MATERIAL SAFETY DATA SHEET

Loteprednol Etabonate Ophthalmic Gel

SECTION 1 - IDENTIFICATION

Product Identifier	:	Loteprednol Etabonate Ophthalmic Gel, 0.5%
Synonyms	:	chloromethyl 17α-[(ethoxycarbonyl)oxy]-11β-hydroxy-3-oxoandrosta-1,4-diene-17β-carboxylate
NDC Code	:	#72485-630-05 (Per bottle: 10 mL)
Recommended Use	:	Corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.
Manufacturer		Ophtapharm AG Riethofstrasse 1 CH-8442 Hettlingen Switzerland
Telephone		+1855-473-6847
Email		quality@sentiss.ch

SECTION 2 - HAZARDS IDENTIFICATION

UN GHS	:	According to: UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS)
Classification of the substance or mixture **UN GHS**		
Health Hazards	:	Reproductive Toxicity Category 2
Symbol(s)	:	
Signal Word	:	Warning
Hazard Statement(s)	:	Suspected of damaging fertility or the unborn child
Precautionary Statement(s)	:	Do not handle until all safety precautions have been read and understood. Wash thoroughly after handling. Use personal protective equipment as required. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention.

Storage/ Disposal	**:**	Keep tightly closed. Store at room temperature 15-25 ºC (59-77ºF), to maintain product integrity. Use before date marked on carton and/or container. Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.
Other Hazards	**:**	No data available

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Substances	:	Material does not meet the criteria of a substance according to United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

COMPOSITION			
Chemical Name	**Identifiers**	**%**	**Classifications According to**
Benzalkonium Chloride	**CAS:**139-07-1 **EINECS:**205-351-5	<0.005%	**UN GHS:** NDA
Boric acid	**CAS:**10043-35-3 **EINECS:**233-139-2	<1 %	**UN GHS:** Skin Irrit. 2; Eye Irrit. 2A; Acute Tox. Oral 5; Repr. 1
Edetate Disodium Dihydrate	**CAS:**139-33-3 **EINECS:**205-358-3	<0.1 %	**UN GHS:** NDA
Glycerin/ Glycerine 99.7%	**CAS:**56-81-5 **EINECS:**200-289-5	<1 %	**UN GHS:** Skin Irrit. 3; Eye Irrit. 2B
Loteprednol	**CAS:**82034-46-6	0.5 %	**UN GHS:** NDA
Polycarbophil	**CAS:**9003-97-8	<1 %	**UN GHS:** NDA
Propylene Glycol	**CAS:**57-55-6 **EINECS:**200-338-0	<1 %	**UN GHS:** Skin Irrit. 3; Eye Irrit. 2B
Sodium chloride	**CAS:**7647-14-5 **EINECS:**231-598-3	<0.05 %	**UN GHS:** Skin Irrit. 2; Eye Irrit. 2A; Acute Tox.
Tyloxapol	**CAS:**25301-02-4	<0.1 %	**UN GHS:** Skin Irrit. 2; Eye Irrit. 2A
Water	**CAS:**7732-18-5 **EINECS:**231-791-2	Balance	**UN GHS:** Classification criteria not met

Sodium Hydroxide (CAS# 1310-73-2, EINECS: 215-185-5) may be added to adjust the pH.

SECTION 4 - FIRST AID MEASURES

Inhalation	:	No inhalation exposure expected with this formulation under normal conditions of use. If signs/symptoms develop, get medical attention.
Eye Contact	:	For accidental and non-therapeutic applications, flush eyes with copious amounts of water for at least 15 minutes. Get medical attention. If eye irritation persists: Get medical advice/attention.
Skin Contact	:	Flush with fresh water if contact with skin or eyes. If skin irritation occurs: Get medical advice/attention
Ingestion	:	No specific treatment is necessary since this material is not likely to be hazardous by ingestion. If large quantities are accidentally ingested (greater than a tablespoon), get medical attention immediately.
Most important symptoms and effects, both acute and delayed	:	Ocular adverse reactions occurring in 5-15 % of patients treated with loteprednol etabonate ophthalmic suspension (0.2 % - 0.5 %) in clinical studies included abnormal vision/blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, injection, and photophobia. Other ocular adverse reactions occurring in less than 5 % of patients include conjunctivitis, corneal abnormalities, eyelid erythema, keratoconjunctivitis, ocular irritation/pain/discomfort, papillae, and uveitis
Indication of any immediate medical attention and special treatment needed **Other information**	:	Have the product container or label with you when calling a poison control center or doctor or going for treatment.

