PRODUCT INFORMATION

DIAMICRON® MR

modified release tablets

Gliclazide

NAME OF THE DRUG

DIAMICRON® MR 30mg: gliclazide 30mg modified release tablet blister pack
DIAMICRON® MR 60mg: gliclazide 60mg modified release tablet blister pack

DESCRIPTION

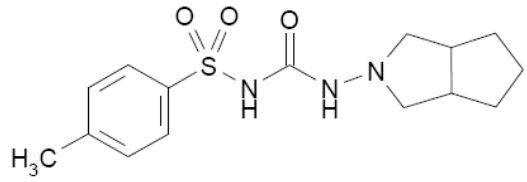
DIAMICRON® MR 30mg and ***DIAMICRON® MR 60mg*** are modified release formulations.

Active Ingredient
Gliclazide is a white or almost white powder, practically insoluble in water, freely soluble in dichloromethane, sparingly soluble in acetone and slightly soluble in ethanol 96%. The melting point of gliclazide is approximately 168°C.

Chemical Name : 1-(3-azabicyclo[3.3.0]oct-3-yl)-3-*p*-tolylsulfonylurea

Molecular Formula : $C_{15}H_{21}N_3O_3S$

Chemical Structure :



Excipients
DIAMICRON® MR 30mg*:* Calcium hydrogen phosphate, maltodextrin, hypromellose, magnesium stearate and silica–colloidal anhydrous.

DIAMICRON® MR 60mg*:* Lactose monohydrate, maltodextrin, hypromellose, magnesium stearate and silica–colloidal anhydrous.

PHARMACOLOGY

Gliclazide is an oral hypoglycaemic sulfonylurea which differs from other related compounds. It has an N-containing heterocyclic ring with an endocyclic bond.

Gliclazide reduces blood glucose levels by stimulating insulin secretion from the β-cells of the islets of Langerhans. Gliclazide shows high affinity, strong selectivity and reversible binding to the β-cell K_{ATP} channels with a low affinity for cardiac and vascular K_{ATP} channels. Increased postprandial insulin and C-peptide secretion persists after two years of treatment. Gliclazide also has extra-pancreatic effects and haemovascular properties.

Effects on insulin release
In type II diabetes, gliclazide restores the first peak of insulin secretion in response to glucose and increases the second phase of insulin secretion. A significant increase in insulin release is seen in response to stimulation induced by a meal or glucose.

Extra-pancreatic effects

Gliclazide has been shown to increase peripheral insulin sensitivity:

- In muscle, euglycaemic hyperinsulinaemic clamp studies with gliclazide have demonstrated significantly increased (35%) insulin mediated glucose uptake which may improve diabetes control. Gliclazide potentiates insulin action on muscle glycogen synthase. These effects are consistent with a post-transcriptional action of gliclazide on GLUT4 glucose transporters.
- Studies on glucose turnover have further shown that gliclazide decreases hepatic glucose production, leading to an improvement in fasting blood glucose levels.

Other actions

Gliclazide has been shown in some studies to have actions independent of that on glucose levels. These haemovascular effects of gliclazide include:

- Partial inhibition of platelet aggregation and adhesion with a decrease in markers of platelet activation (beta thromboglobulin, thromboxane B2)
- Increased vascular endothelial fibrinolytic activity (increased tPA activity)
- Anti-oxidant properties, notably a reduction in plasma lipid peroxides and increased erythrocyte superoxide dismutase activity
- Inhibition of the increased adhesiveness of type II diabetic patient's monocytes to endothelial cells *in vitro*.

The anti-oxidant, platelet inhibiting and fibrinolytic actions of gliclazide involve processes which have been implicated in the pathogenesis of vascular complications of type II diabetes. There is no clinical evidence that the haemovascular effects of gliclazide are of therapeutic benefit in type II diabetes patients.

