For the use only of a Registered Medical Practitioner or hospital or a laboratory

This package insert is continually updated: Please read carefully before using a new pack

Glibenclamide and Metformin Hydrochloride Sustained Release Tablets
Daonil® M

DESCRIPTION

Active Ingredients
Glibenclamide and Metformin Hydrochloride

Therapeutic or Pharmacological Class
Glibenclamide : Antidiabetic. Sulfonylurea
Metformin: Antidiabetic. Biguanide.

Pharmaceutical Form(s)
Bilayer tablet (one layer sustained release)

COMPOSITION

Each uncoated bilayered tablet of Daonil®M contains:
Glibenclamide IP …… 5mg
Metformin Hydrochloride IP.....….. 500mg
(in sustained release form)
Excipients qs
Colour : Lake of Quinoline yellow, Lake of Brilliant Blue

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

Dosage
In principle, the dosage of Daonil®M is governed by the desired blood glucose level. The dosage of Daonil®M must be the lowest which is sufficient to achieve the desired metabolic control.

During treatment with Daonil®M glucose levels in blood and urine must be measured regularly. In addition, it is recommended that regular determination of the proportion of glycated haemoglobin be carried out.

Mistakes, e.g., forgetting to take a dose, must never be corrected by subsequently taking a larger dose.

Measures for dealing with such mistakes (in particular forgetting a dose or skipping a meal) or situations where a dose cannot be taken at the prescribed time must be discussed and agreed between physician and patient beforehand.

As an improvement in control of diabetes is, in itself, associated with higher insulin sensitivity glibenclamide requirements may fall as treatment proceeds. To avoid hypoglycemia timely dose reduction or cessation of Daonil®M therapy must therefore be considered.

Initial dose: One Daonil®M tablet should be administered as 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 divide the administration into 2 doses. Up to 4 tablets of Daonil®M can be given per day.

Due to sustained release preparation, do not crush or chew the tablet. The whole tablet must be taken with water.

SPECIAL POPULATIONS

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. The maximum daily dose of metformin should preferably be divided into 2-3 daily doses. Factors that may increase the risk of lactic acidosis (see Section Warnings) should be reviewed before considering initiation of metformin in patients with GFR<60 mL/min. If no adequate strength of Daonil M is available, individual monocomponents should be used instead of the fixed dose combination.

GFR ml/min	Metformin	Glibenclamide
60-89	Maximum daily dose is 3000 mg. Dose reduction may be considered in relation to declining renal function.	Maximum daily dose is 20mg Glibenclamide (higher daily doses of 20 mg are not recommended because they are more effective only in exceptional cases).
45-59	Maximum daily dose is 2000 mg The starting dose is at most half of the maximum dose.	
30-44	Maximum daily dose is 1000 mg. The starting dose is at most half of the maximum dose.	
<30	Metformin is contraindicated	Glibenclamide is contraindicated

CONTRAINDICATIONS:

Daonil®M must 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
- Severe renal failure (GFR <30 mL/min)

- in patients with known hypersensitivity to glibenclamide or metformin or any excipients
- in pregnant women
- in breast feeding women
- in patients treated with bosentan
- acute conditions with the potential to alter renal function such as dehydration, severe infection, shock)
- disease which may cause tissue hypoxia (especially acute disease, or worsening of chronic disease) such as: decompensated heart failure, respiratory failure, recent myocardial infarction, shock.
- in patients with serious hepatic dysfunction
- hepatic insufficiency, acute alcohol intoxication, alcoholism.

WARNINGS
For 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 to maintain good metabolic control.

Persons allergic to other sulfonamide derivatives may develop an allergic reaction to glibenclamide as well.

For Metformin:
Lactic acidosis
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.

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.

Medicinal 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 associated 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 (see Section “CONTRAINDICATIONS” and Section “INTERACTIONS”).

Patients and/or care-givers should be informed of 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. Diagnostic laboratory findings are decreased blood pH (< 7.35), increased plasma lactate levels (>5 mmol/l) and an increased anion gap and lactate/pyruvate ratio.