SECTION 5 - FIRE-FIGHTING MEASURES

EXTINGUISHING MEDIA		
Suitable extinguishing media	:	SMALL FIRES: Dry chemical, CO2, water spray or regular foam. LARGE FIRE: Water spray, fog or regular foam.
Unsuitable extinguishing media	:	No data available
SPECIFIC HAZARDS ARISING FROM THE SUBSTANCE AND MIXTURE		
Unusual Fire and Explosion Hazards	:	None known
Hazardous Combustion Products	:	None Known
Advice for Firefighters	:	Structural firefighters' protective clothing will only provide limited protection. Wear positive pressure self-contained breathing apparatus (SCBA).

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions	**:**	No special controls or personal protection required under the conditions of intended use. In the event of bulk spills, wear suitable protective eyewear, clothing, protective boots and protective gloves. Evacuate immediate area. Ensure adequate ventilation. Refer to Section 8.
Emergency Procedures	:	Keep unauthorized personnel away. Ventilate closed spaces before entering. Stop leak if you can do it without risk.
Environmental precautions	**:**	Prevent spilled material from entering storm sewers or drains, waterways, and contact with soil.
Methods for containment and cleaning up	**:**	Contain spilled product. For small spills, add suitable absorbent material. Scoop up and place in an appropriate liquid-tight container equipped with a tight cover for disposal. For large spills, dike spilled material or otherwise contain material to ensure runoff does not reach a waterway. Place spilled material in an appropriate, liquid-tight container equipped with a tight cover for disposal. Dispose of in accordance with Section 13.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	**:**	No special handling is required. Refer to Section 8. Use only in accordance with product literature. Use only in accordance with product literature.
Conditions for safe storage, including any incompatibilities	**:**	Keep tightly closed. Store at room temperature 15-25 °C (59-77°F), to maintain product integrity. Use before date marked on carton and/or container.
Incompatible Materials or ignition source	**:**	None specified

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

CONTROL PARAMETERS		
Exposure Limits/Guidelines	:	Refer to the occupational exposure limits / guidelines for the individual product components.

Exposure Limits/Guidelines					
	Result	**ACGIH**	**Canada Quebec**	**NIOSH**	**OSHA**
Boric acid (10043-35-3)	STELs	6 mg/m3 STEL (inhalable fraction, listed under Borate compounds, inorganic)	Not established	Not established	Not established
	TWAs	2 mg/m3 TWA (inhalable fraction, listed under Borate compounds, inorganic)	Not established	Not established	Not established
Glycerin/ Glycerine 99.7% (56-81-5)	TWAs	Not established	10 mg/m3 TWAEV (mist)	Not established	15 mg/m3 TWA (mist, total particulate); 5 mg/m3 TWA (mist, respirable fraction)
Sodium hydroxide (1310-73-2)	Ceiling	2 mg/m3 Ceiling	2 mg/m3 Ceiling	2 mg/m3 Ceiling	Not established
	TWAs	Not established	Not established	Not established	2 mg/m3 TWA

Exposure Control Notations ACGIH		
Boric acid (10043-35-3)	:	Carcinogens: (A4 - Not Classifiable as a Human Carcinogen (listed under Borate compounds, inorganic))

Exposure Controls		
Engineering measure/ Control	:	Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level.

Respiratory	:	In the event of a bulk spill, and where risk assessment shows that air purifying respirators are appropriate, a NIOSH (US) or CEN (EU) -certified air purifying respirator equipped with HEPA cartridges may be permissible under certain circumstances where airborne concentrations are expected to exceed exposure limits, when adequate oxygen is present and as a backup to engineering controls. Use a positive pressure air supplied respirator if there is any potential for an uncontrolled release or any other circumstances where air purifying respirators may not provide adequate protection.
Hands	:	Wear appropriate gloves.
Skin/Body	:	No special personal protection required under the conditions of intended use. In the event of a bulk spill, wear appropriate protective clothing.
Eye/ Face	:	Wear protective eyewear (goggles, face shield, or safety glasses) when handling bulk products before closed in final packaging. In the event of a spill, appropriate eye protection should be worn.
General Industrial Hygiene Considerations	:	Wash thoroughly after handling.
Environmental Exposure consideration	:	No data available