Pharmacokinetics

Hydration of the tablets induces formation of a gel to activate drug release. Plasma levels increase progressively, resulting in a plateau-shaped curve from the sixth to the twelfth hour after administration. Intra-individual variability is low. Gliclazide is completely absorbed and food intake does not affect the rate or degree of absorption. The relationship between the dose administered and the area under the concentration curve as a function of time is linear for doses of gliclazide up to 90mg/day. At the highest evaluated dose (135mg/day), the AUC increases slightly more than proportionally to the dose.

Plasma protein binding is approximately 95%. Gliclazide is mainly metabolised in the liver, the products of which are extensively excreted in the urine. Less than 1% of unchanged drug is recovered in the urine. No active metabolites have been detected in plasma. The clearance of gliclazide has been found to be slightly reduced as a function of age. This reduction, however, is not considered to be clinically significant. The elimination half-life of gliclazide is approximately 16 hours.

No clinically significant modifications in the pharmacokinetic parameters have been observed in elderly patients.

Pharmacokinetic studies have demonstrated bioequivalence between:
-one ***DIAMICRON MR 60mg*** tablet and two ***DIAMICRON MR 30mg*** tablets, and;
-one ***DIAMICRON MR 60mg*** tablet and two halves of one ***DIAMICRON MR 60mg*** tablet.

INDICATIONS

DIAMICRON MR 30mg and ***DIAMICRON MR 60mg*** are indicated for the treatment of type II diabetes in association with dietary measures and with, physical exercise when these measures alone are inadequate to control blood glucose.

During controlled clinical trials in patients with type II diabetes, a modified release formulation of gliclazide (30mg - 120mg), taken as a single daily dose, was shown to be effective long term in controlling blood glucose levels, based on monitoring of HbA1c.

CONTRAINDICATIONS

DIAMICRON MR 30mg and ***DIAMICRON MR 60mg*** are contra-indicated in the following cases:

• hypersensitivity to gliclazide, other sulfonylureas, sulphonamides, or to any of the excipients;
• type 1 diabetes;
• diabetic pre-coma and coma; diabetic keto-acidosis;
• severe renal or hepatic insufficiency: in these cases, the use of insulin is recommended;
• treatment with miconazole (refer to Interactions);
• pregnancy and lactation (refer to Use in pregnancy and Use in lactation).

PRECAUTIONS

Hypoglycaemia:
This treatment should only be prescribed if the patient is likely to have a regular food intake (including breakfast). It is important to have a regular carbohydrate intake due to the increased risk of hypoglycaemia if a meal is delayed, an inadequate amount of food is consumed or the food is low in carbohydrate. Hypoglycaemia is more likely to occur during periods of low-calorie diet, following prolonged or strenuous exercise, following alcohol intake or during treatment with a combination of hypoglycaemic agents.

Hypoglycaemia may occur following administration of sulphonylureas (refer to ADVERSE REACTIONS). Some cases may be severe and prolonged. This may involve hospitalisation and glucose infusion may need to be continued for several days.

Careful selection of patients and of the dose used, as well as provision of adequate information to the patient are necessary to reduce hypoglycaemic episodes.
Hypoglycaemia may be difficult to recognise in elderly patients and those receiving beta-blockers.

Factors which increase the risk of hypoglycaemia:

- patient refuses or (particularly in elderly subjects) is unable to co-operate;
- poor general health, malnutrition, irregular mealtimes, skipping meals, periods of fasting or dietary changes;
- imbalance between physical exercise and carbohydrate intake;
- renal insufficiency;
- severe hepatic insufficiency;
- overdose of ***DIAMICRON***;
- certain endocrine disorders: thyroid disorders, hypopituitarism and adrenal insufficiency;
- concomitant administration of certain other medicines (see Interactions with other medicines).
- Renal and hepatic insufficiency: the pharmacokinetics and/or pharmacodynamics of gliclazide may be altered in patients with hepatic insufficiency or severe renal failure. Hepatic insufficiency may also reduce the capacity for neoglucogenesis. A hypoglycaemic episode occurring in these patients may be prolonged, so appropriate management should be initiated.

