not been reported to have an adverse effect on human pregnancy, the safety of their use in pregnant women has not been absolutely established. In laboratory animals, increases in incidence of fetal abnormalities have been associated with exposure of gestating females to topical corticosteroids, in some cases at rather low dosage levels. Therefore, drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.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, drugs of this class should be used during pregnancy only when the possible benefits outweigh the potential risks.

Lactation

It is not known whether topical corticosteroids are excreted in breast milk. Systemic corticosteroids are excreted in breast milk and may cause unwanted effects in the infant such as growth suppression.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-hydrocortisone topical preparations are not expected to have an influence on the ability to drive or 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

Oxytetracycline (and hydrocortisone) are well tolerated by the epithelial tissues and may be used topically with minimal untoward effects.Allergic reactions including contact dermatitis[7] may occur, but are rare.

Reactions occurring most often from the presence of the anti-infective ingredients are allergic sensitizations. Increased lacrimation, a transient stinging or burning sensation, and a foreign body sensation have been reported occasionally with ophthalmic tetracycline products.

The following reactions are reported with ophthalmic tetracycline:

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.

Secondary Infection: The development of secondary bacterial or fungal infection has occurred after use of combinations containing steroids and antimicrobials. With long-term applications of steroids, the cornea is particularly prone to develop fungal infections. The possibility of fungal invasion must be considered in any persistent corneal ulceration where steroid treatment has been used.

Secondary bacterial ocular infection following suppression of host responses also occurs.

The following reactions are due to the steroid component (hydrocortisone):

Infections and Infestations: Infection, Bacterial infection, Fungal infection.

Eye Disorders: Glaucoma, Optic nerve disorder, Cataract.

General Disorders and Administration Site Conditions: Impaired healing.

Investigations: Intraocular pressure increased

The use of the product should be discontinued if such reactions occur.

4.9 Overdose

There is no specific antidote available. In case of overdosage, discontinue medication, treat symptomatically and institute supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Oxytetracycline hydrocortisone Eye/Ear Suspension combines the anti-infective activity of oxytetracycline (and Polymyxin B for TERRA-CORTRIL Eye/Ear Suspension with polymyxin B) with the anti-inflammatory activity of hydrocortisone.

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*.

Hydrocortisone is an adrenocorticoid. It inhibits the inflammatory reactions of the eye or ear resulting from allergy, infection or trauma.

Oxytetracycline hydrocortisone Eye/Ear Suspension (with Polymyxin B) is useful in the treatment of Eye/Ear conditions in which antibacterial and anti-inflammatory effects are desired.

In the treatment of superficial infections of the eye and ear amenable to oxytetracycline and polymyxin B therapy, the anti-inflammatory action of hydrocortisone in this formulation will afford prompt symptomatic relief while the antibiotics are acting against the causative organisms.

Where topical therapy with hydrocortisone is of value, the added presence of oxytetracycline and polymyxin B will serve to prevent or eradicate secondary bacterial complications.

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 solutions of the drug containing 5 mg/ml.

Hydrocortisone:

Corticosteroids are absorbed into the aqueous humor, cornea, iris, choroid, ciliary body and retina. Systemic absorption occurs, but may be significant only at higher dosages or in extended pediatric therapy.

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

N/A

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium stearate and liquid paraffin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Keep out of the sight and reach of children.
Do not use Terracortrilafter the expiry date which is stated on the label after EXP:. The expiry date refers to the last day of that month.
Medicines should not be disposed of via wastewater or household waste. Ask yourpharmacist how to dispose of medicines no longer required. These measures willhelp to protect the environment.

6.4 Special precautions for storage

Store below 30°C

6.5 Nature and contents of container

Tube 5 and 15 ml.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal <and other handling>

No special requirements.
TERRACORTRIL with Polymyxin B eye/ear drops, suspension can cause discoloration on textiles.

7. MARKING AUTHORIZATION HOLDER AND MANUFACTURER

PfizerAB
191 90 Sollentuna
Sweden

MANUFACTURED

Farmasierra Manufacturing S.L
San Sebastin de los Reyes 28700
Madrid, Spain

8. MARKING AUTHORIZATION NUMBER

04716/06788/REN/2018

9. DATE OF MARKET AUTHORISATION

01-11-2019

10. DATE OF REVISION OF THE TEXT

July 2017