Safety Data Sheet
METFORMIN HYDROCHLORIDE TABLETS

Strength: 500/850/1000mg. **Pack Size:** 90/100/500/1000 Tablets per bottle **Revision No.:** 03

EMERGENCY OVERVIEW

Each Metformin Hydrochloride Tablet intended for oral administration contains Metformin and excipients generally considered to be non- toxic and non-hazardous in small quantities and under conditions of normal occupational exposure.

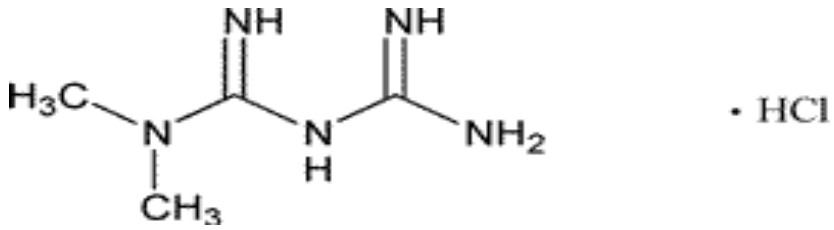
Section 1. Identification

Identification of the product

Product name: Metformin Hydrochloride Tablet

Formula: $C_4H_{11}N_5.HCl$

Chemical Name: N, N-dimethylimidodicarbonimidic diamide hydrochloride



Manufacturer / supplier identification

Company: **Cadila Healthcare Ltd. Ahmedabad, India**

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Recommended use / Therapeutic Category Anti-hyperglycemic

Restriction on Use / Contraindications: Metformin hydrochloride Tablets is contraindicated in patients with:

1. Renal disease or renal dysfunction,
2. Congestive heart failure
3. Known hypersensitivity to metformin hydrochloride
4. Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Diabetic ketoacidosis should be treated with insulin.

5. Should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials.
6. Lactic acidosis is a rare, but serious, metabolic complication that can occur due to metformin accumulation during treatment with metformin; when it occurs, it is fatal in approximately 50% of cases. Metformin must be discontinued in such cases.

Section 2. Hazard(s) Information

Dose and Administration

There is no fixed dosage regimen for the management of hyperglycemia in patients with type 2 diabetes with Metformin hydrochloride Tablets. Dosage of metformin hydrochloride tablets must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended dailydoses. The maximum recommended daily dose of metformin hydrochloride tablets is 2550 mg in adults and 2000 mg in pediatric patients (10-16 years of age. Metformin hydrochloride tablets should be given in divided doses with meals. Metformin hydrochloride tablets should be started at a low dose, with gradual dose escalation, to reduce gastrointestinal side effects and to permit identification of the minimum dose required for adequate glycemic control of the patient. During treatment initiation and dose, fasting plasma glucose should be used to determine the therapeutic response to metformin hydrochloride tablets and identify the minimum effective dose for the patient.

Adverse Effects

In Adults

In a U.S. double-blind clinical study of metformin hydrochloride tablets in patients with type 2 diabetes, a total of 141 patients received metformin
hydrochloride tablets therapy (up to 2550 mg per day) and 145 patients received placebo. Adverse reactions reported in greater than 5% of the metformin hydrochloride tablets patients, and those were more common in metformin hydrochloride tablets- than placebo-treated patients, are Diarrhea, Nausea/Vomiting, Flatulence, Asthenia, Indigestion, Abdominal Discomfort, Headache.

Pediatric Patients

In clinical trials with metformin hydrochloride tablets in pediatric patients with type 2 diabetes, the profile of adverse reactions was similar to that observed in adults.

Over Dose Effect

Overdose of metformin hydrochloride has occurred, including Ingestion of amounts greater than 50 grams. Hypoglycemia was reported in approximately 10% of cases, but no causal association with metformin hydrochloride has been established. Lactic acidosis has been reported in approximately 32% of metformin overdose cases.

