SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DIAMICRON 30 mg, modified release tablet.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains gliclazide 30 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified release tablet.
White, oblong tablet engraved on both faces, 'DIA 30' on one face and  on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Non insulin-dependent diabetes (type 2) in adults when dietary measures, physical exercise and weight loss alone are not sufficient to control blood glucose.

4.2 Posology and method of administration

Posology
The daily dose may vary from 1 to 4 tablets per day, *i.e.* from 30 to 120 mg taken orally in a single intake at breakfast time.
It is recommended that the tablet(s) be swallowed whole.
If a dose is forgotten, there must be no increase in the dose taken the next day.

As with any hypoglycaemic agent, the dose should be adjusted according to the individual patient's metabolic response (blood glucose, HbAlc)

- Initial dose
  The recommended starting dose is 30 mg daily.
  If blood glucose is effectively controlled, this dose may be used for maintenance treatment.
  If blood glucose is not adequately controlled, the dose may be increased to 60, 90 or 120 mg daily, in successive steps. The interval between each dose increment should be at least 1 month except in patients whose blood glucose has not reduced after two weeks of treatment. In such cases, the dose may be increased at the end of the second week of treatment.
  The maximum recommended daily dose is 120 mg.

- Switching from Diamicron 80 mg tablets to Diamicron 30 mg modified release tablets:
  1 tablet of Diamicron 80 mg is comparable to 1 tablet of Diamicron 30 mg. Consequently the switch can be performed provided a careful blood monitoring.

- Switching from another oral antidiabetic agent to Diamicron 30 mg:
  Diamicron 30 mg can be used to replace other oral antidiabetic agents.
  The dosage and the half-life of the previous antidiabetic agent should be taken into account when switching to Diamicron 30 mg.
  A transitional period is not generally necessary. A starting dose of 30 mg should be used and this should be adjusted to suit the patient's blood glucose response, as described above.

When switching from a hypoglycaemic ~~sulphonylurea~~ sulfonylurea with a prolonged half-life, a treatment free period of a few days may be necessary to avoid an additive effect of the two products, which might cause hypoglycaemia. The procedure described for initiating treatment should also be used when switching to treatment with Diamicron 30 mg, *i.e.* a starting dose of 30 mg/day, followed by a stepwise increase in dose, depending on the metabolic response.

- Combination treatment with other antidiabetic agents:
Diamicron 30 mg can be given in combination with biguanides, alpha glucosidase inhibitors or insulin.
In patients not adequately controlled with Diamicron 30 mg, concomitant insulin therapy can be initiated under close medical supervision.

Special Populations

Elderly
Diamicron 30 mg should be prescribed using the same dosing regimen recommended for patients under 65 years of age.

~~*Patients with r*~~*Renal impairment*
In patients with mild to moderate renal insufficiency the same dosing regimen can be used as in patients with normal renal function with careful patient monitoring. These data have been confirmed in clinical trials.

Patients at risk of hypoglycaemia:
- U~~u~~ndernourished or malnourished,
- S~~s~~evere or poorly compensated endocrine disorders (hypopituitarism, hypothyroidism, adrenocorticotrophic insufficiency),
- W~~w~~ithdrawal of prolonged and/or high dose corticosteroid therapy,
- S~~s~~evere vascular disease (severe coronary heart disease, severe carotid impairment, diffuse vascular disease).

It is recommended that the minimum daily starting dose of 30 mg is used.

Paediatric population
The safety and efficacy of Diamicron 30 mg in children and adolescents have not been established. No data are available in children.

4.3 Contraindications

This medicine is contra-indicated in case of:

- Hypersensitivity to gliclazide or to any of the excipients listed in section 6.1, other ~~sulphonylureas~~sulfonylureas, ~~sulphonamides~~sulfonamides,
- ~~t~~Type 1 diabetes,
- D~~d~~iabetic pre-coma and coma, diabetic keto-acidosis,
- S~~s~~evere renal or hepatic insufficiency: in these cases the use of insulin is recommended,
- T~~t~~reatment with miconazole (see Section 4.5),
- L~~l~~actation (see Section 4.6).