Renal function
GFR should be assessed before treatment initiation and regularly thereafter, see Section Dosage and Administration

Metformin is contraindicated in patients with GFR<30 ml/min and should be temporarily discontinued in the presence of conditions that alter renal function, see Section Contraindication

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 agents
Intravascular administration of iodinated contrast agents may lead to contrast induced nephropathy, resulting in metformin accumulation and an increased risk of lactic acidosis.

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 (see Section Dosage and Administration and Section Interactions).

Surgery
Metformin must be discontinued at the time of surgery under general, spinal or epidural anesthesia.
Therapy may be restarted no earlier than 48 hours following surgery or resumption of oral nutrition and provided that renal function has been re-evaluated and found to be stable.

PRECAUTIONS
For Glibenclamide:
To achieve the goal of treatment with Daonil®M - optimal control of blood glucose, adherence to correct diet, regular and sufficient physical exercise and, if necessary, reduction of body weight are just as necessary as regular ingestion of Daonil®M

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.

In accordance with current guidelines (e.g. European NIDDM consensus), the monitoring of certain other parameters is also recommended.

When starting treatment, the patient must be informed about the effects and risks of Daonil®M and about its interaction with dietary measures and physical exercise; the importance of adequate cooperation must also be stressed.

As is necessary during treatment with any blood-glucose-lowering drug, the patient and the physician must be aware of the risk of hypoglycaemia.

Factors favouring hypoglycaemia include:
- unwillingness or (more commonly in older patients) incapacity of the patient to cooperate.
- undernourishment, irregular mealtimes, or missed meals.
- imbalance between physical exertion and carbohydrate intake.
- alterations of diet.
- impaired renal function.
- serious liver dysfunction.
- overdosage with Daonil®M.
- uncompensated disorders of the endocrine system affecting carbohydrate metabolism or counter-regulation of hypoglycaemia (as for example in certain disorders of thyroid function and in anterior pituitary or adrenocortical insufficiency).
- concurrent administration of certain other medicines (see “DRUG INTERACTIONS”).
- treatment with glibenclamide in the absence of any indication.

The patient must inform the physician about such factors and about hypoglycaemic episodes since they may indicate the need for particularly careful monitoring.

If such risk factors for hypoglycaemia are present, it may be necessary to adjust the dosage of Daonil®M or the entire therapy. This also applies whenever illness occurs during therapy or the patient’s life-style changes.

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.

Those symptoms of hypoglycaemia which reflect the body's adrenergic counterregulation (see “ADVERSE REACTIONS”) may be milder or absent where hypoglycaemia develops gradually, where there is autonomic neuropathy or where the patient is receiving concurrent treatment with beta-blockers, clonidine, reserpine, guanethidine, or other sympatholytic drugs.

Hypoglycaemia can, almost always, be promptly controlled by immediate intake of carbohydrates (glucose or sugar, e.g., in the form of sugar lumps, sugar-sweetened fruit juice or tea).

For this purpose, patients must carry a minimum of 20 grams of glucose with them at all times. They may require the assistance of other persons to avoid complications.

Artificial sweeteners are ineffective in controlling hypoglycaemia.

Despite initially successful countermeasures, hypoglycaemia may recur. Patients must, therefore, remain under close observation.

Severe hypoglycaemia, or a protracted episode, which can only be temporarily controlled by usual amounts of sugar, further requires immediate treatment and follow-up by a physician and, in some circumstances, in-patient hospital care.

If treated by different physicians (e.g. hospital stay, after an accident, illness while on holiday), the patients must inform them of their diabetic condition and previous treatment.

Treatment of patients with G6PD-deficiency with sulfonylurea agents can lead to hemolytic anaemia. 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.

For Metformin:
Regular monitoring of thyroid-stimulating hormone (TSH) levels is recommended in patients with hypothyroidism (see Adverse reactions)

Long-term treatment with metformin has been associated with a decrease in vitamin B12 serum levels which may cause peripheral neuropathy. Monitoring of the vitamin B12 level is recommended (see Adverse reactions)

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.

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS

For Glibenclamide:
Alertness and reactions may be impaired by hypo- or hyperglycaemic episodes, especially when beginning or after altering treatment, or when Daonil®M is not taken regularly. This may, for example, affect the ability to drive or operate machinery.

For Metformin:
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 (sulfonylureas, insulin, repaglinide).

