Safety Data Sheet

SECTION 1: Identification

Contact information

General

Kala Pharmaceuticals, Inc.
490 Arsenal Way, Suite 120
Watertown, MA 02472
Main: +1 (781) 996-5252
Fax: +1 (781) 642-0399
E-mail: SDS@kalarx.com

Emergency telephone number

+1 (800) 424-9300 (USA and Canada)
+1 (703) 527-3887 (International; collect calls accepted)
CHEMTREC (24 HOURS)

Product identifier — Loteprednol etabonate ophthalmic suspension 0.25%

Synonyms — KPI-121 0.25%

Trade name — EYSUVIS™

Chemical family — Mixture - containing corticosteroid

Recommended uses and restrictions — Finished pharmaceutical product (prescription drug for ophthalmic use) OR Formulated pharmaceutical mixture for further processing into finished pharmaceutical product. Restrictions: All other uses.

Note — This SDS is written to address potential worker health and safety issues associated with the handling of the mixture. It is not intended to provide information relevant to medicinal use of the product. Patients should consult prescribing information/package insert/product label or consult their pharmacist or physician.

SECTION 2: Hazard(s) identification

Classification of the substance or mixture — Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada. Consult prescribing/packaging information. The classification and labeling listed below is for bulk drug product.

Reproductive toxicity Category 1B
May damage the unborn child.
Specific target organ toxicity (repeated exposure) Category 2
May cause damage to organs (immune system) through prolonged or repeated exposure

Label elements

GHS Hazard pictograms

GHS Signal word — Danger

GHS Hazard statements — H360D - May damage the unborn child.

H373 - May cause damage to organs (immune system) through prolonged or repeated exposure

GHS Precautionary statements — P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. P260 - Do not breathe mist, spray. P280 - Wear protective clothing, eye protection, face protection. P308+P313 - If exposed or concerned: Get medical advice/attention. P314 - Get medical advice/attention if you feel unwell. P405 - Store locked up. P501 - Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation.

Other hazards

Loteprednol etobonate is a synthetic corticosteroid with anti-inflammatory properties. Effects reported in clinical trials following ophthalmic use included blurry vision, dilation and redness of blood vessels in the eye, discomfort on instillation (burning, itching, pain) and sensitivity to light. With prolonged use there is a risk of developing glaucoma, increased intraocular pressure, eye infections, or delayed wound healing.

Corticosteroids, as a class, have been associated with immunosuppression, as well as disturbances of the hypothalmic-pituitary-adrenal (HPA) axis. They have also been associated with fetal growth retardation if administered late in pregnancy. Malformations were also frequently reported with systemic exposure in non-clinical studies. Although loteprednol etobonate is considered a "soft steroid" (designed to be rapidly inactivated upon entering circulation) and it appears to act more locally, a potential for the drug to adversely affect pregnancty outcomes if accidentally inhaled or ingested in a workplace setting cannot be excluded.

Note

This mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3: Composition/Information on ingredients

Ingredient	CAS number	EINECS/ELINCS#	Amount	GHS classification
Ethylenediaminetetraacetic acid disodium salt dihydrate	6381-92-6	205-358-3	< 2 %	Acute Tox. 4 (Inhalation), H332 STOT RE 2, H373
Glycerol	56-81-5	200-289-5	< 2 %	Not classified
Loteprednol etabonate	82034-46-6	639-474-4	0.25 %	Repr. 1B, H360D STOT RE 1, H372

Note

The substance(s) listed above are considered hazardous. The remaining components are not hazardous and/or present at amounts below reportable limits. Glycerol is listed because it has OELs. Amounts are listed as ranges; the exact percentage of composition is withheld as a trade secret.

SECTION 4: First-aid measures

Description of first aid measures

Immediate medical attention and special treatment, if necessary

Yes

Inhalation

Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.

Skin contact

Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.

Eye contact

If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.

Ingestion

If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.

Most Important Symptoms/Effects

Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively.

Expected Symptoms/Effects, Acute and Delayed

See Sections 2 and 11

SECTION 5: Fire-fighting measures

Suitable (and unsuitable) extinguishing media

Suitable extinguishing media

Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.

Specific hazards arising from the chemical

No information identified. May emit carbon monoxide, carbon dioxide, oxides of nitrogen and chlorine containing compounds.

Fire hazard

No information identified.

Explosion hazard

No information identified. As product is an aqueous suspension, it is not expected to be explosive.

Special protective equipment and precautions for fire-fighters

Firefighting instructions

In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6: Accidental release measures

Personal precautions, protective equipment and emergency procedures

Protective equipment — If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated.

Emergency procedures — Do not breathe vapors/mist/spray.

Environmental precautions — Do not empty into drains. Avoid release to the environment.

