Zylet (loteprednol etabonate and tobramycin ophthalmic suspension) 0.5%/3.0% (5 mg/mL and 3 mg/mL).

**INDICATIONS AND USAGE**

Zylet contains 5 mg/mL loteprednol etabonate and 3 mg/mL tobramycin for the treatment of responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial, fungal, or viral pathogens are suspected. (1)

**CONTRAINDICATIONS**

Zylet, as with other steroid anti-infective ophthalmic combination drugs, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye (e.g., tuberculosis). (3)

**WARNINGS AND PRECAUTIONS**

• Intraocular pressure (IOP)-Prolonged use of corticosteroids may result in persistence or increase of any pre-existing eye infection, detect in visual acuity and fields of vision. This product is used for 10 days or longer, IOP should be monitored. (5.1)

• Cataracts-Use of corticosteroids may result in posterior subcapsular cataract formation. (5.2)

• Delayed healing-Use of corticosteroid after surgery may delay the healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of a magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining. (5.3)

• Bacterial infections-Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. (5.4)

• Viral infections-Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution, use of corticosteroids may exacerbate the severity of many viral infections of the eye (including herpes simplex). (5.5)

• Fungal infections-Fungal infections of the cornea are particularly prone to develop coincidentally with long-term topical corticosteroid use. Fungi invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. (5.6)

Most common adverse reactions reported in patients were injection site reactions, superficial punctate keratitis, increased intraocular pressure, burning and stinging upon instillation. (6)

**ADVERSE REACTIONS**

• Use of corticosteroids may result in posterior subcapsular cataract formation, increased intraocular pressure, burning and stinging upon instillation. (6)

To report SUSPECTED ADVERSE REACTIONS, contact BAUSCH + LOMB, a division of Valeant Pharmaceuticals North America LLC, at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 08/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Recommended Dosing
2.2 Prescription Guideline
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Intraocular Pressure (IOP) Increase
5.2 Cataracts
5.3 Delayed Healing
5.4 Bacterial Infections
5.5 Viral Infections
5.6 Fungal Infections
5.7 Aminoglycoside-Hypersensitivity
6 ADVERSE REACTIONS
6.1 Injection Site Reactions
6.2 General Adverse Reactions
6.3 Allergic Reactions
6.4 Cardiovascular Disorders
6.5 Cramps
6.6 Dermatologic Reactions
6.7 Endocrine Disorders
6.8 Gastrointestinal Disorders
6.9 Headache
6.10 Hypoglycemia
6.11 Hypersensitivity Reactions
6.12 Infections
6.13 Injuries: External
6.14 Lovenberg and Dorsalis
6.15 Nervous System Disorders
6.16 Pain
6.17 Perinatal
6.18 Peripheral Nerve Disorders
6.19 Pulmonary Disorders
6.20 Skin and Appendage Disorders
6.21 Special Senses Disorders
6.22 Systemic Disorders
6.23 Urogenital Disorders
6.24 Vision Disorders
6.25 Vomiting
6.26 Other Adverse Reactions
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
9 CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY
10 CLINICAL PHARMACOLOGY
10.1 Mechanism of Action
10.2 Pharmacokinetics
10.3 Pharmacodynamics
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacokinetics
12.3 Pharmacodynamics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenicity
13.2 Mutagenesis
13.3 Impairment of Fertility
14 HOW SUPPLIED/STORAGE AND HANDLING
15 PATIENT COUNSELING INFORMATION
16 ADVERSE REACTIONS
17 PATIENT INFORMATION

Specific sections not listed from the full prescribing information are not listed.
Ocular reactions reported with an incidence less than 4% include visual disorders, discharge, itching, lacrimation disorder, photophobia, conjunctival injection, ocular pain, periorbital edema, and periorbital erythema.

The incidence of non-ocular reactions reported in approximately 14% of subjects was headache; all other non-ocular reactions had an incidence of less than 5%.

