SUMMARY OF PRODUCTS CHARACTERISTICS (SMPC)

1. NAME OF THE MEDICINAL PRODUCT:

METFORMIN HYDROCHLORIDE TABLETS USP 500 MG (**FORMIMET 500**)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each film coated tablet contains:

Metformin Hydrochloride USP	500 mg
Excipients	Q.S.
Colour: Titanium Dioxide BP	

3. PHARMACEUTICAL FORM

Film Coated Tablets

White to off white coloured, round shaped, biconvex film coated, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

Metformin hydrochloride Tablets is indicated as an adjunct to diet and exercise to improve glycemic control in adults and children with type 2 diabetes mellitus.

4.2 Posology and Method of Administration

It is given orally in the treatment of type 2 diabetes mellitus, and is the drug of first choice in overweight patients.

Recommended Dosing Schedule

Adults: Initial dosage is 500 mg two or three times daily or 850 mg once or twice daily with or after meals, gradually increased if necessary, at intervals of at least 1 week, to 2 to 3 g daily; doses of 3 g daily are associated with an increased incidence of gastrointestinal adverse effects.

Child (10-18 years): In children aged 10 years and older with type 2 diabetes mellitus, oral metformin hydrochloride may be used in a starting dose of 500 mg or 850 mg once daily, or 500 mg twice daily, given with or after a meal. It may be gradually increased if needed, at intervals of at least 1 week, to a maximum of 2 g daily given in 2 or 3 divided doses.

Renal impairment

A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at an increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g., every 3 – 6 months.

GFR (mL/min)	Total maximum daily dose (to be divided into 2-3 daily doses)	Additional considerations
60-89	3000 mg	Dose reduction may be considered in relation to declining renal function
45-59	2000 mg	The starting dose maximum is at most half of the
30-44	1000 mg	
< 30	-	Metformin is contraindicated

4.3 Contraindications

Metformin is contraindicated in patients with severe renal impairment (GFR below 30 mL/min), known hypersensitivity to metformin hydrochloride and acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Use of general anaesthesia (suspend metformin on the morning of surgery and restart when renal function returns to baseline) and Iodine-containing X-ray contrast media (Suspend metformin prior to the test; restart no earlier than 48 hours after the test if renal function has returned to baseline) are contraindicated.

4.4 Special warnings and precautions for use

Lactic acidosis: A very rare, but serious metabolic complication, most often occurs at acute worsening of renal function or cardiorespiratory illness or sepsis. Metformin accumulation occurs at acute worsening of renal function and increases the risk of lactic acidosis. Lactic acidosis is characterised by acidotic dyspnoea, abdominal pain, muscle cramps, asthenia and hypothermia followed by coma. In case of suspected symptoms, the patient should stop taking metformin and seek immediate medical attention.

In case of dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), metformin should be temporarily discontinued and contact with a health care professional is recommended.

Renal function: GFR should be assessed before treatment initiation and regularly thereafter. Metformin is contraindicated in patients with GFR<30 mL/min and should be temporarily discontinued in the presence of conditions that alter renal function

Cardiac function: Patients with heart failure are more at risk of hypoxia and renal insufficiency. In patients with stable chronic heart failure, metformin may be used with a regular monitoring of cardiac and renal function. For patients with acute and unstable heart failure, metformin is contraindicated

Other precautions: Metformin alone does not cause hypoglycaemia, but caution is advised when it is used in combination with insulin or other oral antidiabetics (e.g. sulphonylureas or meglitinides).

4.5 Interaction with other medicinal products and other forms of Interaction

Concomitant use not recommended:

Alcohol: Alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in case of fasting, malnutrition or hepatic impairment.

Combinations requiring precautions for use:

Some medicinal products can adversely affect renal function which may increase the risk of lactic acidosis, e.g. NSAIDs, including selective cyclo-oxygenase (COX) II

inhibitors, ACE inhibitors, angiotensin II receptor antagonists and diuretics, especially loop diuretics. When starting or using such products in combination with metformin, close monitoring of renal function is necessary.