4.4 Special warnings and precautions for use

Hypoglycaemia:
This treatment should be prescribed only 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 taken late, if an inadequate amount of food is consumed or if the food is low in carbohydrate. Hypoglycaemia is more likely to occur during low-calorie diets, following prolonged or strenuous exercise, alcohol intake or if a combination of hypoglycaemic agents is being used.

Hypoglycaemia may occur following administration of ~~sulphonylureas~~ sulfonylureas (see Section 4.8.). Some cases may be severe and prolonged. Hospitalisation may be necessary and glucose administration may need to be continued for several days.
Careful selection of patients, of the dose used, and clear patient directions are necessary to reduce the risk of hypoglycaemic episodes.
Factors which increase the risk of hypoglycaemia:

- patient refuses or (particularly in elderly subjects) is unable to co-operate,
- 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 Section 4.5).

Renal and hepatic insufficiency: the pharmacokinetics and/or pharmacodynamics of gliclazide may be altered in patients with hepatic insufficiency or severe renal failure. 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 (see section 4.8), 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 a patient receiving antidiabetic treatment may be affected by any of the following: St. John's Wort (*Hypericum perforatum*) preparations (see section 4.5), fever, trauma, infection or surgical intervention. In some cases, it may be necessary to administer insulin.

The hypoglycaemic efficacy of any oral antidiabetic agent, including gliclazide, is attenuated over time in many patients: 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 which is distinct from primary failure, when an active substance is ineffective as first-line treatment. Adequate dose adjustment and dietary compliance should be considered before classifying the patient as secondary failure.

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, carefull monitoring of blood glucose is recommended in all patients receiving at the same time DIAMICRON 30 mg 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.

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.

4.5 Interactions with other medicinal products and other forms of interaction

~~1)~~ The following products are likely to increase the risk of hypoglycaemia

Formatted: Indent: Left: 0.64", No bullets or numbering

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~~ sulfonylureas (displaces their binding to plasma proteins and/or reduces their elimination).
  It is preferable to use a different anti-inflammatory agent, or else to warn the patient and emphasise the importance of self-monitoring. Where necessary, adjust the dose during and after treatment with the anti-inflammatory agent.

- **Alcohol:** increases the hypoglycaemic reaction (by inhibiting compensatory reactions) that can lead to the onset of hypoglycaemic coma.
  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 when one of the following drugs is taken:
other antidiabetic agents (insulins, acarbose,metformin, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, GLP-1 receptor agonists), beta-blockers, fluconazole, angiotensin converting enzyme inhibitors (captopril, enalapril), H2-receptor antagonists, MAOIs, sulfonamides, clarithromycin and nonsteroidal anti-inflammatory agents.

~~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 active substance cannot be avoided, warn the patient and emphasise the importance of urine and blood glucose monitoring. It may be necessary to adjust the dose of the antidiabetic agent during and after treatment with danazol.

Combinations requiring precautions during use

- **Chlorpromazine** (neuroleptic agent): high doses (>100 mg per day of chlorpromazine) increase blood glucose levels (reduced insulin release).
  Warn the patient and emphasise the importance of blood glucose monitoring. It may be necessary to adjust the dose of the antidiabetic active substance during and after treatment with the neuroleptic agent.

- **Glucocorticoids** (systemic and local route: intra-articular, cutaneous and rectal preparations) and tetracosactrin: increase in blood glucose levels with possible ketosis (reduced tolerance to carbohydrates due to glucocorticoids).
  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 active substance during and after treatment with glucocorticoids.

- **Ritodrine, salbutamol, terbutaline**: (I.V.)
  Increased blood glucose levels due to beta-2 agonist effects.
  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.

The following products may cause dysglycaemia

Combinations requiring precautions during use

- **Fluoroquinolones:** in case of a concomitant use of DIAMICRON 30 mg and a fluoroquinolone, the patient should be warned of the risk of dysglycaemia, and the importance of blood glucose

monitoring should be emphasized.

