

MATERIAL SAFETY DATA SHEET

Issued:	01/05/05	Prepared by:	Gary Wong
Revised:	N/A		Manager EHS
Revision:	Original	Core No.	358

1. PRODUCT AND COMPANY INFORMATION

Product Name: Zylet™
Generic Name: Loteprednol Etabonate 0.5% and Tobramycin 0.3% Ophthalmic Suspension
NDC No. 24208-358-25 (2.5 ml)
 24208-358-05 (5 ml)
 24208-358-10 (10 ml)

Legal Category: Prescription only medicine, filled in dropper-tipped plastic bottle suitable for dispensing, and overpacked inside a cardboard carton.

Drug Composition: Glucocorticoid and Aminoglycoside Antibiotic

BAUSCH & LOMB INCORPORATED
 8500 Hidden River Parkway
 Tampa, FL 33637
 Information: (800) 323-0000 (M-F) 8am-5pm EST
 Emergency: (800) 227-1427 24 hrs

2. PRODUCT AND COMPANY INFORMATION

Description	CAS #	TLV (mg/m ³)	PEL (mg/m ³)	% Content
Loteprednol Etabonate	82034-46-6	NE	NE	0.5
Tobramycin	32986-56-4	NE	NE	0.3
Glycerin	56-81-5	10	NE	>1
Povidone	9003-39-8	NE	NE	>1
Purified Water	NA	NE	NE	>1
Ingredients <1%: Tyloxapol, Edetate Disodium, Benzalkonium Chloride				

3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

Plastic bottle with dropper tip in cardboard box. Milky white to off white suspension, toxic by ingestion. Presents little or no hazard if spilled and no unusual hazard if involved in fire.

POTENTIAL HEALTH HAZARDS

Carcinogenicity: (NTP) No (IARC) No (OSHA) No

Eye: This is an ophthalmic preparation. May cause irritation and hypersensitivity in some individuals. Adverse reactions include localized ocular toxicity, lid itch and swelling and redness of the mucous membrane of the eye (conjunctival erythema). These reactions occur in less than 3% of patients. Signs of overdose of Tobramycin Ophthalmic Solution include inflammation of the cornea, erythema, increased tearing (lacrimation), swelling (edema) and lid itching.

Skin: May cause irritation and localized hypersensitivity in some individuals with itching, swelling and diffused redness of the skin. Repeated or prolonged contact can induce hypersensitivity in some individuals.

Ingestion: May cause irritation and hypersensitivity in some individuals. Large doses can induce vomiting, diarrhea, adrenal gland suppression, Cushing's syndrome, water retention, electrolyte imbalance and hyperglycemia.

Inhalation: May cause irritation to the respiratory tract and hypersensitivity in some individuals.

Chronic Effects: May cause irritation and hypersensitivity in some individuals. Prolonged use of topical antibiotics can give rise to overgrowth of nonsusceptible organisms, including fungi. Bacterial resistance to tobramycin may also develop. In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be administered. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels and absence of response to ACTH stimulation. Prolonged use can result in elevation of intraocular pressure, with damage to the optic nerve, defects in visual acuity and fields of vision and/or posterior subcapsular cataract formation. It may also contribute to secondary ocular infections from fungi or viruses liberated from ocular tissues derived from nonsusceptible organisms.

Target Organs: Eyes, skin, digestive tract, kidney and brain.

Medical Conditions Aggravated by Long Term Exposure: Allergies to aminoglycoside antibiotics or any component of the product. As with other antibiotic preparations, prolonged use may result in overgrowth of other nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. Reproduction studies, in three different types of animals, at doses up to thirty-three times the normal human systemic dose have revealed no evidence of impaired fertility or harm to the fetus due to tobramycin. There are no adequate and well controlled studies in pregnant women. Tobramycin should be used in pregnancy only if the potential benefits justify the risk to the fetus. Because of the potential for adverse reactions in nursing infants from Tobramycin Ophthalmic Solution, a decision should be made whether to discontinue nursing the infant or discontinue taking the drug, taking into account the importance of the drug to the mother.

