



Bristol-Myers Squibb Company

MATERIAL SAFETY DATA SHEET

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

BRISTOL-MYERS SQUIBB
 WORLDWIDE MEDICINES GROUP
 P.O. BOX 191, NEW BRUNSWICK, NJ 08903
 (732)519-3683

August 22, 2000

Product Identification Lysodren Tablets, 500 mg

Chemical Name: 1-Chloro-2-(2,2-dichloro-1-(4-chlorophenyl)ethyl)benzene

Synonym: Mitotane, o,p'-DDD, MJ7236

How Supplied: White, round, biconvex, tablets; bisected on one side and impressed with "BL" over "11" on the other

Product Use: Lysodren tablets contain mitotane, and are used to treat certain neoplastic diseases.

Chemical Family: Chlorobenzene derivative

Molecular Formula: C₁₄H₁₀Cl₄

CAS NUMBER: 53-19-0

EMERGENCY CONTACTS

TRANSPORTATION: CHEMTREC (800)424-9300 For all international transportation emergencies call CHEMTREC at (703)527-3887, collect call accepted.

EMERGENCY OVERVIEW: Lysodren tablets contain mitotane, a potent drug that can cause adrenal suppression and adrenal cytotoxicity. Suspected animal carcinogen.

2. COMPOSITION/ INFORMATION ON INGREDIENTS

COMPONENTS	HAZARDOUS (Y/N)	CONCENTRATION (wt%)	CAS NUMBER	EXPOSURE GUIDELINE
Mitotane	Y	62	53-19-0	none
Microcrystalline Cellulose	N	> 1	9004-36-6	none
Corn Starch	N	> 1	9005-25-8	none
Polyethylene Glycol 3350	N	> 1	25322-68-3	none
Silicon Dioxide, Colloidal	N	<1	60676-86-0	none

3. HEALTH HAZARDS IDENTIFICATION

EFFECTS OF OVEREXPOSURE

Routes of Entry:

1. Inhalation: Because Lysodren is formulated as a tablet, under normal conditions exposure to this material by inhalation is not expected to occur. If tablets are crushed or broken and if material becomes airborne there may be potential for inhalation. The extent of systemic absorption of the material after inhalation is not known.

2. Skin Contact: Because Lysodren is formulated as a tablet, under normal conditions skin contact with this material is not expected



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HEALTH HAZARDS IDENTIFICATION (CONTINUED)

to occur. Exposure may occur via skin contact if tablets are crushed or broken and if gloves and protective clothing are not worn. The extent of systemic absorption of the material after skin contact is not known.

3. Ingestion: Ingestion of large quantities of this material in an occupational setting would not be expected to occur. Ingestion of trace amount of the material might occur if tablets are crushed or broken, if material contacts hands and if hands are not washed prior to eating, drinking, or smoking. Approximately 35-40% of an oral dose of mitotane is absorbed from the gastrointestinal tract.

Acute

Ingestion: Lysodren tablets contain mitotane. Inadvertent ingestion of trace amount is not likely to result in symptoms. Ingestion of therapeutic doses may result in symptoms such as anorexia, nausea, vomiting, diarrhea, lethargy, somnolence, dizziness or vertigo.

Inhalation: There is no information concerning the potential of this material to produce symptoms after inhalation.

Skin Contact:

a. Toxic: There is no information concerning the potential of this material to produce symptoms after skin contact.

b. Irritation: The irritation potential of this material has not been evaluated.

c. Sensitization: This material may cause skin rashes upon contact.

Eye Contact: May cause conjunctivitis.

Chronic: Mitotane is an antineoplastic drug used to treat inoperable adrenal cortical cancer. Repeated ingestion of therapeutic doses produces adrenal suppression in most patients receiving mitotane. Approximately 80% of individuals receiving this drug at therapeutic doses experience adverse gastrointestinal effects, such as anorexia, nausea, vomiting, or diarrhea. Approximately 40% of the patients receiving this drug at therapeutic doses experience adverse central nervous system (CNS) effects, including lethargy, somnolence, dizziness, and vertigo. Prolonged administration of high doses of mitotane may produce brain damage and functional impairment. Approximately 15% of patients receiving mitotane experience skin toxicity in the form of transient maculopapular rash. Frequently, patients treated with mitotane exhibit a decrease in serum uric acid concentration and elevations in serum cholesterol. Gynecomastia has occurred in men receiving mitotane.

