

Irofulven

MGI PHARMA, INC.
Material Safety Data Sheet
HMAF for Injection, 10 mg/Vial
(6-Hydroxymethylacylfulvene)

Document #: MSDS-HMAF FP.2
 Effective Date: 03/05/99
 Supersede Date: 04/07/97
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SECTION 1 - IDENTITY

COMMON NAME	6-Hydroxymethylacylfulvene
CAS NUMBER	Not yet assigned
CHEMICAL NAME	6'-Hydroxy, 3'-hydroxymethyl, 2',4',6'-trimethyl, spiro [cyclopropane-1,5'-5H indene] 7' (6'H) one
MOLECULAR WEIGHT	246.31
CLASSIFICATION	ORM-D
CHEMICAL FAMILY	Fulvene, antineoplastic candidate
FORMULA	C ₁₅ H ₁₈ O ₃

SECTION 2 - HAZARDOUS INGREDIENTS

NAME	PERCENT	THRESHOLD LIMIT VALUE (UNITS)
6-hydroxymethylacylfulvene	100%	None established

SECTION 3 - PHYSICAL AND CHEMICAL CHARACTERISTICS

SOLUBILITY IN WATER	approx. 0.7 mg/mL
ACTIVITY IN WATER	Unknown
APPEARANCE	Yellow-gold to Orange film in a 10cc septum-sealed vial
EXTINGUISHER MEDIA	Water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials.
IGNITION TEMPERATURE	n/a
SPECIAL FIRE FIGHTING	As with all fires, evacuate personnel to safe area. Firefighters should use self-contained breathing equipment and protective clothing.
FIRE AND EXPLOSION CHARACTERISTICS	This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with dry material to dissipate the potential buildup of static electricity. When heated to decomposition, material emits toxic fumes. Emits toxic fumes under fire conditions.

Address: MGI PHARMA, INC. Suite 300 E, Opus Center 9900 Bren Road East Minnetonka, MN 55343-9667 Telephone: (612) 935-7335	Contact: Dr. Robin Dawe Director, Product Development
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SECTION 4 - PHYSICAL HAZARDS

STABILITY () Unstable (X) Stable

CONDITIONS TO AVOID Material is stable from a safety point of view.

INCOMPATIBILITY (MATERIALS TO AVOID) Degraded in the presence of bases, oxidizers, moisture, and light. Degradation products should be considered toxic.

HAZARDOUS DECOMPOSITION PRODUCTS When heated to decomposition, material emits toxic fumes. Emits toxic fumes under fire conditions.

HAZARDOUS POLYMERIZATION () May Occur (X) Will Not Occur

SECTION 5 - HEALTH HAZARDS

THRESHOLD LIMIT VALUE None established

SIGNS AND SYMPTOMS OF OVEREXPOSURE The single intravenous dose LD₅₀ in mice is 14.9 mg/kg. In rats, reversible body weight loss, cardiac lesions, and hematopoietic toxicity are observed at single intravenous doses ≥ 3.3 mg/kg. In dogs, postdose emesis is observed at intravenous doses ≥ 0.15 mg/kg. Hematopoietic toxicity in dogs, consisting primarily of neutropenia and thrombocytopenia, is observed at single intravenous doses of ≥ 0.4 mg/kg. These effects are reversible at single intravenous doses of ≤ 1 mg/kg, but not at 2 mg/kg.

Related mushroom toxins, the illudins, have produced transient vomiting, diarrhea, weakness, and sensation of cold following ingestion in humans.

ACUTE CHRONIC REACTIONS TO CONSIDER Eye, skin and/or respiratory tract irritation
 Possible hypersensitization
 Persons developing hypersensitivity (anaphylactic) reactions must receive immediate medical attention.
 Material may be irritating to mucous membranes and respiratory tract. As a general rule, when handling, avoid all contact and inhalation of dust, fumes, mists, and/or vapors associated with the material. Keep container tightly closed and use with adequate ventilation; wash thoroughly after handling. Individuals working with chemicals should consider all chemicals to be potentially hazardous even if their individual hazards may be uncharacterized or unknown.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE None known