INTERACTIONS

For Glibenclamide:

Not recommended associations

Bosentan:

An increased incidence of elevated liver enzymes was observed in patients receiving glibenclamide concomitantly with bosentan.

Both glibenclamide and bosentan inhibit the bile salt export pump, leading to intracellular accumulation of cytotoxic bile salts. Therefore this combination should not be used (See Section "Warnings").

Take into account

Patients who take or discontinue taking certain other medicines while undergoing treatment with Daonil® M may experience changes in blood glucose control.

Glibenclamide is mainly metabolized by CYP 2C9 and to a lesser extent by CYP 3A4. This should be taken into account when glibenclamide is coadministered with inducers or inhibitors of CYP 2C9.

Potentiation of the blood-glucose-lowering effect and, thus, in some instances hypoglycaemia may occur when taking other drugs, including: insulin and other, oral antidiabetics, ACE inhibitors, anabolic steroids and male sex hormones, chloramphenicol, coumarin derivatives, cyclophosphamide, disopyramide, fenfluramine, fenyramidol, fibrates, fluoxetine, ifosfamide, MAO inhibitors, miconazole, para-aminosalicylic acid, pentoxifylline (high dose parenteral), phenylbutazone, azapropazone, oxyphenbutazone, probenecid, quinolones, salicylates, sulfinpyrazone, sulfonamides, sympatholytic agents such as beta-blockers and guanethidine, clarithromycin, tetracyclines, tritoqualine, trofosfamide.

Weakening of the blood-glucose-lowering effect and, thus, raised blood glucose levels may occur when taking other drugs, including: acetazolamide, barbiturates, corticosteroids, diazoxide, diuretics, epinephrine (adrenaline) and other sympathomimetic agents, glucagon, laxatives (after protracted use), nicotinic acid (in high doses), oestrogens and progestogens, phenothiazines, phenytoin, thyroid hormones, rifampicin.

H2-receptor antagonists, clonidine, and reserpine may lead to either potentiation or weakening of the blood-glucose-lowering effect.

Under the influence of sympatholytic drugs such as beta-blockers, clonidine, guanethidine, and reserpine, the signs of adrenergic counter-regulation to hypoglycaemia may be reduced or absent.

Both acute and chronic alcohol intake may potentiate or weaken the blood glucose-lowering action of glibenclamide in an unpredictable fashion.

Glibenclamide may either potentiate or weaken the effect of coumarin derivatives.

Glibenclamide may increase cyclosporine plasma concentration and potentially lead to its increased toxicity. Monitoring and dosage adjustment of cyclosporin are therefore recommended when both drug are coadministered.

Colesevelam binds to glibenclamide and reduces glibenclamide absorption from the gastro-intestinal tract. No interaction was observed when glibenclamide was taken at least 4 hours before colesevelam. Therefore glibenclamide should be administered at least 4 hours prior to colesevelam.

For Metformin:

Concomitant use not recommended:

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

Avoid consumption of alcohol and alcohol-containing medications.

Iodinated contrast agents : Metformin must be discontinued prior to, or at the time of the image procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable(See Section Dosage and Administration and Warnings).

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.

Glucocorticoids (systemic and local routes), beta-2-agonists and diuretics have intrinsic hyperglycaemic activity. Inform the patient and perform more frequent blood glucose monitoring, especially at the beginning of treatment. If necessary, adjust the dosage of the antidiabetic drug during therapy with the other drug and upon its discontinuation.

ACE-inhibitors may decrease the blood glucose levels. If necessary, adjust the dosage of the antidiabetic drug during therapy with the other drug and upon its discontinuation.

Metformin may decrease the anticoagulant effect of phenprocoumon. Therefore, a close monitoring of the INR is recommended.

Levothyroxine can reduce the hypoglycemic effect of metformin. Monitoring of blood glucose levels is recommended, especially when thyroid hormone therapy is initiated or stopped, and the dosage of metformin must be adjusted if necessary.

Organic cation transporters (OCT)

Metformin is a substrate of both transporters OCT1 and OCT2.

Co-administration of metformin with

• Inhibitors of OCT1 (such as verapamil) may reduce efficacy of metformin.

