

MERCK HUMAN HEALTH DIVISION, U.S. HUMAN HEALTH
 A Division of Merck and Co., Inc.; P.O. Box 4, West Point, PA 19486

***** MATERIAL SAFETY DATA SHEET *****

LABEL NAME: ELSPAR

MHHD-025

Emergency Telephone - 1-800-NSC-MERCK (1-800-672-6372)
 Number Merck National Service Center (NSC)

SECTION 1 - MATERIAL IDENTIFICATION

Chemical Name----- Complex enzyme
 Synonyms (Common)----- L-Asparaginase (active ingredient)
 (Chemical)----- None known
 Material Statistical Number--- Not available
 Material Product Number----- 4612
 Chemical Classification----- Complex enzyme
 Intended Use----- Elspar is indicated in the therapy of
 patients with acute lymphocytic leukemia.
 NDC Number----- 0006-4612-00

SECTION 2 - PRINCIPAL HAZARDOUS COMPONENT(S)

<u>Component</u>	<u>Molecular Formula</u>	<u>Molecular Weight</u>	<u>CAS Number</u>	<u>Percent (%)</u>
L-Asparaginase*	Not avail.	133,000 plus/ minus 5,000	9015-68-3	6.0
Mannitol	C ₆ H ₁₄ O ₆	182.17	69-65-8	94.0

*Each vial contains 10,000 IU of Asparaginase and 80 mg of mannitol.
 IU is defined, according to International Union of Biochemistry, as
 225 IU/mg protein.

SECTION 3 - PHYSICAL PROPERTY DATA

Appearance----- White lyophilized plug or powder. When
 reconstituted, Elspar should be a clear,
 colorless solution. If the solution
 becomes cloudy, discard.
 Odor/Threshold Level (ppm)---- Odorless. Caution: do not test for odor
 to avoid breathing powder.
 Boiling Point (°C/°F)----- Not applicable

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Freezing Point (°C/°F)----- Not applicable
Melting Point----- Not available
pH ----- Not available
Solubility in water----- Freely soluble in water. Practically
insoluble in methanol, acetone,
chloroform.
Specific Gravity (Water = 1)-- Not applicable
Vapor Density (Air=1)----- Not applicable
Vapor Pressure (mm Hg @ °C/°F)-- Not applicable
Volatile Components (% w/w)--- None

SECTION 4 - FIRE AND EXPLOSION HAZARD DATA

Flash Point (°C/°F)----- Not applicable
Flash Point Test Method----- Not applicable
Autoignition Temperature (°C/°F)-- Not available
Flammable Limits -LEL (%)----- Not applicable
 -UEL (%)----- Not applicable
Combustibility Information---- Not available
Dust Explosivity Information-- Not available
Shock Sensitivity Information- Not available
Extinguishing Media----- Use water spray or all purpose dry
 chemical to fight fires
Special Fire Fighting Procedures-- Fire fighters should wear self-
 contained breathing apparatus and full
 protective clothing if compound is
 released during fire or is burning.

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Fire/Explosion Hazards----- None known.

Hazardous Decomposition Products Resulting From A Fire-- None known.

SECTION 5 - REACTIVITY DATA

Stability (Normal Storage Conditions)-- Unstable and does not contain a preservative; therefore open or unused material is at risk of bacterial contamination. Asparaginase is not a stable compound at temperatures above 8°C (46°F).

Storage Conditions to Avoid--- Temperatures above 8°C (46°F).

Thermal Stability/Instability Information-- Not available

Incompatibilities (Chemical Entities)-- None

Incompatibilities (Materials of Construction)-None

Hazardous Polymerizations----- None

SECTION 6 - EMERGENCY AND FIRST AID PROCEDURES

Eye Contact----- In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention immediately.

Skin Contact----- Wash area immediately with soap and water. Get medical attention if symptoms occur.

Inhalation----- Remove from exposure and get medical attention if symptoms appear.

Ingestion----- Do not induce vomiting. May dilute with water, then get medical attention.

Notes to Physician----- None

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SECTION 7 - HEALTH HAZARD DATA

Component	OSHA Permissible Exposure Limit (PEL)	ACGIH Threshold Limit Value (TLV)	Merck Exposure Control Limit (ECL)
L-Asparaginase	Not established	Not established	10 mcg/m ³ (8hr-TWA)
Mannitol	Not established	Not established	Not established

Carcinogen Designation----- Not listed as a carcinogen by IARC, NTP or OSHA.

Effects of Acute Exposure

Eye Contact----- No data available on the formulated product. L-Asparaginase is slightly irritating to the eyes.

Skin Contact----- No data available on the formulated product. L-Asparaginase may be irritating to the skin.