- Anaphylactic cross-reactions may occur for glucocorticoids.
- Preexisting conjunctival or systemic fungal infections may be aggravated.
Appropriate measures should be taken if this occurs.
- Epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella and other viral diseases of the cornea and conjunctiva.
- Tuberculosis of the eye.
- Fungal diseases of the ocular structures.
- Hypersensitivity to any of the ingredients of the medication.
- Various ocular diseases and long-term use of topical corticosteroids have been known to cause corneal and scleral thinning. Use of topical corticosteroids in the presence of thin corneal or scleral tissue may lead to perforation.
- Acute purulent untreated infection of the eye can be masked or activity enhanced by the presence of corticosteroid medication.

Chronic Effects: Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate or tobramycin. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in a chromosome aberration test in human lymphocytes, or *in vivo* in the single dose mouse micronucleus assay. Oral treatment of male and female rats with up to 50 mg/kg/day and 25mg/kg/day of loteprednol etabonate, respectively, (500 and 250 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender. No impairment of fertility was noted in studies of subcutaneous tobramycin in rats at doses of 100 mg/kg/day (1700 times the maximum daily clinical dose).

4. FIRST AID MEASURES

Remove from exposure and in the event of any untoward events, obtain appropriate medical attention. Persons developing serious hypersensitivity reactions must receive immediate medical attention.

Eyes: May cause irritation. Flush immediately with copious amounts of water for at least 20 minutes. Contact a physician.

Skin: May cause irritation. Remove all contaminated clothing and wash skin with copious quantities of water for at least 20 minutes. Contact physician if skin becomes irritated.

Ingestion: May cause irritation. Flush out mouth with water. Give plenty of water and bland fluids. Do not give anything to an unconscious person. Contact physician.

Inhalation: May cause irritation of respiratory tract. Avoid inhalation. Remove person to fresh air, and if breathing stops, use artificial respiration. Contact physician.

Note to Physicians:

Pregnancy: Teratogenic effects: Pregnancy Category C. Loteprednol etabonate was shown to be teratogenic when administered orally to rats and rabbits during organogenesis at 5 and 3 mg/kg/day, respectively (50 and 30 times the maximum daily clinical dose in rats and rabbits, respectively). An oral dose of loteprednol etabonate in rats at 50 mg/kg/day (500 times the maximum daily clinical dose) during late pregnancy through the weaning period showed a decrease in the growth and survival of pups without dystocia. However, no adverse effect in the pups was observed at 5 mg/kg/day (50 times the maximum daily clinical dose).

Parenteral doses of tobramycin did not show any harm to fetuses up to 100 mg/kg/day (1700 times the daily clinical dose) in rats and rabbits.

There are no adequate and well controlled studies in pregnant women. Zylet™ should be used during pregnancy only if potential benefits justifies the potential risks to the fetus.

Nursing Mothers: It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemic steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when Loteprednol Etabonate 0.5% and Tobramycin 0.3% Ophthalmic Suspension is administered to a nursing woman.

Additional details are available in the package insert or in the Physicians Desk Reference.

5. FIRE FIGHTING MEASURES

Flammable Properties: Flash point: NE Method: NE

Hazardous Products: Emits toxic fumes.

Extinguishing Media: Dry chemical, carbon dioxide, halon, water spray or fog, and foam on surrounding materials.

Fire Fighting Instructions: Wear self-contained breathing apparatus and protective clothing. Use water spray to keep fire-exposed containers cool. Do not spray water into the burning material.

6. ACCIDENTAL RELEASE MEASURES

Large/Small Spills: Use personal protective equipment. Contain the spill to prevent drainage into sewers, drains or streams. Use absorbent material to solidify the spill. Shovel or scoop up solidified waste. Dispose of material according to Federal, State and Local regulations.

7. HANDLING AND STORAGE

Handling: Avoid contact with product and use caution to prevent puncturing containers. No special protective equipment or procedures are required in the clinical or home environment.

Storage: Store product upright in original containers with the cap tightly closed at a controlled room temperature 15°-25° C (59°- 77° F). **PROTECT FROM FREEZING. KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.**

8. EXPOSURE CONTROL/PERSONAL PROTECTION

Engineering Controls: In the manufacturing plant, provide adequate ventilation for the raw material handling and compounding process, which will maintain the dust and vapor, levels below the TLV, STEL, and PEL values for the ingredients. Ventilation fans should be explosion proof. Use adequate personal protective equipment e.g. NIOSH-approved respirators, goggles or safety glasses, gloves and protective clothing. Ensure training in the handling of chemical material and use current Material Safety Data Sheets.