Patient information:
The risks of hypoglycaemia, together with its symptoms (refer to ADVERSE REACTIONS), treatment and conditions that predispose to its development, should be explained to the patient and to family members.

The patient should be informed of the importance of following dietary advice, of taking regular exercise, and of regular monitoring of blood glucose levels.

Poor blood glucose control
Blood glucose control in treated patients may be jeopardised by: St John's Wort (*Hypericum Perforatum*) preparations, fever, trauma, infection or surgical intervention. It may be necessary to discontinue treatment and to administer insulin in these cases.

The efficacy of oral antidiabetic agents often decreases in the long term. This may be due to progression in the severity of the diabetes, or to a reduced response to treatment. This phenomenon is known as secondary failure and should be distinguished from primary failure, when the drug is ineffective as first-line treatment. However, before classifying the patient as a secondary failure, dose adjustment and reinforcement of dietary measures should be considered.

Dysglycaemia
Disturbances in blood glucose, including hypoglycaemia and hyperglycaemia have been reported in diabetic patients receiving concomitant treatment with fluoroquinolones, especially in elderly patients. Indeed, careful monitoring of blood glucose is recommended in all patients receiving at the same time ***DIAMICRON MR*** and a fluoroquinolone.

Laboratory tests: measurement of glycated haemoglobin levels (or fasting venous plasma glucose) is recommended in assessing blood glucose control. Blood glucose self-monitoring may also be useful.

Glucose-6-phosphate dehydrogenase deficiency (G6PD)
Treatment of patients with G6PD-deficiency with sulfonylurea agents can lead to haemolytic anaemia. Since gliclazide belongs to the chemical class of sulfonylurea drugs, caution should be used in patients with G6PD-deficiency and a non-sulfonylurea alternative should be considered.

Porphyric patients:
Cases of acute porphyria have been described with some other sulfonylurea drugs, in patients who have porphyria.

Lactose intolerance
Due to the presence of lactose in ***DIAMICRON MR 60mg***, patients with rare hereditary problems of galactose intolerance, glucose galactose malabsorption, or the Lapp lactase deficiency should not take this medicinal product.

Use in pregnancy (Category C)
There is no or limited amount of data (less than 300 pregnancy outcomes) from the use of gliclazide in pregnant women even though there are few data with other sulfonylurea.

In animal studies, gliclazide is not teratogenic.

The use of gliclazide during pregnancy is contraindicated.

Control of diabetes should be obtained before the time of conception to reduce the risk of congenital abnormalities linked to uncontrolled diabetes.

Oral hypoglycaemic agents are not suitable, insulin is the drug of choice for treatment of diabetes during pregnancy. It is recommended that oral hypoglycaemic therapy is changed to insulin before a pregnancy is attempted, or as soon as pregnancy is discovered.

Use in lactation
It is unknown whether gliclazide or its metabolites are excreted in human milk. Given the risk of neonatal hypoglycaemia, the product is therefore contra-indicated in breast-feeding mother. A risk to the newborns/infants cannot be excluded.

Fertility
No effect on fertility or reproductive performance was noted in male and female rats.

Interactions with other medicines

1) The following products are likely to increase the risk of hypoglycaemia
   Contra-indicated combination:
   Miconazole (systemic route, oromucosal gel): increases the hypoglycaemic effect with possible onset of hypoglycaemic symptoms, or even coma.

   Combinations which are not recommended

Phenylbutazone (systemic route): increases the hypoglycaemic effect of sulphonylureas (shifts their binding to plasma proteins and / or reduces their elimination).
It is preferable to use a different anti-inflammatory agent, otherwise, warn the patient and emphasise the importance of self monitoring: if necessary, adjust the dose during and after treatment with the anti-inflammatory.