Medicinal products with intrinsic hyperglycaemic activity (e.g. glucocorticoids (systemic and local routes), sympathomimetics:

More frequent blood glucose monitoring may be required, especially at the beginning of treatment. If necessary, adjust the metformin dosage during therapy with the respective medicinal product and upon its discontinuation.

Organic cation transporters (OCT)

Metformin is a substrate of both transporters OCT1 and OCT 2.

Co-administration of metformin with

- Inhibitors of OCT 1 (such as verapamil) may reduce efficacy of metformin.
- Inducers of OCT 1 (such as rifampicin) may increase gastrointestinal absorption and efficacy of metformin.
- Inhibitors of OCT 2 (such as cimetidine, dolutegravir, ranolazine, trimethoprime, vandetanib, isavuconazole) may decrease the renal elimination of metformin and thus lead to an increase in metformin plasma concentration.
- Inhibitors of both OCT 1 and OCT 2 (such as crizotinib, olaparib) may alter efficacy and renal elimination of metformin.

4.6 Pregnancy and lactation

Pregnancy: Can be used in pregnancy for both pre-existing and gestational diabetes. Women with gestational diabetes should discontinue treatment after giving birth.

Lactation: May be used during breast-feeding in women with pre-existing diabetes.

4.7 Effects on ability to drive and use machines

Metformin monotherapy does not cause hypoglycaemia and therefore has no effect on the ability to drive or to use machines. However, patients should be alerted to the risk of hypoglycaemia when metformin is used in combination with other antidiabetic agents (e.g. sulfonylureas, insulin or meglitinides).

4.8 Undesirable effects

Common or very common: Abdominal pain, anorexia, diarrhoea (usually transient), nausea, taste disturbance, vomiting.

Rare: Decreased vitamin-B12 absorption, Erythema, lactic acidosis (withdraw treatment), pruritus, urticaria.

Frequency not known: Hepatitis

Gastro-intestinal side-effects are initially common with metformin, and may persist in some patients, particularly when very high doses are given. A slow increase in dose may improve tolerability.

4.9 Overdose

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. Metformin is dialyzable with a clearance of up to 170 mL/min under good

hemodynamic conditions. Therefore, hemodialysis may be useful for removal of accumulated drug from patients in whom metformin overdosage is suspected.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Metformin is an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Its pharmacologic mechanisms of action are different from other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Unlike sulfonylureas, metformin does not produce hypoglycemia in either patients with type 2 diabetes or normal subjects and does not cause hyperinsulinemia. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

5.2 Pharmacokinetic properties

Metformin hydrochloride is slowly and incompletely absorbed from the gastrointestinal tract; the absolute bioavailability of a single 500 mg dose is reported to be about 50 to 60%, although this is reduced somewhat if taken with food. Once absorbed, protein binding in plasma is negligible; the drug is excreted unchanged in the urine. The plasma elimination half-life is reported to range from about 2 to 6 hours after oral doses. Metformin crosses the placenta and is distributed into breast milk in small amounts.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipient(s)

Maize Starch, Povidone (PVP-30), Purified water, Purified Talc, Croscarmellose Sodium, Magnesium Stearate, DR Coat FCU (W/011/014)

6.2 Shelf-life

24 months

6.3 Special precautions for storage

Store below 30°C. Store in the original package.

6.4 Nature and contents of container

10 Tablets are Blister packed. Such 10 Blisters are packed in a Printed Carton with packing insert.

10 Tablets are Blister packed. Such 3 Blisters are packed in a Printed Carton with packing insert.

7. MARKETING AUTHORISATION HOLDER

BIOMATRIX HEALTHCARE PVT LTD.
Survey No. 624, Sarkhej – Bavla Highway, Vil.: Rajoda,
Tal.: Bavla, Dist.: Ahmedabad – 382220, Gujarat, INDIA.

8. Marketing authorisation number(s)
09407/10402/NMR/2022

9. Date of first authorisation/renewal of the authorisation
Jan 7, 2024

10. Date of revision of the text

Not Applicable