Section1: Chemical Product and Company Identification

Product Name: Metformin Hydrochloride tablets 850 mg film-coated tablets

Synonyms: --

CAS No.: 1115-70-4

Chemical Formula: --

Molecular Weight: --

NFPA Rating:

Health: - ; Flammability: - ; Reactivity: - ; Specific Hazard: -

Contact Information:

Corporate Address :
Laurus Labs Limited,
2nd Floor, Serene Chambers, Road No # 7, Banjara Hills, Hyderabad – 500034
Ph: 040 – 3980 4333

Section 2: Hazards Identification

Classification and Labelling Common to All Jurisdictions

Classification

Acute Toxicity - Oral - Category 4
Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 1

Symbol

Signal Word Danger

Hazard Statements

Harmful if swallowed.
Causes damage to organs (endocrine system, gastrointestinal tract, eyes) through prolonged or repeated exposure.

Precautionary Statements

Do not breathe dust.
Do not eat, drink or smoke when using this product.
Wash thoroughly after handling.

Section 3: Composition/ Information on Ingredients

CAS #	Chemical name	Percent
1115-70-4	Metformin Hydrochloride	93 – 95
9004-65-3	Hydroxypropyl Methylcellulose	< 5

Section 4: First Aid Measures

Eye contact

Rinse immediately with plenty of water for at least 15 minutes. Keep eye wide open while rinsing. Obtain medical attention.

Skin contact

Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water for at least 15 minutes. If skin irritation persists, call a physician.

Inhalation

Move to fresh air. Oxygen or artificial respiration if needed. Get medical attention/advice if you feel unwell.

Ingestion

IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell.

Notes to Physician

Medical conditions aggravated include: kidney disorders, liver disorders, acidosis. This product has been reported to interact with the following medications: Sulfonulurea antidiabetic agents, diuretics, Nifedipine, Cimetidine, ß-adrenergic blocking agents, ACE inhibitors, drugs that cause hyperglycemia, and, alcohol. Refer to Section 11.

Medical Surveillance

The need for a pre-placement physical examination and history for employees with potential exposure to this compound is to be evaluated by a physician that is thoroughly knowledgeable about both the toxicity of this compound and the extent of work place exposure. Baseline testing would include: a blood test for kidney function, a blood test for liver function, blood glucose test. Based on opportunity for exposure and duration of exposure a periodic follow-up examination may be considered. This exam should be overseen by a physician thoroughly knowledgeable about both the toxicity of this compound and the extent of work place exposure. It is recommended that the content be similar to the pre-placement exam. Employees 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 worker's health.

Section 5: Fire and Explosion Data

Flammable Properties

Not available

Extinguishing Media Suitable extinguishing media: Dry chemical, Water spray, Foam

Unsuitable extinguishing media: Do NOT use water jet.

Protection of Firefighters

Specific hazards: Not available

Protective equipment: Use personal protective equipment. In the event of fire, wear self-contained breathing apparatus.

Hazardous Combustion Products: carbon oxides (COx), nitrogen oxides (NOx), and, gaseous hydrogen chloride (HCl).

Further Information: HCl gas can form flammable or explosive mixtures with alcohols or metals. In the event of fire and/or explosion do not breathe fumes.

Other information

Decontaminate protective clothing and equipment before reuse. Heating can release hazardous gases.

Section 6: Accidental Release Measures

Personal precautions

Refer to protective measures listed in sections 7 and 8. Use personal protective equipment. Examples include tightly fitting safety goggles, lab coat and impervious gloves. Wear respiratory protection. Depending on the nature of the spill (quantity and extent of spill) additional protective clothing and equipment such as a self-contained breathing apparatus may be needed.

Environmental precautions

Prevent release to drains and waterways. Prevent release to the environment.

Containment Methods

Wet down any dust to prevent generation of aerosols, if appropriate. Cover with suitable material.

Cleanup Methods

Contain and collect spillage and place in container for disposal according to local regulations (see Section 13). Handle waste materials, including gloves, protective clothing, contaminated spill cleanup material, etc., as appropriate for chemically and pharmacologically similar materials.

Section 7: Handling and Storage

Handling Precautions

Avoid exposure - obtain special instructions before use. Avoid formation of dust and aerosols. Keep away from heat and sources of ignition. When handling broken or crushed tablets or capsules, ensure worker exposure is below the recommended exposure limit. Prevent release to drains and waterways.

Container Requirements

Store in the original primary packaging as provided. Container should be light resistant.