Alcohol: increases the hypoglycaemic reaction (by inhibiting compensatory reactions) and may potentiate the onset of hypoglycaemic coma. Ingestion of alcohol may also cause a disulfiram-like reaction with characteristic flushing of the face, throbbing headache, giddiness, tachypnoea, tachycardia or angina pectoris. Chronic alcohol abuse may, as a result of liver enzyme induction, increase the metabolism of sulfonylurea drugs, shortening the plasma half life and duration of action.

Avoid alcohol or medicines containing alcohol.

Combinations requiring precautions for use
Potentiation of the blood glucose lowering effect and thus, in some instances, hypoglycaemia may occur during concomitant treatment with the following drugs: other antidiabetics (insulin, acarbose, metformin, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, GLP-1 receptor agonists), clofibrate, salicylates (high doses), chloramphenicol, beta-blockers, fluconazole, angiotensin converting enzyme inhibitors (captopril, enalapril), H2-receptor antagonists, MAOIs, sulphonamides, clarithromycin, and nonsteroidal anti-inflammatory drugs.

Warn the patient and emphasise the importance of self-monitoring of blood glucose levels. It may be necessary to adjust the dose of the antidiabetic agent during treatment with these substances.

2) The following products may cause an increase in blood glucose levels

Combination which is not recommended
Danazol: diabetogenic effect of danazol.
If the use of this drug cannot be avoided, warn the patient and emphasise the importance of urine and blood glucose self monitoring. It may be necessary to adjust the dose of the antidiabetic during and after treatment with danazol.

Combinations requiring precautions during use
As with all hypoglycaemics, caution should be observed in administering thiazide diuretics, since these diuretics have been reported to aggravate the diabetic state.

Chlorpromazine (neuroleptics): at high doses (> 100 mg per day of chlorpromazine) this increases blood glucose levels (reduced insulin release).

Warn the patient and emphasise the importance of blood glucose self-monitoring. It may be necessary to adjust the dose of the antidiabetic agent during treatment with the neuroleptic agent and after its discontinuation.

Glucocorticoids (systemic route and local route: intra-articular, cutaneous and rectal preparations) and tetracosactrin: increase in blood glucose with possible ketosis (reduced tolerance to carbohydrates by corticosteroids).
Warn the patient and emphasise the importance of blood glucose monitoring, particularly at the start of treatment. It may be necessary to adjust the dose of the antidiabetic during treatment with corticosteroids and after discontinuation.

Ritodrine, salbutamol, terbutaline: (I.V. route)
Increased blood glucose levels due to beta-2 agonists.
Emphasise the importance of monitoring blood glucose levels. If necessary, switch to insulin.

Saint John's Wort (Hypericum perforatum) preparations:
Gliclazide exposure is decreased by Saint John's Wort – *Hypericum perforatum*.
Emphasize the importance of blood glucose levels monitoring.

Barbiturates, oestrogens and progestogens

3) The following products may cause dysglycaemia

   Combinations requiring precautions during use
   Fluoroquinolones:
   In case of a concomitant use of ***DIAMICRON MR*** and a fluoroquinolone, the patient should be warned of the risk of dysglycaemia, and the importance of blood glucose monitoring should be emphasized.

4) *Combinations which should be taken into account*
   Anticoagulants (e.g. warfarin)
   Sulphonylureas may lead to potentiation of anticoagulation during concurrent treatment.
   It may be necessary to adjust the dose of the anticoagulant.

Laboratory tests
Glycated haemoglobin should be monitored regularly. Blood glucose measurement may also be useful.

Effects on ability to drive and use machines
DIAMICRON MR has no or negligible influence on the ability to drive and use machines. However, patients should be made aware of the symptoms of hypoglycaemia and should be careful if driving or operating machinery, especially at the beginning of treatment.

ADVERSE REACTIONS

Good clinical acceptability of gliclazide, has been established in many studies as well as in medical practice.

The safety of a modified release formulation of gliclazide (30mg - 120mg) has been evaluated in controlled clinical trials in 955 patients, of which 728 patients were treated in long-term comparative trials, against a gliclazide immediate release formulation (80mg - 320mg), for up to 10 months. In these comparative trials, the overall incidence and type of adverse events were similar in both groups. Adverse events were generally mild and transient, not requiring discontinuation of therapy.