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Material Description			
Physical Form	Liquid Gel	Appearance	White to off-white gel
Color	White to off-white	Odor	No odor
Taste	Not Relevant	Odor Threshold	Not Relevant
General Properties			
Boiling Point	No data available	Melting Point	No data available
Decomposition Temperature	No data available	pH	6 to 7
Specific Gravity/Relative Density	= 1.007 Water=1	Water Solubility	No data available
Viscosity	No data available		
Volatility			
Vapor Pressure	Not relevant	Vapor Density	Not relevant
Evaporation Rate	Not relevant		
Flammability			
Flash Point	Not relevant	UEL	Not relevant
LEL	Not relevant	Autoignition	Not relevant
Environmental			
Octanol/Water Partition coefficient	No data available		

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	:	No dangerous reaction known under conditions of normal use.
Chemical stability	:	Stable under normal temperatures and pressures.
Possibility of Hazardous Reactions	:	No data available
Conditions to avoid	:	Extreme heat or cold. Do not freeze.
Incompatible materials	:	No data available
Hazardous Decomposition Products	:	No data available

SECTION 11 - TOXICOLOGICAL INFORMATION

Components		
Chemical name	**CAS No.**	**Toxicological data**
Glycerin/Glycerine 99.7%	56-81-5	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 12600 mg/kg; *Behavioral*:**General anesthetic**; *Behavioral*:**Muscle weakness**; *Liver*:**Other changes**
Propylene Glycol	57-55-6	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 20 g/kg
Sodium chloride	7647-14-5	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 3000 mg/kg
Benzalkonium Chloride	139-07-1	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 400 mg/kg
Polycarbophil	9003-97-8	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 20 g/kg; *Gastrointestinal*:**Other changes**
Tyloxapol	25301-02-4	**Acute Toxicity**: Ingestion/Oral-Rat LD50 • >5 g/kg
Sodium hydroxide (2N)	1310-73-2	**Acute Toxicity:** Intraperitoneal-Mouse LD50 • 40 mg/kg
Edetate Disodium Dihydrate	139-33-3	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 2 g/kg
Boric acid	10043-35-3	**Acute Toxicity:** Ingestion/Oral-Rat LD50 • 2500 mg/kg; *Behavioral*:**Convulsions or effect on seizure threshold**; *Behavioral*:**Ataxia**

GHS Properties	:	**Classification**
Acute toxicity	:	**UN GHS** • Classification criteria not met
Aspiration Hazard	:	**UN GHS** • Classification criteria not met
Carcinogenicity	:	**UN GHS** • Classification criteria not met
Germ Cell Mutagenicity	:	**UN GHS** • Classification criteria not met
Skin corrosion/Irritation	:	**UN GHS** • Classification criteria not met
Skin sensitization	:	**UN GHS** • Classification criteria not met
STOT-RE and STOT-SE	:	**UN GHS** • Classification criteria not met
Toxicity for Reproduction	:	**UN GHS** • Classification criteria not met
Respiratory sensitization	:	**UN GHS** • Classification criteria not met
Serious eye damage/Irritation	:	**UN GHS** • Classification criteria not met
Potential Health Effects		

Inhalation		
Acute (Immediate)	:	Under normal conditions of use, no health effects are expected.
Chronic (Delayed)	:	No data available
Skin		
Acute (Immediate)	:	Not expected to cause skin irritation.
Chronic (Delayed)	:	No data available
Eye		
Acute (Immediate)	:	Non-irritating to the eyes when used as directed. Ocular adverse reactions occurring in 5-15 % of patients treated with loteprednol etabonate ophthalmic suspension (0.2 %- 0.5 %) in clinical studies included abnormal vision/blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, injection, and photophobia. Other ocular adverse reactions occurring in less than 5 % of patients include conjunctivitis, corneal abnormalities, eyelid erythema, keratoconjunctivitis, ocular irritation/pain/discomfort, papillae, and uveitis.
Chronic (Delayed)	:	Reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. Refer to the product insert and/or product prescribing information for comprehensive information regarding adverse reactions and other important symptoms and effects.
Ingestion		
Acute (Immediate)	:	Not expected to be an exposure route. However, may cause gastric and intestinal irritation if ingested.
Chronic (Delayed)	:	No data available

Carcinogenic Effects		
	CAS	**NTP**
Boric acid	10043-35-3	Evidence of Carcinogenicity