Storage Conditions

Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F).
Dispense in light-resistant containers.

Section 8: Exposure Controls/ Personal Protection

Exposure limit(s)	Company Guideline	ACGIH	Germany OEL	UK MEL
Metformin Hydrochloride	1000 µg/m3	--	--	--
Magnesium Stearate		10 mg/m3 TWA	--	--
Povidone		--	--	--
Hydroxypropyl Methylcellulose		--	--	--
Polyethylene Glycol		--	1,000 mg/m3 TWA 8,000 mg/m3 Peak Average molecular weight 200-600 1,000 mg/m3 MAK average molecular weight 200-600	--

Magnesium Stearate

Occupational Exposure Limits have been established by:

- Belgium - Spain - Ireland - Portugal – Sweden

Polyethylene Glycol

Occupational Exposure Limits have been established by:

- Austria - Switzerland - The Netherlands

Recommended Industrial Hygiene Monitoring Methods

General - The health hazard risk of handling this material is dependent on many factors, including physical form, % API in material being handled, duration and frequency of process task, and effectiveness of controls. If it is necessary to handle this compound outside of engineering controls, an exposure risk assessment should be conducted and procedures

documented by a qualified EHS professional. See Section 4 "Notes to Physician" for information on medical surveillance.

EXPOSURE CONTROLS / PERSONAL PROTECTION FOR MATERIAL AS SUPPLIED

2 -- Material is assigned to Exposure Control Band 2 (range 100 – 1000 µg/m3).

Engineering Controls and Ventilation

When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed. When handling broken or crushed tablets or capsules, ensure worker exposure is below the recommended exposure limit. If significant dust is generated, use process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit.

For Manufacturing Processes (Bulk): When handling quantities up to 15 milligrams, a standard laboratory with general laboratory dilution ventilation (e.g. 6-12 air changes per hour) is appropriate. When handling quantities from 15 milligrams to 1 kilogram, work in a standard laboratory using a fume hood, biological safety cabinet(Class II, all types), or approved vented enclosure. Quantities exceeding 1 kilogram should be handled in a designated laboratory. A laminar flow/powder containment booth is recommended for handling >1 kilograms of active substance. For manufacturing and pilot plant operations, use direct coupling and closed transfer systems for all bulk transfers. Use dust tight valves as appropriate. HEPA filtration of local exhaust ventilation (LEV) is required.

For Clinical Setting Use (Drug Product): When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed. When handling broken or crushed tablets or capsules, ensure worker exposure is below the recommended exposure limit. If significant dust is generated, use process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit.

Respiratory protection

Normally not required for handling a small number of capsules. Use the indicated respiratory protection if the occupational exposure limit is exceeded and/or in case of product release.

Eye protection

Safety glasses with side-shields are recommended (EN 166). Face shields or chemical safety goggles (EN 166) may be required if splash potential exists or if corrosive materials are present. Note: Choice of eye protection may be influenced by the type of respirator which is selected.

Hand protection

Impervious nitrile, rubber and latex gloves are recommended. Please note that employees who are allergic to natural rubber latex should use nitrile gloves.

Skin and body protection

FOR CLINICAL SETTING USE (DRUG PRODUCT): Follow good chemical hygiene practices when using clinical or consumer presentations. FOR MANUFACTURING PROCESSES (BULK): Wear a laboratory coat (EN 340) when handling quantities up to 1 kilogram.

Hygiene

Wash hands and face before breaks and immediately after handling the product.

Environmental exposure controls

Prevent release to drains and waterways.

Section 9: Physical and Chemical Properties

Appearance	
Physical State	: Solid

Color	: white to off-white
Form	: film coated tablets
Odour	: Not available
pH	: Not available
Flash point	: Not available
Melting Point	: Not available

Section 10: Stability and Reactivity Data

Stability

Chemical Stability

Stable under normal conditions.

Conditions to avoid

Not available

Materials to avoid

Not available

Hazardous decomposition products

Hazardous decomposition products formed under fire conditions.: carbon oxides (COx), nitrogen oxides (NOx), and, gaseous hydrogen chloride (HCl).

Hazardous reactions

None known.

Sensitivity to static discharge/Dust exp.

Summary Statements

Although material has not been specifically tested, fine dust suspended in air in sufficient concentration and in the presence of an ignition source may pose a potential explosion hazard. Provide appropriate bonding and grounding protection to control static charge. Powder handling equipment such as dust collectors, dryers, and mills may require additional protective measures (e.g. explosion venting, inerting, etc.).

