For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

DAONIL® M
Glibenclamide & Metformin Tablets

Abridged Prescribing Information

COMPOSITION

Daonil® M: Each tablet contains Glibenclamide IP 5mg + Metformin Hydrochloride IP 500mg (in sustained release form)

THERAPEUTIC INDICATIONS

For the management of type II diabetes mellitus when diet, exercise and single drug therapy do not result in adequate glycemic control.

DOSAGE AND ADMINISTRATION

Initial dose: 1 tablet of Daonil M should be administered once daily with meals. Maximum Dosing: For once daily administration maximum 2 tablets of Daonil M can be given. For higher doses, it may be necessary to administer in 2 doses. Upto 4 tablets of Daonil M can be given per day. Do not crush or chew the tablet.

As data on the safety and effectiveness in children is not available, Daonil M is not recommended for this age group.

Renal impairment : A GFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at 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.

SAFETY-RELATED INFORMATION

Contraindications: Should not be used in patients with insulin-dependent (type 1) diabetes mellitus (for example diabetics with a history of ketoacidosis), in treatment of diabetic ketoacidosis , in treatment of diabetic precoma or coma, any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis, diabetic pre-coma), in patients with serious renal dysfunction, in severe renal failure (GFR <30 mL/min), in patients with known hypersensitive to glibenclamide, metformin or any of the excipients, pregnant women and in breast feeding women, in patients treated with bosentan, in acute conditions with the potential to alter renal function (dehydration, severe infection, shock); disease which may cause tissue hypoxia such as decompensated heart failure, respiratory failure, recent myocardial infarction, shock; in patients with serious hepatic dysfunction; hepatic insufficiency; acute alcohol intoxication, alcoholism.

Warnings: Glibenclamide: Epidemiological studies suggest that the administration of glibenclamide is associated with an increased risk of cardiovascular mortality, when compared to treatment with metformin or gliclazide. This risk was especially observed in patients with diagnosed coronary diseases.Clinical signs of hyperglycaemia are: increased urinary frequency, intense thirst, dryness of the mouth, and dry skin. In exceptional stress situations (e.g. trauma, surgery, febrile infections), blood glucose regulation may deteriorate, and a temporary change to insulin may be necessary. Persons allergic to other sulfonamide derivatives may develop an allergic reaction to glibenclamide. Metformin : 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. Medicinal products that can acutely impair renal function (such as antihypertensives, diuretics and NSAIDs) should be initiated with caution in metformin-treated patients.

Precautions : Glibenclamide: During treatment with Daonil®M, glucose levels in blood and urine must be measured regularly. In addition, it is recommended that regular determinations of the proportion of glycated haemoglobin be carried out. Monitoring of glucose levels in blood and urine also serves to detect failure of therapy - either primary or secondary. As is necessary during treatment with any blood-glucose-lowering drug, the patient and the physician must be aware of the risk of hypoglycaemia. Elderly patients are particularly susceptible to hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly. The initial and maintenance dosing should be conservative to avoid hypoglycemic reactions. Since glibenclamide belongs to the class of sulfonylurea agents, caution should be used in patients with G6PD-deficiency and a nonsulfonylurea alternative should be considered. Metformin: GFR should be assessed before treatment initiation and regularly thereafter. 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. Intravascular administration of iodinated contrast agents may lead to contrast induced nephropathy. Metformin should be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable. Metformin must be discontinued at the time of surgery under general, spinal or epidural anesthesia. Other precautions include regular monitoring of thyroid-stimulating hormone (TSH) levels is recommended in patients with hypothyroidism; monitoring of the vitamin B12 level is recommended

Pregnancy & Lactation: Contraindicated in pregnancy and lactation; patients must switch to insulin during pregnancy or when planning pregnancy. Patients may change over to insulin when breast feeding or must stop breast feeding.

Adverse Reactions: Very common and common adverse reactions for glibenclamide: Metabolism and nutrition disorders: Hypoglycaemia, sometimes prolonged and even life-threatening, may occur. Clinical picture of a severe hypoglycaemic attack may resemble that of a stroke. The symptoms of hypoglycaemia nearly always subside when hypoglycaemia is corrected. Gastrointestinal disorders : Commonly nausea, abdominal pain and diarrhoea may occur. Skin and subcutaneous disorders : rashes. Glibenclamide, like all sulfonylureas can cause weight gain.

For metformin – Gastrointestinal symptoms such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite (>10%) are very common, Metallic taste (3%). Hepatobiliary disorders: There are reports of liver function tests abnormalities and hepatitis resolving upon metformin discontinuation

For full prescribing information write to Sanofi India Ltd, Sanofi House, CT Survey No 117-B, L&T Business Park, Saki Vihar Road, Powai, Mumbai 400072

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Sources: Glibenclamide CCDS version 10.1 dated 23rd March2017, Metformin and Glibenclamide combination CCSI Version 2 dated 17th October 2017, Glimepiride Plus Metformin Fixed Dose Combination CCDS Version 11 dated 17th October 2017