3) Combination which must be taken into account

- **Anticoagulant therapy** (Warfarin ...):
  Sulfonylureas may lead to potentiation of anticoagulation during concurrent treatment.
  Adjustment of the anticoagulant may be necessary.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no experience or limited amount of data (less than 300 pregnancy outcomes) from with the use of gliclazide in pregnant women during pregnancy in human, even though there are few data with other sulfonylurea.
In animal studies, gliclazide is not teratogenic (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of Gliclazide during pregnancy.

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 first 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.

Breast-feeding
It is not unknown whether gliclazide or its metabolites are excreted in human breast 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 (see section 5.3).

4.7 Effects on ability to drive and use machines

Diamicron 30 mg has no known 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.

4.8 Undesirable effects

Based on the experience with gliclazide, the following undesirable effects have been reported.

The most frequent adverse reaction with gliclazide is h Hypoglycaemia
As for other sulfonylureas, treatment with Diamicron can cause hypoglycaemia, if mealtimes are irregular and, in particular, if meals are skipped. 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 lethal outcome.
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 carbohydrates (sugar). However, artificial sweeteners have no effect. Experience with other sulphonylureas sulfonylureas shows that hypoglycaemia can recur even when measures prove effective initially.

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 are required.

Gastrointestinal disturbances, 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.

The following undesirable effects have been more rarely reported:

- Skin and subcutaneous tissue disorders: rash, pruritus, urticaria, angioedema, erythema, maculopapular rashes, bullous reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis), and exceptionally, drug rash with eosinophilia and systemic symptoms (DRESS).

- Blood and lymphatic system disorders: Changes in haematology are rare. They may include anaemia, leucopenia, thrombocytopenia, granulocytopenia. These are in general reversible upon discontinuation of medication.

- Hepato-biliary disorders: raised hepatic enzyme levels (AST, ALT, alkaline phosphatase), hepatitis (isolated reports). Discontinue treatment if cholestatic jaundice appears.

These symptoms usually disappear after discontinuation of treatment.

- Eye disorders
  Transient visual disturbances may occur especially on initiation of treatment, due to changes in blood glucose levels.

- Class attribution effects:
  As for other ~~sulphonylureas~~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 sulfonylurea or led to life-threatening liver failure in isolated cases.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 listed in Appendix V.

4.9 Overdose

An overdose of ~~sulphonylureas~~ sulfonylureas may cause hypoglycaemia.
Moderate symptoms of hypoglycaemia, without any loss of consciousness or neurological signs, must be corrected by carbohydrate intake, dose adjustment and/or change of diet. Strict monitoring should be continued until the doctor is sure that the patient is out of danger.
Severe hypoglycaemic reactions, with coma, convulsions or other neurological disorders are possible and must 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 that will maintain blood glucose levels above 1 g/L. Patients should be monitored closely and, depending on the patient's condition after this time, the doctor will decide if further monitoring is necessary.
Dialysis is of no benefit to patients due to the strong binding of gliclazide to proteins.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ~~sulphonamides~~sulfonamides, urea derivative
ATC code: A10BB09

Mechanism of action
Gliclazide is a hypoglycaemic ~~sulphonylurea~~ sulfonylurea oral antidiabetic active substance differing from other related compounds by 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. Increase in postprandial insulin and C-peptide secretion persists after two years of treatment.
In addition to these metabolic properties, gliclazide has haemovascular properties.

Pharmacodynamic effects
Effects on insulin release
In type 2 diabetics, 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 response is seen in response to stimulation induced by a meal or glucose.

Haemovascular properties~~:~~
Gliclazide decreases microthrombosis by two mechanisms which may be involved in complications of diabetes:

- A~~a~~ partial inhibition of platelet aggregation and adhesion, with a decrease in the markers of platelet activation (beta thromboglobulin, thromboxane B_2).
- ~~a~~An action on the vascular endothelium fibrinolytic activity with an increase in tPA activity.