Eye Protection: (29 CFR 1910.133) Recommend goggles or chemical safety glasses.

Skin Protection: Thick impermeable gloves and protective clothing.

Respiratory Protection: (29 CFR 1910.134) NIOSH approved respirator, with organic vapor, acid gas and HEPA filter recommended for handling raw materials.

Warning: Do not use air-purifying respirators in oxygen-depleted environments. No respiratory protection is required in the clinical or home environment.

Other: None

Ventilation: Recommended

Contaminated Equipment: Wash contaminated clothing separately. Wash contaminated equipment with soap and water. Release rinse water into an approved wastewater system or according to Federal, State and Local regulations.

9. CHEMICAL & PHYSICAL PROPERTIES

Appearance & Odor:	Milky white to off-white suspension, odorless.		
Boiling Point:	N/A	Evaporation Rate:	NE
Specific Gravity	1.0	Vapor Density:	NE
Vapor Pressure:	NE	Viscosity:	4 cps

10. STABILITY AND REACTIVITY

Chemical Stability: Stable

Conditions to avoid: Extreme heat or cold. Avoid freezing.

Incompatibility: This product has the incompatibilities of water e.g. strong acids, bases, alkali metals, alkali hydrides and silver preparations.

Hazardous Decomposition Products: Emits toxic fumes.

Hazardous Polymerization: Should not occur.

11. TOXICOLOGY

Summary of Risks: Toxicological information refers to raw materials product. Concentrations and toxicological effects are substantially reduced in the product. For more detailed information see MSDS on chemical material

CAS #

82034-46-6 **Loteprednol Etabonate**

May cause irritation to the eyes, skin and respiratory tract. Can cause hypersensitivity in some individuals. Adverse reactions to corticosteroids include suppression of adrenal gland secretion, Cushing's syndrome, water retention, electrolyte imbalance and hyperglycemia. Studies in animals indicate that topical adrenocorticoids, when used in large amounts, can be systemically absorbed and can cause fetal abnormalities. Immune suppression may result from chronic high doses.

32986-56-4 **Tobramycin**

Topical or parenteral contact with high concentrations of some of the components of this ophthalmic formulation are known to produce hypersensitivity reactions in a small number of persons. The most adverse reactions are localized ocular toxicity and hypersensitivity, including conjunctiva erythema, itching, swelling. Material may be irritating to mucous membranes and respiratory tract. As a general rule, individuals working with chemicals should consider all chemicals to be potentially hazardous even if their individual hazards may be unknown or uncharacterized.

12. ECOLOGICAL INFORMATION

Chemical Fate Information: Product administered to patients presents a negligible impact on the environment.

13. DISPOAL INFORMATION

Dispose of material according to Federal, State, and Local regulations. The method typically used is incineration.

EPA Designations: RCRA Hazardous Waste: Not Listed

SARA Title III: Not Listed

14. TRANSPORTATION INFORMATION

Transportation Data: Not classified as hazardous by DOT regulations.

15. PRODUCT AND COMPANY INFORMATION

DOT Designations: Not classified as hazardous by DOT regulations.

EPA Designations: RCRA Hazardous Waste
(40 CFR 261.33) Not Listed

FDA Designations: Prescription only medication.
NDC No. 24208-358-25 (2.5 ml)
NDC No. 24208-358-05 (5 ml)
NDC No. 24208-358-10 (10 ml)

OSHA Designations: (29 CFR 1910.1000, Table Z)
Not Listed

SARA Title III: Not listed under Section 313 of Toxic Release Reporting.

CALIFORNIA PROPOSITION 65: Not Listed

16. OTHER INFORMATION

None

The information contained herein is furnished without warranty of any kind. The above information is believed to be correct but does not purport to be all-inclusive and should be used only as a guide. Users should make independent determinations of the suitability and completeness of information from all sources to assure proper use and disposal of these materials and the safety and health of employees and customers.

NE- Not Established

< - Less Than

> - Greater Than