• Inducers of OCT1 (such as rifampicin) may increase gastrointestinal absorption and efficacy of metformin.

• Inhibitors of OCT2 (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 OCT1 and OCT2 (such as crizotinib, olaparib) may alter efficacy and renal elimination of metformin.

Caution is therefore advised, especially in patients with renal impairment, when these drugs are coadministered with metformin, as metformin plasma concentration may

increase. If needed, dose adjustment of metformin may be considered as OCT inhibitors/inducers may alter the efficacy of metformin

PREGNANCY
Daonil®M must not be taken during pregnancy. The patient must change over to insulin during pregnancy.

Patients planning a pregnancy must inform their physician. It is recommended that such patients change over to insulin.

LACTATION
To prevent possible ingestion with breast milk, Daonil®M must not be taken by breast-feeding women. If necessary the patient must change over to insulin, or must stop breast-feeding.

ADVERSE REACTIONS
The following CIOMS frequency rating is used, when applicable:
Very common ≥ 10%; Common ≥ 1 and < 10%; Uncommon ≥ 0.1 and < 1%;
Rare ≥ 0.01 and < 0.1%; Very rare < 0.01%; Not known (cannot be estimated from available data).

For Glibenclamide:
• ***Metabolism and nutrition disorders***

Hypoglycaemia (very common frequency), sometimes prolonged and even life-threatening, may occur as a result of the blood-glucose-lowering action of glibenclamide. This happens when there is imbalance between glibenclamide dosage, carbohydrate intake (diet), physical exercise and other factors influencing metabolism.

Possible symptoms of hypoglycaemia include headache, ravenous hunger, nausea, vomiting, lassitude, sleepiness, disordered sleep, restlessness, aggressiveness, impaired concentration, alertness and reactions, depression, confusion, speech disorders, aphasia, visual disorders, tremor, pareses, sensory disturbances, dizziness, helplessness, loss of self-control, delirium, cerebral convulsions, somnolence and loss of consciousness up to and including coma, shallow respiration and bradycardia.

In addition, signs of adrenergic counter-regulation may be present such as sweating, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris, and cardiac arrhythmias.

The clinical picture of a severe hypoglycaemic attack (very common frequency) may resemble that of a stroke.

The symptoms of hypoglycaemia nearly always subside when hypoglycaemia is corrected.

In isolated cases, sodium concentration in the serum may decrease (not known frequency).

• ***Eye disorders***
Especially at the start of treatment, there may be temporary visual impairment (not known frequency) due to the change in blood glucose levels. The cause is a temporary alteration in the turgidity and hence the refractive index of the lens, this being dependent on blood glucose level.

• ***Gastrointestinal disorders***
Gastrointestinal symptoms such as nausea (common frequency), vomiting **(**not known frequency), sensations of pressure or fullness in the epigastrium **(**uncommon frequency), abdominal pain **(**common frequency) and diarrhea **(**common frequency) may occur. However, despite continued treatment, these often subside and usually do not necessitate discontinuing glibenclamide.

• ***Hepatobiliary disorders***
There may be hepatitis **(**not known frequency), elevation of liver enzyme levels **(**not known frequency)and/or cholestasis **(**not known frequency)and jaundice **(**not known frequency) which may progress to life-threatening liver failure **(**not known frequency)but can regress after withdrawal of Daonil®M

• ***Blood and lymphatic system disorders***
Potentially life-threatening changes in the blood picture may occur. They may include - rarely - mild to severe thrombopenia (e.g. presenting as purpura) **(**not known frequency) and – in isolated cases - haemolytic anaemia**(**not known frequency), erythrocytopenia **(**not known frequency), leucopenia, granulocytopenia **(**not known frequency), agranulocytosis **(**not known frequency), and (e.g. due to myelosuppression) pancytopenia **(**not known frequency). In principle, these reactions are reversible once Daonil®M has been withdrawn.

• ***Immune system disorders***
Hypersensitivity reactions allergic or pseudoallergic reactions**(**not known frequency) may occur; they may be directed against glibenclamide itself, but may alternatively be triggered by excipients. Allergy to sulfonamide derivatives may also be responsible for an allergic reaction to glibenclamide. Mild reactions in the form of urticaria **(**not known frequency)may develop into serious and even life-threatening reactions with dyspnoea and fall in blood pressure, sometimes progressing to shock **(**not known frequency). In the event of urticaria, a physician must therefore be notified immediately.