5.2 Pharmacokinetic properties

Absorption
Plasma levels increase progressively during the first 6 hours, reaching a plateau which is maintained from the sixth to the twelfth hour after administration.
Intra-individual variability is low.
Gliclazide is completely absorbed. Food intake does not affect the rate or degree of absorption.

Distribution
Plasma protein binding is approximately 95%. The volume of distribution is around 30 litres.
A single daily intake of Diamicron 30 mg maintains effective gliclazide plasma concentrations over 24 hours.

Biotransformation
Gliclazide is mainly metabolised in the liver and excreted in the urine: less than 1% of the unchanged form is found in the urine. No active metabolites have been detected in plasma.

Elimination
The elimination half-life of gliclazide varies between 12 and 20 hours.

Linearity/non-linearity
The relationship between the dose administered ranging up to 120 mg and the area under the concentration time curve is linear.

Special populations
Elderly
No clinically significant changes in pharmacokinetic parameters have been observed in elderly patients.

Formatted: Font: Italic, No underline

Formatted: Font: Italic, No underline

Formatted: Underline

Formatted: Underline

Formatted: Underline

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of repeated dose toxicity and genotoxicity. Long term carcinogenicity studies have not been done. No teratogenic changes have been shown in animal studies, but lower fœtal body weight was observed in animals receiving doses 25 fold higher than the maximum recommended dose in humans. Fertility and reproductive performance were unaffected after gliclazide administration in animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate dihydrate,
Maltodextrin,
Hypromellose,
Magnesium stearate,
Anhydrous colloidal silica.

Formatted: Not All caps

Formatted: Not All caps

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

7, 10, 14, 20, 28, 30, 56, 60, 84, 90, 100, 112, 120, 180 and 500 tablets in Aluminium/Poly(vinylchloride) blister, packed in cardboard boxes.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

To be completed nationally.
For RMS (France):
Les Laboratoires Servier
50, rue Carnot
92284 Suresnes cedex– France

8. MARKETING AUTHORISATION NUMBER

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}
Date of latest renewal: {DD month YYYY}

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

MM/YYYY

[To be completed nationally]

LABELLING AND PACKAGE LEAFLET

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Diamicron 30 mg, modified release tablets.
Gliclazide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains: gliclazide 30 mg

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

7 modified release tablets
10 modified release tablets
14 modified release tablets
20 modified release tablets
28 modified release tablets
30 modified release tablets
56 modified release tablets
60 modified release tablets
84 modified release tablets
90 modified release tablets
100 modified release tablets
112 modified release tablets
120 modified release tablets
180 modified release tablets
500 modified release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Swallow your tablets whole. Do not chew or crush.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally-]
For RMS (France):
Les Laboratoires Servier
50, rue Carnot
92284 Suresnes cedex- France

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch {number}

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]
~~Medicinal product subject to medical prescription.~~

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]-
For RMS (France):
Diamicron 30 mg

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Diamicron 30 mg, modified release tablets.
Gliclazide

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally].
For RMS (France):
Les Laboratoires Servier

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch {number}

5. OTHER

PACKAGE LEAFLET

Package Leaflet: Information for the patient~~user~~

DIAMICRON® 30 mg modified release tablets
Gliclazide

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects , talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Diamicron 30 mg is and what it is used for

Diamicron 30 mg is a medicine that reduces blood sugar levels (oral antidiabetic medicine belonging to the ~~sulphonylurea~~ sulfonylurea group).
Diamicron 30 mg is used in a certain form of diabetes (type 2 diabetes mellitus) in adults, when diet, exercise and weight loss alone do not have an adequate effect on keeping blood sugar at the correct level.