Medical Conditions

General

The risk of metformin accumulation and lactic acidosis increases with the degree of impairment of renal function. Thus, patients with serum creatinine levels above the upper limit of normal for their age should not receive metformin.

Hypoxic states–Cardiovascular collapse (shock) from whatever cause, acute congestive heart failure, acute myocardial infarction and other conditions characterized by hypoxemia have been associated with lactic acidosis and may also cause prerenal azotemia. When such events occur in patients on metformin therapy, the drug should be promptly discontinued.

Alcohol intake–Alcohol is known to potentiate the effect of metformin on lactate metabolism. Patients, therefore, should be warned against excessive alcohol intake, acute or chronic, while receiving metformin.

Contraindications

Metformin hydrochloride Tablets is contraindicated in patients with:

1. Renal disease or renal dysfunction
2. Congestive heart failure
3. Known hypersensitivity to metformin hydrochloride
4. Acute or chronic metabolic acidosis, including diabetic ketoacidosis,
5. Should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials.
6. Lactic acidosis is a rare, but serious, metabolic complication that can occur due to metformin accumulation during treatment with metformin; when it occurs, it is fatal in approximately 50% of cases. Metformin must be discontinued in such cases.

Pregnancy Comments

Teratogenic Effects: Pregnancy Category B

Recent information strongly suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities.

Most experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible. Because animal reproduction studies are not always predictive of human response, metformin should not be used during pregnancy unless clearly needed.

There are no adequate and well-controlled studies in pregnant women with metformin. Metformin was not teratogenic in rats and rabbits at doses up to 600 mg/kg/day. This represents an exposure of about two and six times the maximum recommended human daily dose of 2000 mg based on body surface area comparisons for rats andrabbits, respectively. Determination of fetal concentrations demonstrated a partial placental barrier to metformin.

Nursing Mothers
Studies in lactating rats show that metformin is excreted into milk and reaches levels comparable to those in plasma. Similar studies have not been conducted in nursing mothers. Because the potential for hypoglycemia in nursing infants may exist, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. If metformin is discontinued, and if diet alone is inadequate for controlling blood glucose, insulin therapy should be considered.

Pregnancy Category **B**

Section 3. Composition / information on ingredients

Component	Exposure Limit	CAS No.
Principle Component:		
Metformin Hydrochloride 500mg, 850mg and 1000mg	Not Found	1115-70-4
Inactive Ingredients :		
Hypromellose	Not Found	9004-65-3
magnesium stearate,	Not Found	557-04-0
microcrystalline cellulose	Not Found	9004-34-6
polyethylene glycol	Not Found	25322-68-3
povidone	Not Found	9003-39-8

Section 4. First - aid measures

General Remove from exposure. Remove contaminated Clothing. Person developing serious hypersensitivity reaction must receive medical attention

Overdose Treatment In a patient with acidosis who is taking metformin, the drug should be discontinued immediately and general supportive measures promptly instituted. Because metformin hydrochloride is dialyzable (with a clearance of up to 170 mL/min under good hemodynamic conditions), prompt hemodialysis is recommended to correct the acidosis and remove the accumulated metformin. Such management often results in prompt reversal of symptoms and recovery. Other treatment modalities should be employed at the physician's discretion and which may be symptomatic and supportive.

Section 5. Fire - fighting measures

Flash point	Not Found	**Upper Flammable Limit:**	Not Found
Auto-Ignition Temperature:	Not Found	**Lower Flammable Limit:**	Not Found
Extinguishing Media	Water Spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and material.	**Fire and Explosion Hazard**	This material is assumed to be combustible. As with all dry powders it is advisable to ground mechanical equipment in contact with the dry material to dissipate the potential build-up of static electricity.

Fire Fighting Procedure As with all fires, evacuate personnel to a safe area. Fire fighter should use self- contained breathing equipment and protective clothing.

Section 6. Accidental Release Measures

Spill Response Wear approved respiratory protection, chemically compatible gloves and protective clothing. Wipe up spillage or collect spillage using high efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labelled container for disposal. Wash spill site.