Loteprednol etabonate ophthalmic suspension 0.2% - 0.5%: Reactions associated with ophthalmic steroids include intraocular pressure, which may be associated with intraocular nerve pressure and increased fluid pressure in the eye. After ophthalmic steroid administration, postoperative pain and visual impairment may occur in patients with corneal transplants. The incidence of significant elevations of intraocular pressure (>18 mm Hg) was 2% (15/701) among patients receiving loteprednol etabonate, 7% (11/164) among patients receiving 1% prednisolone acetate and 0.5% (5/109) among patients receiving placebo.

Loteprednol etabonate ophthalmic suspension 0.3%: The most frequent adverse reactions to topical tobramycin are hypersensitivity and localized ocular toxicity, including lid itching and stinging.

16 USE ONLY IF IMPRINTED NECKBAND IS INTACT.

5 mL (NDC 24208-358-05) in a 7.5 mL bottle

12.1 Mechanism of Action

The development of secondary infection has occurred after use of combinations containing steroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop concurrently with long-term applications of steroids. 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.

12 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

The levels of loteprednol etabonate and tobramycin suspension is sterile, multiple dose topical anti-inflammatory ophthalmic agent and anti-infective combination for use in the treatment of ocular inflammation and infection.

Chemical name: chloromethyl 17-deoxy-3-oxoandrosta-1,4-diene-17β-carboxylate

Loteprednol etabonate (PJ 91), its primary, inactive metabolite, were below the limit of quantitation (1 ng/mL) at all sampling times.

Results from a bioavailability study in normal volunteers established that plasma levels of loteprednol etabonate and Δ1 cortienic acid were comparable with 0.5% loteprednol etabonate.

In a controlled clinical study of ocular penetration, the levels of loteprednol etabonate in the aqueous humor were found to be comparable with 0.5% loteprednol etabonate.

Chemical name: chloromethyl 17-deoxy-3-oxoandrosta-1,4-diene-17β-carboxylate

Chemical name: chloromethyl 17-deoxy-3-oxoandrosta-1,4-diene-17β-carboxylate

13 Nonionic Topical Ed 0.5 mg/kg/day in female rats and at 0.1 mg/kg/day in male rats. In the oral administration study, maternally toxic treatment regimen (significantly decreased body weight gain), gave rise to decreased growth and survival and retardation in development in the offspring during lactation; the NOEL for these effects was 5 mg/kg/day. Loteprednol etabonate had no effect on the development of male offspring, when administered to pregnant rats at doses of up to 50 mg/kg/day during the preimplantation period.

Reproductive studies have been performed in rats and rabbits with loteprednol etabonate at doses up to 100 mg/kg/day parenterally and have revealed no evidence of impaired fertility or harm to the fetus. There are no adequate and well-controlled studies in pregnant women. Therefore, Zylet should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Reproductive studies have been performed in rats and rabbits with loteprednol etabonate at doses up to 100 mg/kg/day parenterally and have revealed no evidence of impaired fertility or harm to the fetus. There are no adequate and well-controlled studies in pregnant women. Therefore, Zylet should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

If Zylet is administered to a nursing woman, caution should be exercised when Zylet is administered to a nursing woman.

2,3,6-trideoxy-4)-O-[2,6-diamino-3-Amino-3-deoxy-

Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Proteus mirabilis, Morganella morgani, most Pseudomonas vulgaris, Proteus vulgaris, Providencia rettgeri, Aeromonas hydrophila, Escherichia coli, and some species of enterobacteria.

Antibiotics in the treatment of bacterial infection (Table 15). 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.

Topical antibiotic agents such as tobramycin have been shown to be effective in the treatment of bacterial infection in the eye.

Primary bacteria include Staphylococcus aureus and some Staphylococcus species, and some (coagulase-negative) Staphylococcus species.

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

Topical antibiotic agents such as tobramycin have been shown to be effective in the treatment of bacterial infection in the eye.

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.

Topical antibiotic agents such as tobramycin have been shown to be effective in the treatment of bacterial infection in the eye.

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.