Reproductive Effects	:	Teratogenic effects: Pregnancy Category C. Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocele, abnormal left common carotid artery, and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (35 times the maximum daily clinical dose), a dose which caused no maternal toxicity. The no-observed-effect-level (NOEL) for these effects was 0.5 mg/kg/day (6 times the maximum daily clinical dose). Oral treatment of rats during organogenesis resulted in teratogenicity (absent innominate artery at ≥5 mg/kg/day doses, and cleft palate and umbilical hernia at ≥50 mg/kg/day) and embryotoxicity (increased post implantation

		losses at 100 mg/kg/day and decreased fetal body weight and skeletal ossification with ≥50 mg/kg/day). Treatment of rats with0.5 mg/kg/day (6 times the maximum clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥5 mg/kg/day. Oral exposure of female rats to 50 mg/kg/day of loteprednol etabonate from the start of the fetal period through the end of lactation, a maternally toxic treatment regimen (significantly decreased body weight gain), gave rise to decreased growth and survival, and retarded development in the offspring during lactation; the NOEL for these effects was 5 mg/kg/day. Loteprednol etabonate had no effect on the duration of gestation or parturition when administered orally to pregnant rats at doses up to 50 mg/kg/day during the fetal period.

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity	**:**	This material has not been tested for environmental effects.
Persistence and Degradability	**:**	No data available
Bioaccumulative Potential	**:**	No data available
Mobility in Soil	**:**	No data available
Other Adverse Effects:	**:**	No data available

SECTION 13- DISPOSAL CONSIDERATIONS

Waste treatment methods		
Product waste	:	Waste characterizations and compliance with applicable laws are the responsibility solely of the waste generator.
Packaging waste	:	Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

SECTION 14 - TRANSPORT INFORMATION

	UN number	**UN proper shipping name**	**Transport hazard class (es)**	**Packing group**	**Environmental hazards**
DOT	NDA	Not regulated	NDA	NDA	NDA
TDG	NDA	Not regulated	NDA	NDA	NDA
IMO/IMD	NDA	Not regulated	NDA	NDA	NDA
IATA/ICA	NDA	Not regulated	NDA	NDA	NDA

Special precautions for user	:	No data available
Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code	:	No data available

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture.

SARA hazard classification: No data available

Inventory				
Component	**CAS**	**Canada DSL**	**EU EINECS**	**TSCA**
Propylene Glycol	57-55-6	Yes	Yes	Yes
Edetate Disodium dihydrate	139-33-3	Yes	Yes	Yes
Benzalkonium Chloride	139-07-1	Yes	Yes	Yes
Boric acid	10043-35-3	Yes	Yes	Yes
Polycarbophil	9003-97-8	No	No	No
Glycerin/Glycerine 99.7%	56-81-5	Yes	Yes	Yes
Loteprednol Etabonate	82034-46-6	No	No	No
Tyloxapol	25301-02-4	Yes	No	No
Sodium chloride	7647-14-5	Yes	Yes	Yes
Sodium hydroxide	1310-73-2	Yes	Yes	Yes
Water	7732-18-5	Yes	Yes	Yes

UNITED STATES

ENVIRONMENT		
U.S. - CERCLA/SARA - Hazardous Substances and their Reportable Quantities		
Edetate Disodium Dihydrate	139-33-3	Not Listed
Propylene Glycol	57-55-6	Not Listed
Sodium hydroxide	1310-73-2	1000 lb final RQ; 454 kg final RQ
Glycerin/Glycerine 99.7%	56-81-5	Not Listed
Sodium chloride	7647-14-5	Not Listed
Boric acid	10043-35-3	Not Listed
Benzalkonium Chloride	139-07-1	Not Listed
Tyloxapol	25301-02-4	Not Listed
Water	7732-18-5	Not Listed
Polycarbophil	9003-97-8	Not Listed
Loteprednol Etabonate	82034-46-6	Not Listed

United States California		
ENVIRONMENT		
U.S. California Proposition 65 Carcinogens List/ Developmental Toxicity/ Reproductive Toxicity (Male and Female)		
Edetate Disodium Dihydrate	139-33-3	Not Listed
Propylene Glycol	57-55-6	Not Listed
Sodium hydroxide	1310-73-2	Not Listed
Glycerin/Glycerine 99.7%	56-81-5	Not Listed
Sodium chloride	7647-14-5	Not Listed
Boric acid	10043-35-3	Not Listed
Benzalkonium Chloride	139-07-1	Not Listed
Tyloxapol	25301-02-4	Not Listed
Water	7732-18-5	Not Listed
Polycarbophil	9003-97-8	Not Listed
Loteprednol Etabonate	82034-46-6	Not Listed

SECTION 16 - OTHER INFORMATION

The information given herein is in good faith and to the best of our knowledge, but no warranty expressed or implied is made.

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