Exposure Guideline Summary: Exposure guideline not established.

Carcinogen Lists

IARC: No

NTP: No

OSHA: No

Target Organs: Target organs identified in humans after oral treatment with therapeutic doses include the adrenal cortex and central nervous system. Medical Conditions Aggravated by Exposure: Therapeutic doses of this material may aggravate shock or severe trauma by adrenal suppression.

Medical Surveillance Recommendation: A pre-placement physical examination and history (noting any risk factors) for employees with potential exposure to Lysodren is recommended. A complete blood count, including differential, and serum electrolytes may be taken to provide a baseline. Periodic follow-up



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HEALTH HAZARDS IDENTIFICATION (CONTINUED)

examinations should be given in accordance with institutional policy, overseen by a physician thoroughly knowledgeable about both the toxicity of the substance and the extent of work place exposure. A permanent registry of all staff who routinely prepare or administer Lysodren should be considered.

Staff members who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring workers' health.

FOR MORE INFORMATION REFER TO SECTION 11: TOXICOLOGICAL INFORMATION

4. FIRST AID MEASURES

Ingestion: Seek medical attention immediately. Vomiting may be induced if person is conscious and not experiencing convulsions. Never give anything by mouth to an unconscious person.

Inhalation: Remove exposed person to fresh air. If person is not breathing give artificial respiration. If breathing is difficult administer oxygen. Get medical attention.

Skin Contact: Immediately flush with large amounts of water. Use soap if available. Remove contaminated clothing, including shoes after flushing has begun. Get medical attention.

Eye Contact: Hold eyelids apart and flush with running water for at least 15 minutes. Get medical attention.

Note to physicians: Product contains a drug which can suppress adrenal function and is used to treat neoplasms of the adrenal cortex.

5. FIRE FIGHTING MEASURES

Flash point: Not Determined.

Autoignition Temperature: Not Determined.

Flammability Limits

LEL: Not Determined.

UEL: Not Determined.

Combustibility of Dusts: Fine powders are considered to be combustible. Provide appropriate bonding and grounding protection to control static charges. Powder handling equipment such as dust collectors, dryers and mills may require additional protective measures (i.e. explosion venting).

Extinguishing Media: In case of fire use water, carbon dioxide, foam or dry chemical.

Firefighting Instructions: Firefighters should wear self contained breathing apparatus, flame and chemical resistant clothing, boots and gloves. Evacuate personnel to upwind direction, remove unneeded material and cool container(s) with water from a maximum distance.

Hazardous Combustion Products: Oxides of carbon, HCl

Unusual Hazards: None known.



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6. ACCIDENTAL RELEASE MEASURES

Spill/Clean-up: Scoop up tablets and place in suitable container. If tablets are crushed, clean powder with damp cloth or towels. Treat products and contaminated materials as hazardous materials. Incineration is recommended.

7. HANDLING AND STORAGE

Handling Precautions: Avoid inhalation, skin or eye contact with crushed or broken tablets.

Container Requirements: Tight, light-resistant containers.

Storage Conditions: Store at room temperature; avoid excessive heat.

8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

Ventilation Requirements: Local exhaust recommended when handling quantities of broken or crushed tablets.

Respiratory Protection: Normally not required. Approved HEPA respirators recommended when handling large quantities of broken or crushed tablets in the absence of suitable exhaust ventilation.

Eye Protection: Wear safety glasses (ANSI Z87.1) when handling crushed or broken tablets.

Protective Gloves: Wear latex surgical gloves when handling quantities of broken or crushed tablets.

Special Clothing: Wear overalls when the potential for severe dusty conditions exists.

Hygiene: Wash hands after handling compound and before eating, smoking, using lavatory, and at end of day.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance/Physical State/Color: White, round, biconvex, tablets; bisected on one side and impressed with "BL" over "L1" on the other.

Boiling point: Not applicable.

Evaporation rate (degree C): Not applicable.

Flash point: Not applicable.

Freezing point: Not applicable.

Melting point: 76-78 degree C.

Octanol/water partition coefficient: Not determined.