Section 11: Toxicological Information

Routes of Entry

Ingestion, inhalation, Eye contact, Skin contact

Eye Irritation

Metformin Hydrochloride

Mildly and/or transiently irritating to eyes

Hydroxypropyl Methylcellulose

Dust may cause mechanical irritation.

Skin Irritation

Metformin Hydrochloride

Mildly and/or transiently irritating to skin.

Respiratory Irritation

Not available

Sensitization

Not available

Acute Toxicity Study

Acute Oral

Metformin Hydrochloride

LD50 (rat, males and females): 1,770 mg/kg High exposure effects include: hypoactivity, ataxia, tremors, diarrhoea, mortality.

LD50 (monkey, males): 463 - 694 mg/kg High exposure effects include: vomiting.

hypoactivity, decreased respiratory rate, loss of reflexes, mortality.

Acute toxicity (other routes of administration)

Metformin Hydrochloride

LD50 (rat, subcutaneous): 300 mg/kg
LD50 (mouse, subcutaneous): 225 mg/kg
LD50 (rabbit, subcutaneous): 150 mg/kg
LD50 (guinea pig, subcutaneous): 150 mg/kg

Hydroxypropyl Methylcellulose

LD50 (rat, intraperitoneal): 5,200 mg/kg
LD50 (mouse, intraperitoneal): 5,000 mg/kg

Repeated Dose

Toxicity

Metformin Hydrochloride

7 - 104 weeks dietary (daily) mouse, rat study (males and females): LOAEL = 120 mg/kg; High dose effects include: decreased body weight, decreased food consumption, abnormal posture, uncoordination, labored respiration, changes in red blood cell parameters, changes in clinical chemistry parameters, mortality, increased liver weight, increased organ weights included:, kidney, liver, testes. High dose microscopic effects include: kidney, male reproductive organs, female reproductive organs.

6 - 24 months oral (daily) dog, monkey study (males and females): LOAEL = 50 mg/kg; Low dose effects include (< = 100 mg/kg): abnormal posture, vomiting, salivation, diarrhoea, labored respiration, convulsions, uncoordination, tremors, loss of reflexes, hair loss, changes in red blood cell parameters, changes in clinical chemistry parameters, increased liver enzymes, mortality. Low dose microscopic effects include: brain, heart, kidney, liver, gastrointestinal tract. High dose microscopic effects include: skeletal muscles.

Genetic Toxicity

Metformin Hydrochloride

In vitro

Ames reverse-mutation assay -- negative
Chromosome aberrations assay -- negative
-- Weakly positive only at high doses

In vivo

Mutagenicity (micronucleus test) (mouse) -- negative

Mutagenicity Assessment

The weight of evidence demonstrates that this material is not genotoxic. Not classified as mutagen according to GHS criteria.

Carcinogenicity

Metformin Hydrochloride

104 Weeks rat study : Tumor NOAEL = 900 mg/kg (males and females). No treatmentrelated tumors were observed.

91 Weeks mouse study : Tumor NOAEL = 1,500 mg/kg (males and females). No treatment-related tumors were observed.

Carcinogenicity Assessment

This material did not show carcinogenic potential in animal studies.

Carcinogenicity	ACGIH	IARC	NTP
Metformin Hydrochloride	--	--	--
Hydroxypropyl Methylcellulose	--	--	--

