

SUMMARY OF PRODUCT CHARACTERISTICS

1-Name of the Drug Product:

- 1.1 Product Name**
Diabetmin Tablet 500mg
- 1.2 Strength**
Metformin Hydrochloride 500 mg
- 1.3 Pharmaceutical/Dosage Form**
Tablet

2-Quality and Quantitative Composition:

ACTIVE INGREDIENTS	PER TABLET (MG)
Metformin Hydrochloride	500 mg

For excipients, see 6.1

3-Pharmaceutical Form:

11mm, round, white film-coated tablet, bevel-edged and shallow convex faces, "HD" embossed on one face.

4-Clinical Particulars

- 4.1 Therapeutic indications**
Metformin is used in the treatment of non-insulin-dependent diabetes mellitus (type 2) in adults, not responding to exercise and dietary modification. Diabetmin may be used as monotherapy or in combination with other oral antidiabetic agents, or with insulin.
- 4.2 Posology/Dosage and method of administration**
For Oral use

Monotherapy and combination with other oral antidiabetic agents:

Usual adult dose:

Diabetmin 500mg Tablet: Initial dose of one tablet 2 to 3 times daily with or after meals.

If necessary, medication can be increased gradually to a maximum of 3g daily. If transfer from another oral antidiabetic agent is intended; discontinue the other agent and initiate metformin at the dose indicated above.

Combination with insulin:

Metformin and insulin may be used in combination therapy to achieve better blood glucose control. Metformin is given at the usual starting dose of one tablet 2-3 times daily while insulin dosage is adjusted on the basis of blood glucose measurements.

Usual children dose: Metformin is not recommended for use in children.
Usual geriatric dose: Please refer to adult dose. (Due to potential for decreased renal function, the dosage should be adjusted based on renal function and maximum doses are not advised for use in the elderly.)

Note: The information given here is limited. For further information, kindly consult your doctor or pharmacist.

4.3 Contraindications

This medication is contraindicated in patients with the following medical problems:

- Hypersensitivity to metformin.
- Any condition needing close blood glucose control, such as: severe burns, dehydration, diabetic coma, diabetic ketoacidosis, hyperosmolar nonketotic coma, severe infection, major surgery, and severe trauma.
- Conditions associated with hypoxemia, such as: cardiorespiratory insufficiency, cardiovascular collapse, congestive heart failure, acute myocardial infarction.
- Severe, acute, or chronic hepatic disease.
- Active or history of lactic acidosis.
- Renal function impairment or renal disease.
- Diagnostic or medical examinations using intravascular iodinated contrast media such as: angiography, intravenous cholangiography, computed tomography (CT) scan, pyelography and urography

4.4 Special warning and precautions for use

Lactic Acidosis:

Lactic acidosis is a rare, but serious (high mortality in the absence of prompt treatment), metabolic complication that can occur due to metformin accumulation. Reported cases of lactic acidosis in patients on metformin have occurred primarily in diabetic patients with significant renal failure. The incidence of lactic acidosis can and should be reduced by assessing also other associated risk factors such as poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake, hepatic insufficiency and any condition associated with hypoxia.

Diagnosis: Lactic acidosis is characterized by acidosis dyspnea, abdominal pain and hypothermia followed by coma. Diagnostic laboratory findings are decreased blood pH, plasma lactate levels above 5 mmol/L, and an increased anion gap and lactate/pyruvate ratio. If metabolic acidosis is suspected, metformin should be discontinued and the patient should be hospitalized immediately.

Renal Function:

As metformin is excreted by the kidney, serum creatinine levels should be determined before initiating treatment and regularly thereafter:

- at least annually in patients with normal renal function;
- at least 2 to 4 times a year in patients with serum creatinine levels at the upper limit of normal and in elderly subjects.

Decreased renal function in elderly subjects is frequent and asymptomatic. Special caution should be exercised in situations where renal function may become impaired, for example when initiating antihypertensive therapy or diuretic therapy and when starting therapy with an NSAID.

Administration of iodinated contrast agent: As the intravascular administration of iodinated contrast materials in radiologic studies can lead to renal failure, metformin should be discontinued prior to, or at the time of the test and not reinstated until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal.