Methods and material for containment and cleaning up

Methods for cleaning up — DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g, paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice with an appropriate solvent (see Section 9).

Other information — Dispose of materials or solid residues at an authorized site.

Reference to other sections — See Sections 8 and 13 for more information.

SECTION 7: Handling and storage

Precautions for safe handling — Follow recommendations for handling pharmaceutical agents (i.e, use of engineering controls and/or other personal protective equipment if needed). Avoid contact with eyes, skin, and other mucous membranes. Wash thoroughly after handling. Do not breathe vapor/mist/spray.

Conditions for safe storage, including any incompatibilities

Storage conditions — The product is safe when stored tightly closed, away from incompatible materials and extreme temperatures. For ensuring product integrity, store refrigerated (2°C to 8°C; 36°F to 46°F) or at room temperature (15°C to 25°C; 59°F to 77°F), do not freeze.

Specific end use(s) — Pharmaceuticals.

SECTION 8: Exposure controls/personal protection

Control parameters/Occupational Exposure Limits

Name	Issuer	Value
Ethylenediaminetetraacetic acid disodium salt dihydrate	No data available	No data available
Glycerol	BE - Limit value [mg/m³]	10 mg/m³
	CH - KZGW (mg/m³)	100 mg/m³
	CH - VME [mg/m³]	50 mg/m³
	CZ - Exposure limits (NPK-P) (mg/m³)	15 mg/m³
	CZ - Exposure limits (NPK-P) (ppm)	3.66 ppm
	CZ - Exposure limits (PEL) (mg/m³)	10 mg/m³
	CZ - Exposure limits (PEL) (ppm)	2.44 ppm
	ES - VLA-ED (mg/m³)	10 mg/m³
	FI - HTP-arvo (8h) (mg/m³)	20 mg/m³
	FR - VME [mg/m³]	10 mg/m³
	IE - OEL (8 hours ref) (mg/m³)	10 mg/m³
	PL - NDS (mg/m³)	10 mg/m³
	SK - NPHV (priemerná) (mg/m³)	10 mg/m³
	GB - WEL TWA (mg/m³)	10 mg/m³
	ACGIH TWA (mg/m³)	10 mg/m³
	OSHA PEL (TWA) (mg/m³)	15 mg/m³ (total)
	SI - OEL STEL (mg/m³)	400 mg/m³
Loteprednol etabonate	No data available	No data available

Appropriate engineering controls — Control exposures to below the OEL (for the active ingredient(s) if available). Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at aerosol/mist-generating points. Use engineered local exhaust ventilation (LEV) and/or enclosure for procedures where aerosolization may occur such as opened transfers, pumping, and spraying. Solutions can be handled outside a containment system or without LEV during procedures with no potential for aerosolization. All containers for solutions and slurries must be covered while being transferred.

Respiratory protection — Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. At a minimum, a tight-fitting full-face respirator with HEPA filters is required when performing aerosol-generating operations. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required for spill cleanup.

Hand protection — Wear nitrile or other impervious gloves if skin contact is possible. When the material is diluted in an organic solvent, wear gloves that provide protection against the solvent.

Eye protection	Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Skin and body protection	Wear disposable coveralls appropriate to the task, booties, and safety glasses with side shields. Ensure gloves are protective against solvents in use. Protective garments (coveralls, disposable coveralls, lab coats) are not to be worn in common areas (e.g., cafeterias) or out-of-doors. Employees must be trained in proper gowning and degowning practices
Other protective measures	Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).
Environmental exposure controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.

SECTION 9: Physical and chemical properties

Physical state	Liquid
Appearance	Aqueous suspension.
Formula	Not applicable (mixture)
Molecular mass	Not applicable
Color	White.
Odor	Odorless.
pH	No data available
Melting point	No data available
Freezing point	No data available
Boiling point	No data available
Flash point	No data available
Relative evaporation rate (butyl acetate=1)	No data available
Flammability (solid, gas)	Not applicable.
Vapor pressure	No data available
Relative vapor density at 20 °C	No data available
Relative density	No data available
Solubility	In water, material is partially soluble.
Log Kow	No data available
Auto-ignition temperature	No data available
Decomposition temperature	No data available
Viscosity, kinematic	No data available
Viscosity, dynamic	No data available
Explosion limits	No data available
Explosive properties	As an aqueous suspension, not likely to explode.
Oxidizing properties	No data available

SECTION 10: Stability and reactivity

Reactivity	The product is non-reactive under normal conditions of use, storage and transport.
Chemical stability	Stable under normal conditions.
Possibility of hazardous reactions	No dangerous reactions known under normal conditions of use.
Conditions to avoid	(See section 7: Handling and Storage).
Incompatible materials	No data available
Hazardous decomposition products	Under normal conditions of storage and use, hazardous decomposition products should not be produced.