Reproductive Toxicity
Metformin Hydrochloride
oral Study of Fertility and Early Embryonic Development (rat)
(males and females) NOAEL = 600 mg/kg. No effects were found on mating or fertility.
Developmental Toxicity
Metformin Hydrochloride
Study of Embryo-Fetal Development (rat)
NOAEL = 600 mg/kg No effects were observed in the fetus/embryo. No adverse maternal effects were observed.
oral Study of Embryo-Fetal Development (rabbit)
(parent, females) LOAEL = 50 mg/kg
(embryo/fetus) NOAEL = 140 mg/kg
Maternal effects include: decreased body weight, decreased food consumption, fecal changes, hypoactivity, convulsions, mortality. No effects were observed in the fetus/embryo.
oral Study of Pre- and Postnatal Development (rat)
(parent, females) NOAEL = 600 mg/kg
(F1 offspring) NOAEL = 600 mg/kg
No effects were observed in the offspring.
Developmental Toxicity Assessment
Did not show teratogenic effects in animal experiments. This material has been shown to cross the placenta. The potential for this compound to cause hypoglycemia in pregnant animals has not been evaluated. Maternal hypoglycemia in test animals has been found to cause malformations and/or embryo-fetal mortality. This compound and/or its metabolites may be excreted into the milk.
Human experience Experiences with Human Exposure
Metformin Hydrochloride
General effects therapeutic use low exposure - acute effects include: gastrointestinal disturbance, nausea, vomiting, flatulence, stool changes, headache, weakness, hypoglycemia, taste disturbance, muscle pain, fatigue, chills, skin flushing, sweating, breathing difficulties, dizziness, lightheadedness, palpitation, chest pain, rash, nail changes. severe exposure – acute effects include: acidosis, hypoglycemia.
Target Organs
Metformin Hydrochloride
endocrine system, gastrointestinal tract
Symptoms
Metformin Hydrochloride
See "Human Experience".
Pharmacokinetics/Toxicokinetics
Metformin Hydrochloride
Absorption: Not available
Distribution: Not available
Metabolism: Not available
Elimination: Half-life = 17 Hour(s) (Human).
Other Toxicity Information
Not available

Section 12: Ecological Information

Ecotoxicity effects

Acute Toxicity to Fish
Metformin Hydrochloride
LC50 (Bluegill sunfish, 96 H): > 982 mg/l.
Acute Toxicity to Aquatic Invertebrates
Metformin Hydrochloride
NOEC (Daphnia magna (Water flea), 48 H): 78 mg/l.
EC50 (Daphnia magna (Water flea), 48 H): 130 mg/l.
Toxicity to aquatic plants
Metformin Hydrochloride
EC50 (Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum), 72 H): > 100 mg/l
Toxicity to microorganisms
Metformin Hydrochloride
Minimum inhibitory concentration (MIC) (Other): 100 mg/l
Chronic toxicity to fish
Metformin Hydrochloride
LOEC (Pimephales promelas (fathead minnow)): > 10 mg/l
NOEC: 10 mg/l
Chronic toxicity to aquatic invertabrates
Metformin Hydrochloride
EC50 (Daphnia magna (Water flea), 21 D): 97 mg/l
EC50 (Daphnia magna (Water flea), 21 D): 103 mg/l (reproduction rate)
Mobility Not available
Persistence and degradability
Biodegradation
Metformin Hydrochloride
Ultimate aerobic biodegradation (28 D): 0.6 %; Not readily biodegradable.
Stability in water
Metformin Hydrochloride
Hydrolysis (50 °C, pH 5): Degree of hydrolysis - 5 D (0 %)
Hydrolysis (50 °C, pH 7): Degree of hydrolysis - 5 D (0 %)
Hydrolysis (50 °C, pH 9): Degree of hydrolysis - 5 D (0 %)
Metformin Hydrochloride
Koc (Activated Sludge) : 15.9
PBT and vPvB assessment Not available

Section 13: Disposal Considerations

Advice On Disposal And Packaging
Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements. This information presented only applies to the material as supplied.
Other information
Disposal by incineration is recommended.

Section 14: Transport Information

UN number
ADR/RID: - IMDG: - IATA: -
UN proper shipping name
ADR/RID: Not dangerous goods

IMDG: Not dangerous goods
IATA: Not dangerous goods

Transport hazard class(es)

ADR/RID: -	IMDG: -	IATA: -

Packaging group

ADR/RID: -	IMDG: -	IATA: -

Environmental hazards

ADR/RID: no	IMDG Marine pollutant: no	IATA: no

Special precautions for user
No data available

Section 15: Other Regulatory Information

United States of America
313 Toxic Release Inventory
No components listed on the SARA 313 inventory.
TSCA Inventory
Not listed. Food, drug and cosmetic products are exempt from TSCA.
EU Directive 1999/45/EC
BULK MATERIAL
Symbol(s) T: Toxic
R-phrase(s) R22: Harmful if swallowed.
R48/25: Toxic: danger of serious damage to health by prolonged exposure if swallowed.
S-phrase(s) S22: Do not breathe dust.
S36/37/39: Wear suitable protective clothing, gloves and eye/face protection.
S45: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible).
S60: This material and its container must be disposed of as hazardous waste.
DRUG PRODUCT
Classification Medicinal products are exempt from classification and labeling requirements under EU Preparations Directive 1999/45/EC.
Regulatory Authorizations and Restrictions:
Not available

Section 16: Other Information

Disclaimer:
The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product.

Revision Log:

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