- ***Skin and subcutaneous disorders***

Itching(not known frequency), rashes(common frequency), bullous reactions(not known frequency), erythema multiforme(not known frequency), dermatitis exfoliative(not known frequency) have been observed. Hypersensitivity of the skin to light(not known frequency) may occur.

Allergic vasculitis (not known frequency) may arise and, in some circumstances, may be life-threatening.

- ***Investigations***

Glibenclamide, like all sulfonylureas, can cause weight gain (common frequency).

For Metformin:
Gastrointestinal symptoms such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite (>10%) are very common: these occur most frequently during initiation of therapy and resolve spontaneously in most cases. To prevent these gastrointestinal symptoms, it is recommended that metformin be taken in 2 or 3 daily doses during or after meals. A slow increase of the dose may also improve gastrointestinal tolerability.

- Metallic taste (3%) is common.
- Mild erythema has been reported in some hypersensitive individuals. The incidence of such effects is regarded as very rare (<0.01%).
- A decrease of vitamin B12 absorption with decrease of serum levels has been observed in patients treated long-term with metformin and appears generally to be without clinical significance (<0.01%).
  However, cases of peripheral neuropathy in patients with vitamin B12 deficiency have been reported in post-marketing experience (frequency not known) (see Precautions)
- Lactic acidosis (0.03 cases/1000 patient-years) is very rare (see Warnings).
- Hemolytic anemia (frequency unknown)
- Reduction of thyrotropin level in patients with hypothyroidism (see Precautions) (frequency unknown)
- Hypomagnesemia in the context of diarrhea (frequency unknown)
- Encephalopathy (frequency unknown)
- Photosensitivity (frequency unknown)
- Hepatobiliary disorders: Reports of liver function tests abnormalities and hepatitis resolving upon metformin discontinuation

OVERDOSE
For Glibenclamide:
Signs and symptoms
Acute overdose as well as long-term treatment with too high a dose of glibenclamide may lead to severe, protracted, life-threatening hypoglycaemia.

Management
As soon as an overdose of glibenclamide has been discovered, a physician must be notified without delay. The patient must immediately take sugar, if possible in the form of glucose, unless a physician has already undertaken responsibility for treating the overdose.

Careful monitoring is essential until the physician is confident that the patient is out of danger. It must be remembered that hypoglycaemia and its clinical signs may recur after initial recovery.

Admission to hospital may sometimes be necessary - even as precautionary measure. In particular, significant overdoses and severe reactions with signs such as loss of consciousness or other serious neurological disorders are medical emergencies and require immediate treatment and admission to hospital.

If, for example, the patient is unconscious, an intravenous injection of concentrated glucose solution is indicated (for adults starting with 40 ml of 20% solution, for example). Alternatively in adults, administration of glucagon, e.g. in doses of 0.5 to 1 mg i.v., s.c. or i.m., may be considered.

In particular when treating hypoglycaemia in infants and young children, the dose of glucose given must be very carefully adjusted in view of the possibility of producing dangerous hyperglycaemia, and must be controlled by close monitoring of blood glucose.

Patients who have ingested life-threatening amounts of Daonil®M require detoxification (e.g. by gastric lavage and medicinal charcoal).

After acute glucose replacement has been completed, it is usually necessary to give an intravenous glucose infusion in lower concentration so as to ensure that the hypoglycaemia does not recur. The patient's blood glucose level should be carefully monitored for at least 24 hours. In severe cases with a protracted course, hypoglycaemia, or the danger of slipping back into hypoglycaemia, may persist for several days.

For Metformin:
Hypoglycaemia has not been seen with metformin doses of up to 85 g, although lactic acidosis has occurred in such circumstances. High overdose or concomitant risks of metformin may lead to lactic acidosis. Lactic acidosis is a medical emergency and must be treated in hospital. The most effective method to remove lactate and metformin is haemodialysis.

Pancreatitis may occur in the context of a metformin overdose.

STORAGE CONDITIONS
Keep in a cool dry place. Keep out of reach of children

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