GLIBOMET®400 mg + 5 mg film-coated tablets

PHARMACOTHERAPEUTIC CATEGORY
Combinations of oral blood-glucose lowering drugs

THERAPEUTIC INDICATIONS
Non-insulin-dependent type 2 diabetes mellitus that cannot be controlled with diet alone or with diet and sulphanylureas or biguanides.

CONTRAINDICATIONS
Hypersensitivity to the single active ingredients (glibenclamide, metformin) or to any of the excipients; gestational diabetes, type 1 diabetes (insulin dependent); diabetic coma and pre-coma; serum levels of creatinine higher than 12 mg/l; diabetics with previous episodes of lactic acidosis; seriously impaired hepatic or renal function; ongoing treatment with diuretics or anti-hypertensive agents capable of provoking alterations in the renal function or during intravenous urography; severe cardio-circulatory disorders (heart failure, cardiogenic or toxinfective shock, disorders of the peripheral arterial circulation); severe respiratory diseases; adrenal insufficiency; chronic alcoholism; very low-calorie diets and above all, fasting; severe dystrophic diseases; severe acute haemorrhages; shock; gangrene; pregnancy and breastfeeding. During the two days prior to or following surgery.

PRECAUTIONS FOR USE
Patients under treatment must be frequently monitored to detect possible factors or conditions which may favour the onset of lactic acidosis, bearing in mind that the risk of this disorder is more frequent in cases of hepatic and/or renal insufficiency, cardiorespiratory failure, alcohol intoxication, prolonged fasting, treatment with diuretics and gastrointestinal disorders; in any case, patients must be instructed to recognise the symptoms of lactic acidosis (anorexia, nausea, fever, vomiting, muscle cramps, increased respiratory frequency and volume, malaise, abdominal pain, diarrhoea, possible obnubilation or loss of consciousness) and of hypoglycaemia (headache, irritability, sleep disorders, nervous depression, tremors, excessive sweating) so that they can immediately contact the physician, who should also be informed of ongoing febrile illnesses or digestive disorders. In this case, the physician should conduct all necessary tests. Since even a slight impairment of renal function may considerably increase the risk of lactic acidosis, it is necessary to repeatedly monitor renal function before starting the treatment and then at least every eight weeks during the first six months of therapy, and subsequently every six months.

INTERACTIONS
The hypoglycaemic action of glibenclamide may be increased by dicumarol and its derivatives, by monoamine oxidase inhibitors, sulphonamides, phenylbutazone and its derivatives, chloramphenicol, cyclophosphamide, probenecid, phenyramidol and salicylates, oral miconazole, sulfinpyrazone, perhexiline and ingestion of large amounts of alcohol; whereas it may be decreased by adrenalin, corticosteroids, oral contraceptives, thiazide diuretics and barbiturates.
Caution should be exercised when the medicine is administered at the same time as beta-blockers. It must be borne in mind that metformin may intensify the action of anticoagulants.

SPECIAL WARNINGS
Each treatment, and in particular the switch from or to other blood-glucose lowering drugs, must be prescribed by the physician.
The patient should strictly follow the medical prescriptions concerning dosage and type of administration as well as the concomitant diet and exercise regimes.
Use must be limited to patients with Diabetes Mellitus Type 2 which cannot be controlled by diet alone.
In case of hypoglycaemic symptoms (see *Undesirable Effects*), administer carbohydrates (sugar). More serious cases, which on rare occasions may lead to loss of consciousness, require the intervention of a physician.
In concomitance with trauma, surgery, infective and febrile diseases, it may be necessary to temporarily administer insulin therapy in order to maintain adequate metabolic control.
After the ingestion of alcoholic beverages, it is recommended to consider the possibility of reactions such as general malaise, respiratory difficulty, palpitations, headache, nausea, and vomiting.
Treatment must be suspended 48 hours prior to an angiography or urography and resumed, if necessary, 48 hours after the test.
Treatment with sulphonylureas may give rise to haemolytic anaemia in patients with a G6PD deficiency. Glibenclamide must therefore be administered with caution to these patients and another therapeutic

alternative considered.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
The patient must be informed about the risk of hypoglycaemia and the consequent reduction in concentration and reaction capacities, and therefore take this into account before driving or using machinery.

POSOLOGY, METHOD AND DURATION OF ADMINISTRATION
The daily dose, administration and duration of treatment must be established by the physician for each patient on the basis of metabolic tests. As a rule, the starting dose is 2 tablets daily with the main meals. Doses should never exceed 4 tablets of Glibomet 400 mg/5 mg. Subsequently the daily dose must be gradually decreased until the minimum amount needed to control the glycaemia is reached.
Overdosing
Ingestion of an excessive dose can give rise to the onset of symptoms of hypoglycaemia (see *Precautions for Use*) that may require administration of sugar or, in serious cases, intervention by a physician. Gastrointestinal disorders and symptoms of lactic acidosis may also occur (see *Precautions for Use*) that require intervention by a physician.

UNDESIRABLE EFFECTS
Although rare, there may be the onset of hypoglycaemic phenomena, especially in debilitated or elderly patients, in case of excessive physical stress, irregular eating habits or consumption of alcoholic beverages, and in case of impaired renal and/or hepatic function (see also *Special warnings and precautions for use*). Headache and gastrointestinal disorders (nausea, loss of appetite, stomach pain, vomiting or diarrhoea) are sometimes possible and may require the interruption of treatment.
Rarely, allergic skin reactions may occur, however these are transitory and in general disappear as the treatment continues. Patients with a predisposition due to existing renal insufficiency, severe cardio-circulatory disorders or respiratory insufficiency may show symptoms of lactic acidosis, though rarely, (see *Precautions for Use*) that require adequate treatment by the physician. Lactic acidosis may be favoured by the simultaneous ingestion of alcohol.
Alterations to the number of blood cells are very rare and generally reversible.
Observance of the instructions in the illustrative leaflet reduces the risk of undesirable effects.
It is important to inform your physician or pharmacist at the onset of any undesirable effects even if not described in the illustrative leaflet.

SHELF-LIFE AND STORAGE
Expiry: see the "use by" date printed on the package.
Warning: do not use the product after the "use by" date printed on the package.
The "use by" date refers to the product correctly stored in its unopened package.
This medicinal product does not require any special storage conditions.

COMPOSITION
Glibomet 400 mg + 5 mg film-coated tablets
Each film-coated tablet contains:

Glibenclamide	5 mg
Metformin hydrochloride	400 mg

Excipients
Microcrystalline cellulose, Macrogol 6000, Povidone, Croscarmellose sodium, silicon dioxide, glyceryl dibehenate, magnesium stearate, Opadry white (Hydroxypropyl methyl cellulose, titanium dioxide, talc, Macrogol 6000).

PHARMACEUTICAL FORM AND CONTENTS
Glibomet 400 mg + 5 mg 60 film-coated tablets

MARKETING AUTHORISATION HOLDER
Laboratori Guidotti S.p.A. - Via Livornese, 897 – PISA – La Vettola - Italy

MANUFACTURER RESPONSIBLE FOR RELEASE OF BATCHES
A. Menarini Manufacturing Logistics and Services Srl - Campo di Pile, L'Aquila - Italy.
Menarini – Von Heyden GmbH – Leipzinger Strasse, 7 - 13 – Dresden – Germany.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

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