However, where patients did discontinue due to adverse events, the percentage was lower in the modified release group (2.9%) than in the immediate release group (4.5%).

The most frequent adverse reaction with gliclazide is **hypoglycaemia** (refer to **PRECAUTIONS** and **OVERDOSAGE**)

As is the case with all sulphonylurea drugs, hypoglycaemic reactions have been reported following gliclazide administration. However, a number of studies have shown that hypoglycaemia is less common with gliclazide than with glibenclamide.

Possible symptoms of hypoglycaemia are: headache, intense hunger, nausea, vomiting, lassitude, sleep disorders, agitation, aggression, poor concentration, reduced awareness and slowed reactions, depression, confusion, visual and speech disorders, aphasia, tremor, paresis, sensory disorders, dizziness, feeling of powerlessness, loss of self-control, delirium, convulsions, shallow respiration, bradycardia, drowsiness and loss of consciousness, possibly resulting in coma and/or death.

In addition, signs of adrenergic counter-regulation may be observed: sweating, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris and cardiac arrhythmia.

Usually, symptoms disappear after intake of carbohydrate such as sugar (artificial sweeteners have no effect). Experience with other sulphonylureas shows that hypoglycaemia can recur even when these measures are initially effective.

If a hypoglycaemic episode is severe or prolonged, and even if it is temporarily controlled by intake of sugar, immediate medical treatment or even hospitalisation is required.

Gastrointestinal disorders, including abdominal pain, nausea, vomiting, dyspepsia, diarrhoea and constipation have been reported; if these should occur they can be avoided or minimised if gliclazide is taken with breakfast.

In long-term comparative studies, the percentage of patients experiencing hypoglycaemic episodes was similar between patients treated with the modified release formulation of gliclazide (11.6%) and those treated with the immediate release formulation of gliclazide (11.1%). However, the number of hypoglycaemic episodes per 100 patient months was lower in the modified release group (3.5) than in the immediate release group (4.8).

Analysis of elderly patients (over 65 years old) showed less hypoglycaemia than in the general population, with a prevalence of hypoglycaemic episodes lower in the modified release group (2.6 hypoglycaemic episodes for 100 patient months) than in the immediate release group (4.1).

The percentage of patients experiencing hypoglycaemic episodes in the sub-population with renal failure, was similar to that observed in the general population.

Other adverse events
Adverse events reported during controlled clinical trials with the modified release formulation of gliclazide were those expected in an ageing population with diabetes.

Adverse events that were reported in at least 2.0% of patients, in long-term controlled clinical studies, are presented in the following table. The most frequent adverse events were not specifically related to the disease (such as respiratory infections or back pain).

Treatment emergent adverse events* (listed by body system) occurring in ≥2.0% of patients in long-term controlled clinical trials

	Gliclazide modified release tablets (30mg-120mg) n=728 %	Gliclazide immediate release tablets (80mg – 320mg) n=734 %
Resistance mechanism		
Infection viral	7.7	5.6
Respiratory		
Rhinitis	4.4	4.6
Bronchitis	4.4	4.6
Pharyngitis	4.3	3.5
Upper respiratory infection	3.3	3.7
Coughing	2.1	2.0
Musculo-skeletal		
Back pain	5.2	4.1
Arthralgia	3.0	3.5
Arthrosis	2.2	2.2
Secondary term		
Inflicted injury	4.3	4.5
Body as a whole		
Headache	3.8	4.6
Asthenia	2.2	2.6
Cardiovascular		
Hypertension	3.2	3.7
Angina pectoris	2.1	2.2
Urinary		
Urinary tract infections	2.6	3.0

Gastrointestinal		
Diarrhoea	2.5	2.0
Central, periph., nervous system		
Dizziness	2.2	2.3
Metabolism and nutrition		
Hyperglycaemia	1.9	2.2

*whatever the relationship to treatment

Analysis of adverse events in sub-populations showed a similar pattern to that seen in the general population. Gender, age and renal insufficiency had no significant influence on the safety profile of the modified release formulation of gliclazide.