Section 7. Handling and Storage

Storage Store at 20° to 25°C (68° to 77°F)**.**
Dispense in a tight, light-resistant container.

Incompatibilities: No data available

Section 8. Exposure controls / personal protection

Respiratory Protection Protection from inhalation is not normally necessary. If ventilation is inadequate or dust is likely to generate, use of suitable dust mask would be appropriate.

Skin Protection Skin protection is not normally necessary, however it is good practice to avoid contact with chemical to use suitable gloves when handling.

Eye protection Eye protection is not normally necessary. If concerned wear protective goggles or glasses. Wash hands prior to touching eye and in particular handling contact lenses.

Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Engineering Control	Engineering Controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. Physical and chemical properties

Appearance

- Metformin hydrochloride 500 mg tablets are white to off-white, round shaped, film coated tablets debossed with the logo of "70" on one side and "Z" on the other side.
- Metformin hydrochloride 850 mg tablets are white to off-white, oval shaped, film coated tablets debossed with the logo of "69" on one side and "Z" on the other side.
- Metformin hydrochloride 1000 mg tablets are white to off white, oval shaped, biconvex, film coated tablets with a bisect line on both the sides, one surface is debossed with "Z" and "71" on each side of bisect.

Solubility in water	No Data Available	**Odour**	Odourless
Boiling point	No Data Available	**Melting Point**	No Data Available
Evaporation rate	No Data Available	**Vapour density**	No Data Available
Reactivity in water	No Data Available	**Evaporation rate**	No Data Available
% Volatile by volume	No Data Available	**Specific gravity**	No Data Available
		Vapour pressure	No Data Available

Other information Metformin hydrochloride is a white crystalline compound with a molecular formula of $C_4H_{11}N_5 \cdot HCl$ and a molecular weight of 165.63. Metformin hydrochloride is freely soluble in water, slightly soluble in alcohol and is practically insoluble in acetone and methylene chloride. The pKa of metformin is 12.4. The pH of a 1 % aqueous solution of metformin hydrochloride is 6.68.

Section 10. Stability and Reactivity

Condition to avoid	Avoid exposure to extreme heat, light and moisture.	**Stable**	Stable under normal ambient and anticipated storage and handling conditions.
Decomposition Products	No Data Available	**Hazardous Reaction**	No data available.
Incompatibilities:	No Data Available		

Section 11. Toxicological information

General

Handling of formulated product is not expected to cause any toxicological affects. The data pertains to the ingredient in formulations, rather than this specie formulation.

Target organ

Eye contact, Skin contact and inhalation is not great risk as this product is tablet.

Other

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies have been performed in rats (dosing duration of 104 weeks) and mice (dosing duration of 91 weeks) at doses up to and including 900 mg/kg/day and 1500 mg/kg/day, respectively. These doses are both approximately four times the maximum recommended human daily dose of 2000 mg based on body surface area comparisons. No evidence of carcinogenicity with metformin was found in either male or female mice. Similarly, there was no tumorigenic potential observed with metformin in male rats. There was, however, an increased incidence of benign stromal uterine polyps in female rats treated with 900 mg/kg/day. There was no evidence of a mutagenic potential of metformin in the following in vitro tests: Ames test (S. typhimurium), gene mutation test (mouse lymphoma cells), or chromosomal aberrations test (human lymphocytes). Results in the in vivo mouse micronucleus test were also negative. Fertility of male or female rats was unaffected by metformin when administered at doses as high as 600 mg/kg/day, which is approximately three times the maximum recommended human daily dose based on body surface area comparisons.

Section 12. Ecological information

Do not allow product to enter drinking water supplies, waste water or soil

Section 13. Disposal Consideration

Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. Transport Information

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. Regulatory Information

Generic Medicine. Approved by USFDA & the ANDA Number is 77064

Section 16. Other information

None

Date of issue: 28/05/2015 **Supersedes edition of:** 02

The information contained herein is based on the state of our knowledge. It Characterises the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.