Inhalation----- No data available on the formulated product. L-Asparaginase may be irritating to the upper respiratory tract. Workers exposed occupationally to pure L-Asparaginase have experienced chills, fever, slight respiratory distress and diarrhea. Effects are thought to be immunologically mediated and are reversible within 24-48 hours. In clinical use, adverse reactions following intravenous administration include skin rashes, joint pain, respiratory distress and anaphylaxis. Rare serious reactions include hemorrhage due to low fibrinogen, pancreatitis, liver dysfunction, bone marrow suppression and CNS effects.

Ingestion----- Not considered a potential route of systemic exposure.

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Effects of Chronic Exposure-- L-Asparaginase is an antineoplastic agent. It removes an exogenous source of L-asparagine for malignant cells that depend on this essential amino acid for survival. The compound has been shown to cause birth defects in laboratory animals when given intravenously at doses of 50-100 IU/kg. In repeat-dose intravenous studies, L-asparaginase produced changes in serum proteins and G.I. distress in dogs and liver changes in monkeys (LOAEL = 100 IU/kg/day). A small increase in pulmonary adenomas was reported in newborn Swiss mice injected with 2500 IU/kg/day for 4 days.

Medical Conditions Aggravated by Exposure-- Hypersensitivity to L-Asparaginase, pancreatitis or liver impairment.

Quantitative Toxicity Data

L-Asparaginase

<u>Test</u>	<u>Species</u>	<u>Route</u>	<u>Result</u>
LD50	Mouse	Oral	10,000 IU/kg (44 mg/kg)
LD50	Rat	Oral	10,000 IU/kg (44 mg/kg)
LD50	Mouse	I.V.	500,000 IU/kg (222 mg/kg)
LD50	Rabbit	I.V.	22,000 IU/kg (98 mg/kg)

SECTION 8 - SPILL/LEAK/DISPOSAL PROCEDURE

Steps to be taken in case materials released:

Immediately contact emergency response personnel. Keep unnecessary persons away. If emergency response personnel are unavailable, HEPA vacuum dry material or shovel wetted spilled material and place in an appropriate container for disposal. Use suitable protective equipment (Section 9). Follow all fire prevention procedures (Section 4).

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For additional assistance, CHEMTREC provides a toll-free Hotline for chemical emergencies regarding spills, leaks, exposure or accidents: 1-800-424-9300.

Environmental Data----- Not available

Waste Disposal Information--- Dispose of residual product and spill residues, including contaminated soils following all federal, state and local regulations for the handling of hazardous waste.

SECTION 9 - SPECIAL PROTECTION INFORMATION

Respiratory----- Not required for handling vials. Use of a BSC (Biological Safety Cabinet) is recommended for reconstitution and preparation of doses. Workers who are not protected by the containment environment of a BSC should use respiratory protection such as a HEPA-filter powered air purifying respirator.

Hands/Arms----- Gloves made of rubber or other impervious material should be worn when reconstituting Elspar.

Eye/Face----- Reconstitution should be carried out in a biological Safety Cabinet (BSC).

Additional Protective Equipment-- Disposable work uniform or outer garment, preferably made of tyvek, is recommended.

Ventilation----- Ventilation is not necessary if material is handled in a vial. In the laboratory, material should be handled in a chemical fume hood or ventilated enclosure whenever possible.

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SECTION 10 - SPECIAL PRECAUTIONS

Special Precautions to be taken when:

Handling----- Elspar should be reconstituted in a Biological Safety Cabinet. This drug may be a contact irritant and both powder and solution must be handled and administered with care. Inhalation of dust or vapors and contact with skin or mucous membranes, especially those of the eyes, must be avoided.

Storing----- Asparaginase is an enzymatic protein. It should be stored below 8°C (46°F); unused reconstituted solution should be stored at 2-8°C (36-46°F) and discarded after 8 hours or if solution becomes cloudy.

Other----- It is preferable that material be handled in a dissolved state. Confine any operation so that spilled or released material does not affect unprotected workers. Emphasize control by containment.

SECTION 11 - BASIC TRANSPORTATION DESCRIPTION

U.S. DOT----- Not regulated

ICAO/IATA----- Not regulated

IMO----- Not regulated

Hazardous Substance-Reportable Quantity (RQ)--- Not applicable

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SECTION 12 - MSDS PREPARATION

Date Prepared----- February 1991
Last Revision Date----- December 1999
Section 11: Effects of Chronic Exposure
MSDS Coordinator----- 1-908-423-7926

SECTION 13 - MERCK DISCLAIMER

While this information and recommendations set forth are believed to be accurate as of the date hereof, MERCK & CO., INC. makes no warranty with respect hereto and disclaims all liability from reliance thereon.