Gastrointestinal disturbances (reported with gliclazide), including nausea, dyspepsia, diarrhoea, abdominal pain, vomiting and constipation may be avoided or minimised if gliclazide is taken with breakfast.

The following adverse events have been rarely reported:

- Skin and mucosae reactions pruritus, urticaria, angioedema, maculopapular rashes, rash, erythema and, bullous reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis and autoimmune bullous disorders), and exceptionally, drug rash with eosinophilia and systemic symptoms (DRESS).
- Haematological disorders (as with other sulfonylurea drugs): a few rare cases of anaemia, leucopenia, thrombocytopenia and, agranulocytosis.
- Occasional elevations of serum creatinine, blood urea nitrogen, serum bilirubin and hepatic enzyme (AST, ALT, alkaline phosphatase) levels and exceptionally, hepatitis. Treatment should be discontinued if cholestatic jaundice appears. These symptoms usually disappear after discontinuation of treatment.
- As with any glucose lowering medication, transient visual disorders may occur on initiation of treatment, due to changes in blood glucose levels.

Class attribution effects:
As for other sulfonylureas, the following adverse events have been observed: cases of erythrocytopenia, agranulocytosis, haemolytic anaemia, pancytopenia, allergic vasculitis, hyponatraemia, elevated liver enzyme levels and even impairment of liver function (e.g. with cholestasis and jaundice) and hepatitis which regressed after withdrawal of the sulphonylurea or led to life threatening liver failure in isolated cases.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

DOSAGE AND ADMINISTRATION

Oral use.

For adult use only.

DIAMICRON MR 30mg tablets do not have a break bar and must not be broken in half. Tablets must be administered whole.

DIAMICRON MR 60mg tablets have a break bar and may be administered as whole or as half tablets (see Pharmacokinetics).

So that the modified release properties of the product can be maintained, ***DIAMICRON MR 30mg*** and ***DIAMICRON MR* 60mg** tablets should not be chewed or crushed.

These products should be taken with food because there is an increased risk of hypoglycemia if a meal is taken late, if an inadequate amount of food is consumed or if the food is low in carbohydrate. It is recommended that the medication be taken at breakfast time. If a dose is forgotten, the dose taken on the next day should not be increased.

- A single daily dose provides an effective blood glucose control. The initial recommended dose for these products is 30mg daily, even in elderly patients (≥ 65 years). For ***DIAMICRON MR 30mg*** the single daily dose may be between one (30mg) and four (120mg), tablets.

- For ***DIAMICRON MR 60mg*** the single daily dose may be between half a tablet (30mg) and two tablets (120mg).

For both ***DIAMICRON MR 30mg*** and ***DIAMICRON MR 60mg***, the daily dose should not exceed 120mg.

Previously untreated patients should commence with a dose of 30mg and will benefit from dose titration until the appropriate dose is reached.
As with all hypoglycaemic agents, doses should be titrated according to the individual patient's response. Titration should be carried out in steps of 30mg, according to the fasting blood glucose response. Each step should last for at least one month between each increment, except in patients whose blood glucose do not decrease after two weeks of treatment. In this case, it is possible to propose a dosage increase at the end of the 2nd week treatment.

Across the dose range, one half of a ***DIAMICRON MR 60mg*** tablet, can replace one tablet of ***DIAMICRON MR 30mg***, or one tablet of gliclazide 80mg immediate release (refer to the following table for other dose equivalences).

Dose equivalences between *DIAMICRON MR* 60mg*, DIAMICRON MR* 30mg and Gliclazide 80mg immediate release formulation.