Odor (threshold): Aromatic odor.

pH: Not applicable.

Solubility in water (degree C): Mitotane is practically insoluble in water. (Mitotane is soluble in ethanol and iso-octane.)



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PHYSICAL AND CHEMICAL PROPERTIES (CONTINUED)

Specific gravity: (degree C): Not determined.

Vapor density (degree C): Not determined.

Vapor pressure: Not determined.

Viscosity (degree C): Not determined.

Hydrolysis rate: Not determined.

10. STABILITY AND REACTIVITY

Stability: Stable to expiration when stored at room temperature in original container.

Incompatibilities: None known.

Conditions of Reactivity: Not determined.

Hazardous Decomposition Products: Oxides of carbon, HCl

Hazardous Polymerization: Will not occur.

Explosion data relative to mechanical impact: Not determined.

Explosion data relative to static discharge: Not determined.

11. TOXICOLOGICAL INFORMATION (for mitotane)

RTECS NUMBER (U.S.): KH7880000

ACUTE

LD 50: Not available.

LC 50: Not available.

NOTE: Substantial doses have been tolerated without mortality over a period of several weeks. Compound is not expected to be classified as toxic or highly toxic.

CHRONIC

Carcinogenicity: In studies conducted by NCI in mice and rats, mitotane was found to have weak, slightly positive carcinogenic potential. The carcinogenic potential of mitotane in humans is unknown. However, the mechanism of action of this compound suggests that it probably has less carcinogenic potential than other cytotoxic therapeutic agents.

Mutagenicity: The mutagenic potential of mitotane has not been characterized.

Teratogenicity: Animal teratogenicity studies with mitotane have yielded conflicting and irreproducible results. It is not known whether mitotane can cause fetal harm when administered to pregnant women.

Reproductive Effects: Animal reproduction studies have not been performed with mitotane. It is not known whether mitotane can affect reproduction capacity in humans. It is not known whether mitotane is distributed into milk.



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TOXICOLOGICAL INFORMATION (CONTINUED)

Toxicological synergistic products: Therapeutic exposure to mitotane may result in increased metabolism of drugs such as barbiturates, coumarin anticoagulants, or phenytoin. Additive CNS depression may occur when mitotane is administered concomitantly with other CNS depressants. Spironolactone may block the therapeutic action of mitotane.

12. ECOLOGICAL INFORMATION

Ecotoxicological Information: Not determined.

Chemical Fate Information: Not determined.

13. DISPOSAL CONSIDERATIONS

Disposal: Dispose of in accordance with national, state, local or applicable country regulations. Treat products and contaminated materials as hazardous materials. Incineration at an approved facility is recommended.

14. TRANSPORT INFORMATION

DOMESTIC

Hazard Class (UN NUMBER): Not regulated by D.O.T.

Proper shipping name: Not applicable.

Label requirements: Not applicable.

Placard requirements: Not applicable.

Limited Quantity Exemption: Not applicable.

INTERNATIONAL

Hazard Class (UN NUMBER or PIN NUMBER): Not regulated.

Proper shipping name: Not applicable.

Label requirements: Not applicable.

Placard requirements: Not applicable.

Limited Quantity Exemption: Not applicable.

15. REGULATORY/STATUTORY INFORMATION -- not meant to be all inclusive

U.S. Federal: None noted.

International: None noted.

EC Labeling: None noted.

16. OTHER INFORMATION

8-22-2000. The MSDS dated 1/8/93 was revised to change the emergency telephone numbers.

Therapeutic agents are intended for use under direction of a physician and/or under the conditions of use described on the label. As a general precaution, personnel who handle drug substances should avoid contact (ingestion, inhalation, skin and eye contact) with these substances.

This material safety data sheet is intended for use by personnel who handle this material as part of their job responsibilities. It does not address the therapeutic use of this material. Information concerning the therapeutic use of this drug substance should be obtained from formulated product package inserts and other appropriate references.



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OTHER INFORMATION (CONTINUED)

Federal law prohibits dispensing without prescription. See package insert for recommended medical use.

The information contained in this MSDS is believed to be accurate and represents the best information available at the time of preparation. However, we make no warranty, express or implied, with respect to such information, and we assume no liability from its use.
