December 2023

SUMMARY OP PRODCUT CHARACTERISTICS (SPC)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Glucomet (Metformin 500mg tablet)

2. Qualitative and quantitative composition:

Each tablet contains 500mg metformin hydrochloride.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form:

Tablet

4. Clinical Particulars:

4.1 Therapeutic indication:

Treatment of type 2 diabetes mellitus in adults, when dietary management and exercise alone does not result in adequate glycemic control. Metformin may be used as monotherapy or in combination with other oral antidiabetic agents, or with insulin. A reduction of diabetic complications has been shown in overweight type-2 diabetic patients treated with Metformin as 1st – line therapy after diet failure. In type 1 diabetes, Metformin may be given as an adjuvant to patients whose symptoms are poorly controlled.

4.2 Posology and method of administration:

The usual dose is 500mg three times daily, taken with food or after meals; maximum 3g daily in divided doses. To be taken orally.

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 preferably 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	Factors that may increase the risk of lactic acidosis should be reviewed before considering initiation of Metformin. The starting dose is at most half of the maximum dose.
30-44	1000 mg	
<30	-	Metformin is contraindicated.

Method of administration: Oral

4.3 Contraindication:

(a) Hypersensitivity to biguanides.

(b) Diabetic coma and serious ketoacidosis.

(c) Impaired renal function, impaired hepatic function, and impaired cardiovascular function including cardiac failure and recent myocardial infarction.

(d) History of, or state associated with lactic acidosis, eg. shock or pulmonary insufficiency, alcoholism.

(e) Condition associated with hypoxaemia.

(f) Severely reduced kidney function (GFR <30mL/min)

(g) Any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis).

4.4 Special warnings and special precautions for use:

(a) Metformin is excreted by the kidney and regular monitoring of renal function is advised in all diabetics.

(b) Care must be taken when administering this drug in conditions which may cause dehydrations or in patients suffering from serious infection or trauma, and in those undergoing surgery.

(c) Metformin may impair absorption of Vitamin B_{12}. Patients receiving Metformin continuously should have an annual check up of vitamin B_{12} levels.

(d) Use in children: Metformin is not recommended for use in children.

(e) Use in the elderly: Metformin is indicated in the elderly but not when renal function is impaired.

(f) Lactic acidosis: Lactic acid, 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. 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. Medical products that can acutely impair renal function (such as antihypertensives, diuretics and NSAIDs) should be initiated with caution in Metformin-treated patients. Other risk factors for lactic acidosis are excessive alcohol intake, hepatic insufficiency, inadequately controlled diabetes, ketosis, prolonged fasting and any conditions associated with hypoxia, as well as concomitant use of medicinal products that may cause lactic acidosis.

Patients and/or care-givers should be informed of the risk of lactic acidosis. Lactic acidosis is characterized by acidotic dyspnea, 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. Diagnostic laboratory findings are decreased blood pH (< 7.35), increased plasma lactate levels (> 5mmol/L) and an increased anion gap and lactate pyruvate ratio.

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

4.5 Interaction with other FPPs and other forms of interaction:

(a) Alcohol causes enhanced hypoglycemic effect and risk of lactic acidosis with Metformin.

(b) Concomitant therapy with sulfonylurea may cause hypoglycemia, therefore blood glucose should be monitored.

(c) Reduced renal clearance of Metformin has been reported during Cimetidine therapy, so a dose reduction should be considered.

(d) An interaction of Metformin with anticoagulants is a possibility and the dosage of anticoagulants may need adjustment.

4.6 Pregnancy and lactation:

The use of Metformin during pregnancy is not advisable. It is not known if Metformin is excreted in breast milk; however, hypoglycemia in infant is possible.

4.7 Effects on ability to drive and use machines:

None has been mentioned.

4.8 Undesirable effects:

(a) Concomitant therapy with sulfonylurea may cause hypoglycemia, therefore blood glucose should be monitored.

(b) Metformin may impair absorption of Vitamin B_{12}. Patients receiving Metformin continuously should have an annual checkup of vitamin B_{12} levels.

(c) Reduced renal clearance of Metformin has been reported during Cimetidine therapy, so a dose reduction should be considered.

(d) An interaction of Metformin with anticoagulants is a possibility and the dosage of anticoagulants may need adjustment.

(e) The most frequently reported adverse effects are: metallic taste in the mouth, epigastric discomfort, nausea and vomiting, lactic acidosis, decreased vitamin B_{12} absorption: rarely diarrhea and anorexia. Most of these reactions are transient and can be controlled by reducing the dosage or by discontinuing therapy.

4.9 Overdose:

Hypoglycemia may occur when Metformin is given concomitantly with a sulfonylurea, insulin or alcohol. In excessive dosage, lactic acidosis may develop. Intensive supportive therapy is recommended which should be particularly directed at correcting fluid loss and metabolic disturbance.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

(a) The biguanide Metformin is an oral antihyperglycemic agent use in the management of non-insulin-dependent diabetes mellitus (NIDDM). It reduces blood glucose levels, predominantly by improving hepatic and peripheral tissue sensitivity to insulin without affecting the secretion of this hormone.Since Metformin does not promote weight gain or hypoglycemia, it should be considered first-line pharmacotherapy in

obese patients with NIDDM that is inadequately controlled by nonpharmacological measures.

(b) Metformin decrease gluconeogenesis from lactate (pyruvate) and elevates the glucose utilization of peripheral tissues.

(c) Metformin reduces elevated blood glucose concentrations in patients with diabetes, but it does not increase insulin secretion. This is probably the reason why it does not cause hypoglycemia.

(d) Metformin has no effect on the pancreatic beta cells. It has been postulated that Metformin may potentiate the effect of insulin or enhance insulin's effect on peripheral receptor sites.

(e) A lipolytic action of Metformin has been suggested and a lipid-lowering effect has been demonstrated, including reduction of plasma triglycerides and, to a lesser degree, of total cholesterol.

(f) Metformin improves the blood lipoprotein profile not only in diabetics but also in non-diabetic subjects with hyperlipoproteinemia.

5.2 Pharmacokinetic properties:

Metformin oral bioavailability of usual doses is 50 ~ 60%, and the mean plasma elimination half-life ranges from 1.5 ~ 4.5 hours.

5.3 Preclinical safety data:

No information available.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Magnesium aluminometasilicate

Polyethylene glycol

Magnesium stearate

Colloidal silicon dioxide

Hydroxypropyl cellulose

Sodium lauryl sulphate

Isopropyl alcohol

6.2 Incompatibilities

No information available.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Keep in a tight container. Store at temperature below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

Blister packing 10's x 10

6.6 Instructions for use and handling and disposal:

None has been mentioned.

7. MARKETING AUTHORIZATION HOLDER

Y. S. P. INDUSTRIES (M) SDN. BHD.
Lot 3, 5 & 7, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor Darul Ehsan,
Malaysia.

8. MARKET AUTHORIZATION NUMBER

YSP / MAA / 003

9. DATE OF ~~FIRST AUTHORIZATION~~/ RENEWAL OF THE AUTHORIZATION:

24 Aug 2020

10. DATE OF REVISION OF THE TEXT

28 July 2023