SECTION 11: Toxicological information

Note	No data on product formulation. The following information is for loteprednol etabonate and other ingredients, where applicable.
Likely routes of exposure	May be absorbed by inhalation, skin contact and ingestion.

Toxicological information

Acute toxicity

Component	Type	Dose

Ethylenediaminetetraacetic acid disodium salt dihydrate	LD50 oral rat	> 2000 mg/kg
Glycerol	LD50 oral rat	12600 mg/kg
	LD50 dermal rabbit	> 10000 mg/kg
Loteprednol etabonate	LD50 oral rat	> 4000 mg/kg
	LD50 oral mouse	> 4000 mg/kg

Serious eye damage/irritation	No data available
Skin corrosion/irritation	No data available
Sensitization	No data available
STOT-single exposure	No data available
STOT-repeated exposure	Systemic exposure to corticosteroids can cause immune suppression. Inhaled edetate disodium caused lung damage in rats.
Reproductive toxicity	For loteprednol etobonate, no fertility impairment was observed in male or female rats treated orally with doses up to 50 or 25 mg/kg/day.
Developmental toxicity	Embryotoxicity and teratogenicity was observed following oral administration of loteprednol etabonate to rats and rabbits during organogenesis at maternally toxic doses of 50 and 3 mg/kg/day, respectively. Malformations included cleft palate, umbilical hernia, and aortic arch abnormalities in rats, and meningocele (a form of spina bifida) and carotid artery abnormalities in rabbits. The oral NOAEL in both species for developmental and maternal toxicity was 0.5 mg/kg/day. In a peri-/post-natal rat study with loteprednol etabonate, low birth weight was noted at oral doses of 5 mg/kg/ day, while embryotoxicity (e.g., developmental retardation and poor survival) was evident at 50 mg/kg/day (the NOAEL was 0.5 mg/kg/day). Developmental effects were considered to be independent of maternal toxicity which occurred in the same dose range
Genotoxicity	Loteprednol etabonate was not not genotoxic in the Ames bacterial mutagenesis assay, an in vitro mouse lymphoma cell assay, an in vitro chromosomal aberration test using cultured human lymphocytes, and an in vivo mouse micronucleus test.
Carcinogenicity	No data available. None of the components of the product mixture at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen.
Aspiration hazard	No data available
Experience with humans	See "Section 2 - Other Hazards".

SECTION 12: Ecological information

Toxicity

Component	Type	Concentration
Ethylenediaminetetraacetic acid disodium salt dihydrate	EC50 crustacea	140 mg/l 48 h
Glycerol	No data available	No data available
Loteprednol etabonate	No data available	No data available

Persistence and degradability	No data available
Bioaccumulative potential	No data available
Mobility in soil	No data available
Results of PBT assessment	No data available
Other adverse effects	No data available
Note	The environmental characteristics of this mixture have not been fully investigated. Releases to the environment should be avoided.

SECTION 13: Disposal considerations

Waste treatment methods	Used product should be disposed of according to local, state, and federal regulations. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g, appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g, appropriately permitted municipal or on-site wastewater treatment facility.

SECTION 14: Transport information

Transport	Based on the available data, this mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN number	None assigned.
UN proper shipping name	None assigned.
Transport hazard class(es) (DOT)	None assigned.

Packing group	None assigned.
Marine pollutant	Based on the available data, this mixture is not regulated as an environmental hazard or a marine pollutant.
Special transport precautions	Avoid release to the environment.
Transport in bulk according to Annex II of Marpol and the IBC Code	Not applicable

SECTION 15: Regulatory information

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
Chemical safety assessment	No chemical safety assessment has been carried out
TSCA	Drugs are exempt from TSCA.
SARA Section 313 - Emission Reporting	This substance or mixture is not known to contain a toxic chemical or chemicals in excess of the applicable de minimis concentration as specified in 40 CFR §372.38(a) subject to the reporting requirements of section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40 CFR Part 372.
California Proposition 65	California Proposition 65 - This product does not contain any substances known to the state of California to cause cancer, developmental and/or reproductive harm
Additional information	No additional information available

SECTION 16: Other information

Full text of H phrases and GHS classification	Acute Tox. 4 (Inhalation) - Acute toxicity (inhalation) Category 4. Repr. 1B - Reproductive toxicity Category 1B. STOT RE 1 - Specific target organ toxicity (repeated exposure) Category 1. STOT RE 2 - Specific target organ toxicity (repeated exposure) Category 2. H332 - Harmful if inhaled. H360D - May damage the unborn child.. H372 - Causes damage to organs through prolonged or repeated exposure. H373 - May cause damage to organs through prolonged or repeated exposure.
Data sources	Information from published literature and internal company data.
Abbreviations and acronyms	ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PBT - Persistent, Bioaccumulative, and Toxic; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
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