Surgery:

Metformin should be discontinued before elective surgery with general anaesthesia and should not be usually resumed earlier than 48 hours afterwards.

Other precautions:

- All patients should continue their diet with a regular distribution of carbohydrate intake during the day. Overweight patients should continue their energy-restricted diet.
- The usual laboratory tests for diabetes monitoring should be performed regularly.
- Metformin alone never causes hypoglycaemia, although caution is advised when it is used in combination with insulin or sulfonylureas.

4.5 Interaction with other drug products and other forms of interactions

Concurrent use of this medication with the following may interact with metformin:

- Acute or chronic ingestion of alcohol.
- Cimetidine or other cationic medications excreted by renal tubular transport.
- Furosemide.
- Hyperglycemia-causing and hypoglycemia-causing medications.

4.6 Fertility, pregnancy and lactation

For fertility and pregnancy problems, adequate and well-controlled studies in humans have not been done and documented. For patient plans to become pregnant or during pregnancy, control of blood glucose with diet alone or a combination of diet and insulin is recommended, while use of metformin is discouraged. Metformin is distributed into breast milk, but safety for use in nursing mothers has not been established

4.7 Effects on ability to drive and use machine

None known.

4.8 Undesirable effects

Metformin can cause:

- Gastrointestinal adverse effects including anorexia, diarrhea, dyspepsia, flatulence, nausea, vomiting.
- Headache, metallic taste, weight loss.
- Anemia, megaloblastic, hypoglycemia, lactic acidosis.

- Long-term metformin therapy may cause a decrease of vitamin B12 absorption with decrease of serum levels

4.9 Overdose

Symptoms of overdose: Hypoglycemia and lactic acidosis. Treatment of overdose:

- For hypoglycemia: Treating with immediate ingestion of a source of glucose and counseling patient to obtain emergency medical assistance immediately.
- For lactic acidosis: Hemodialysis with sodium bicarbonate.

5-Pharmacological Properties :

5.1 Pharmacodynamic properties

Metformin is an oral biguanide antidiabetic agent. Its mode of action is thought to be multifactorial and includes delayed uptake of glucose from the gastrointestinal tract; increased peripheral glucose utilization mediated by increased insulin sensitivity; and inhibition of increased hepatic and renal gluconeogenesis.

5.2 Pharmacokinetic properties

Metformin Hydrochloride is slowly and incompletely absorbed from the gastrointestinal tract. The absolute bioavailability of a single 500mg dose is reported to be about 50 to 60%, although this is reduced somewhat if taken with food. Plasma protein binding is negligible. It is excreted unchanged in the urine. The plasma elimination half-life is reported to range from about 2 to 6 hours after oral administration.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies on safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and reproductive toxicity.

6-Pharmaceutical Particulars:

6.1 List of excipients

Microcrystalline Cellulose
Pregelatinised Cornstarch
Kollidon
Magnesium Stearate
Sodium Starch Glycolate
Isopropyl Alcohol (IPA)
Polyethylene Glycol
Hydroxypropyl Methylcellulose
Hydroxypropyl Methylcellulose
Purified water

6.2 Incompatibilities

None known

6.3 Shelf life

3 years from date of manufacture

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

Descriptions of each packaging material for Diabetmin 500mg Tablet is as below:

Immediate Container/Packaging:

Rigid Polyvinyl chloride (PVC) Film

Appearance: Glass clear transparent

Aluminium blister foil

Appearance: Bright surface and heal seal on dull surface

Secondary packing components:

Outer Container/Packaging

Type: Unit Box

Material: Paper carton

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Not applicable

7- Applicant/ Holder of Certificate of Product Registration:

Marketing Authorization Holder:

Name : HOVID Bhd.
Address : 121, Jalan Tunku Abdul Rahman,
(Jalan Kuala Kangsar)
30010 Ipoh, Perak, Malaysia

8-Drug Product Manufacturer:

Manufacturer : Hovid Bhd.
Lot 56442, 7 ½ Miles Jalan Ipoh / Chemor,
31200 Chemor, Perak, Malaysia

9-NAFDAC Registration Number(s)

04-0810