CHEMICAL LISTED AS CARCINOGEN OR POTENTIAL CARCINOGEN NATIONAL TOXICOLOGY PROGRAM () Yes (X) No
 I.A.R.C. Monographs () Yes (X) No
 OSHA () Yes (X) No

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Similar to other anticancer agents that alkylate DNA, HMAF has been found to be carcinogenic in rats. Intravenous administration of HMAF to rats on an intermittent basis for 6 months has been shown to induce tumors primarily of the blood and breast. HMAF has also been found to be mutagenic in bacterial reverse mutation assays in both the presence and absence of mammalian biotransformation enzymes and clastogenic in the mouse micronucleus assay at intravenous doses ≥ 5 mg/kg. HMAF did not produce chromosomal aberrations in cultured peripheral human lymphocytes in either the presence or the absence of mammalian biotransformation enzymes.

TERATOGEN

Similar to other anticancer agents that alkylate DNA, HMAF has been shown to produce developmental toxicity in rats and rabbits. In rats, HMAF administration resulted in reduced fetal body weights, increased postimplantation loss and increased incidences of malformations and/or developmental variations. In rabbits, HMAF has produced developmental toxicity, consisting of increased incidences of malformations and skeletal variations.

PERMISSIBLE EXPOSURE

Limit not established

EXPOSURE LIMIT USED

Limit not established

**EMERGENCY AND
 FIRST AID PROCEDURES**

Remove from exposure. Remove contaminated clothing. Person developing serious hypersensitivity reactions must receive immediate medical attention. Upon eye or skin contact, flush affected area with copious quantities of water. Obtain medical attention. If not breathing give artificial respiration. If breathing is difficult give oxygen.

INHALATION

May cause irritation of respiratory tract. Remove to fresh air.

EYES

May cause irritation. Flush with copious quantities of water.

SKIN

May cause irritation. Flush with copious quantities of water.

INGESTION

May cause irritation. Flush out mouth with water. Induce vomiting, if emesis has not already occurred.

SECTION 6 - SPECIAL PROTECTION INFORMATION

RESPIRATORY PROTECTION

NIOSH approved respirators

VENTILATION

Adequate

LOCAL EXHAUST

Recommended

MECHANICAL (GENERAL)

Recommended

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PROTECTIVE GLOVES Rubber/latex, neoprene, or vinyl

EYE PROTECTION Safety goggles

OTHER PROTECTIVE CLOTHING AND EQUIPMENT Appropriate laboratory apparel, protect exposed skin.

SECTION 7 - SPECIAL PRECAUTIONS AND SPILL/LEAK PROCEDURES

PRECAUTIONS TO BE TAKEN IN HANDLING AND STORAGE Store in tight container. This material should be handled and stored per label and other instructions to ensure product integrity.

OTHER PRECAUTIONS Avoid contact with eyes, skin or clothing. Avoid breathing dust or mist. Use with adequate dust control. Wash thoroughly after handling. Wear fresh clothing daily. Wash contaminated clothing before reuse. Do not permit eating, drinking or smoking near material.

STEPS TO BE TAKEN IN CASE MATERIAL IS SPILLED OR RELEASED Wear approved respirator and chemically compatible gloves. Vacuum or sweep up spillage. Avoid dust. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse. Ventilate area and wash spill site with aqueous basic solution (sodium hydroxide, pH 10) containing 10% Alcohol (Ethanol or Isopropanol, if available) then water.

SAFE DISPOSAL METHODS Dispose of waste in accordance with all applicable Federal, State and local laws.

APPROVAL SIGNATURES ON FILE:

QUALITY ASSURANCE	R. JOHNSON
MANUFACTURING	S. DYKSTRA
PRODUCT DEVELOPMENT	R. DAWE
RESEARCH & DEVELOPMENT	S. WATERS

Change History:

MS-97-015 New- MSDS for HMAF Finished Product
 MSDS-97-048 Revise - MSDS HMAF FP, update carcinogen section
 MSDS-98-253 Revise - Included genotoxicity and teratology data

MSDS Verified By/Date: M. Hanson 3/5/99 *M. Hanson* 3/5/99

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