***DIAMICRON MR* 60mg**	***DIAMICRON MR* 30mg**	**Gliclazide 80mg immediate release**
half tablet (30 mg)	1 tablet (30 mg)	1 tablet (80 mg)
1 tablet (60 mg)	2 tablets (60 mg)	2 tablets (160 mg)
1.5 tablets (90 mg)	3 tablets (90 mg)	3 tablets (240 mg)
2 tablets (120 mg)	4 tablets (120 mg)	4 tablets (320 mg)

DIAMICRON MR 30mg or ***DIAMICRON MR 60mg****,* may be used to replace other antidiabetic treatments without any transitional period. If a patient is switched from a hypoglycaemic sulfonylurea with a prolonged half-life he/she should be carefully monitored (for one to two weeks) in order to avoid hypoglycaemia due to possible residual effects of the previous therapy.

DIAMICRON MR 30mg or ***DIAMICRON MR 60mg***, may be given in combination with biguanides, alpha glucosidase inhibitors or insulin.

In patients not adequately controlled with ***DIAMICRON MR*** concomitant insulin therapy can be initiated under close medical supervision.

Elderly subjects: The efficacy and tolerance of the modified release formulation of gliclazide (30mg - 120mg) has been confirmed in clinical trials in subjects over 65 years who were given the same dosage regimen as the general population. The dosage is therefore identical to that recommended for adults under the age of 65 years.

Renal insufficiency: The efficacy and tolerance of the modified release formulation of gliclazide (30mg - 120mg) has been confirmed in clinical trials of subjects with mild to moderate renal failure (creatinine clearance of between 15 and 80mL/min) who were given the same dosage regimen as the general population. No dosage adjustment is therefore required in subjects with impaired renal function.

In patients at risk of hypoglycaemia:
- states of undernourishment or malnutrition,

- severe or poorly compensated endocrine pathologies (hypopituitarism, hypothyroidism, adrenal insufficiency),
- withdrawal from prolonged and /or high dose corticosteroid therapy,
- severe vascular disease (severe coronary heart disease, severe carotid impairment, diffuse vascular disease)

It is recommended that treatment be systematically initiated with a minimal dose of 30mg / day.
There are no data or clinical studies in children.

OVERDOSAGE

Overdose of sulfonylureas may cause hypoglycaemia.

Moderate symptoms of hypoglycaemia, (without any loss of consciousness or neurological signs), should be corrected by carbohydrate intake, dose adjustment and/or modification of diet. Strict monitoring should be continued until the doctor is sure that the patient is out of danger.

Severe hypoglycaemic reactions are possible (with coma, convulsions or other neurological disorders) and should be treated as a medical emergency, requiring immediate hospitalisation.

If hypoglycaemic coma is diagnosed or suspected, the patient should be given a rapid I.V. injection of 50 ml of concentrated glucose solution (20 to 30%). This should be, followed by continuous infusion of a more dilute glucose solution (10%) at a rate necessary to maintain blood glucose levels above 5mmol/L.

It is recommended that patients should be monitored closely for a 48 hour period at least.

Plasma clearance of gliclazide may be prolonged in patients with hepatic disease. However, due to the strong binding of gliclazide to proteins, dialysis is not effective in these patients.

PRESENTATION AND STORAGE CONDITIONS

Presentation:

DIAMICRON MR 30mg gliclazide 30mg modified release tablets:

Modified release tablets, 30mg available in 60's.

The tablets are white oblong tablets with an engraving of "DIA 30" on one face and  on the other face.

DIAMICRON MR 60mg gliclazide 60mg modified release tablets:

Modified release tablets, 60mg available in 30s.

The tablets are white oblong tablets, scored with a break bar on both sides with an engraving of "DIA 60" on both faces.

Storage conditions:

Store below 30°C.

Shelf-life:

3 years.

Date of Last Revision of Pack Insert: April 2020

Les Laboratoires Servier – France
Manufacturer:

Les Laboratoires Servier Industrie
45520 Gidy – France

Servier (Ireland) Industries Ltd
Gorey Road – Arklow
Co. Wicklow – Ireland