2. What you need to know before you take Diamicron 30 mg

Do not take Diamicron 30 mg
- if you are allergic to gliclazide or any of the other ingredients of Diamicron 30 mg (listed in section 6), or to other medicines of the same group (~~sulphonylureas~~sulfonylureas), or to other related medicines (hypoglycaemic ~~sulphonamides~~sulfonamides);
- if you have insulin-dependent diabetes (type 1);
- if you have ketone bodies and sugar in your urine (this may mean you have diabetic keto-acidosis), a diabetic pre-coma or coma;
- if you have severe kidney or liver disease;
- if you are taking medicines to treat fungal infections (miconazole) (~~,~~see ~~S~~section "~~Taking o~~Other medicines and Diamicron 30 mg");
- if you are breastfeeding (see s~~S~~ection "Pregnancy and breastfeeding").

Warnings and precautions
Talk to your doctor before taking Diamicron 30 mg.
You should observe the treatment plan prescribed by your doctor to achieve proper blood sugar levels. This means, apart from regular tablet intake, ~~you~~ to observe the dietary regimen, have physical exercise and, where necessary, reduce weight.

During gliclazide treatment regular monitoring of your blood (and possibly urine) sugar level and also your glycated haemoglobin (HbA1c) is necessary.

In the first few weeks of treatment the risk of having reduced blood sugar levels (hypoglycaemia) may be increased. So particularly close medical monitoring is necessary~~:~~.

Low blood sugar (Hypoglycaemia) may occur:
- if you take meals irregularly or skip meals altogether,
- if you are fasting,
- if you are malnourished,
- if you change your diet,
- if you increase your physical activity and carbohydrate intake does not match this increase,
- if you drink alcohol, especially in combination with skipped meals,
- if you take other medicines or natural remedies at the same time,
- if you take too high doses of gliclazide,
- if you suffer from particular hormone-induced disorders (functional disorders of the thyroid gland, of the pituitary gland or adrenal cortex),
- if your kidney function or liver function is severely decreased.

If you have low blood sugar you may have the following symptoms:
headache, intense hunger, nausea, vomiting, weariness, sleep disorders, restlessness, aggressiveness, poor concentration, reduced alertness and reaction time, depression, confusion, speech or visual disorders, tremor, sensory disturbances, dizziness, and helplessness.
The following signs and symptoms may also occur: sweating, clammy skin, anxiety, fast or irregular heart beat, high blood pressure, sudden strong pain in the chest that may radiate into nearby areas (angina pectoris).

If blood sugar levels continue to drop you may suffer from considerable confusion (delirium), develop convulsions, lose self control, your breathing may be shallow and your heart beat slowed down, you may become unconscious.

In most cases the symptoms of low blood sugar vanish very quickly when you consume some form of sugar, ~~*e.g.*~~ for instance glucose tablets, sugar cubes, sweet juice, sweetened tea.
You should therefore always carry some form of sugar with you (glucose tablets, sugar cubes). Remember that artificial sweeteners are not effective. Please contact your doctor or the nearest hospital if taking sugar does not help or if the symptoms recur.

Symptoms of low blood sugar may be absent, less obvious or develop very slowly or you are not aware in time that your blood sugar level has dropped. This may happen if you are an elderly patient taking certain medicines (for instance ~~*e.g.*~~ those acting on the central nervous system and beta blockers).
If you are in stress-situations (~~*e.g.*~~ accidents, surgical operations, fever etc.) your doctor may temporarily switch you to insulin therapy.

Symptoms of high blood sugar (hyperglycaemia) may occur when gliclazide has not yet sufficiently reduced the blood sugar, when you have not complied with the treatment plan prescribed by your doctor, if you take St John's Wort (*Hypericum perforatum*) preparations (see section "Other medicines and Diamicron 30 mg"), or in special stress situations. These may include thirst, frequent urination, dry mouth, dry itchy skin, skin infections and reduced performance.

If these symptoms occur, you must contact your doctor or pharmacist.

Blood glucose disturbance (low blood sugar and high blood sugar) can occur when gliclazide is prescribed at the same time than medicines belonging to a class of antibiotics called fluoroquinolones, especially in elderly patients. In this case, your doctor will remind you the importance of monitoring your blood glucose.

If you have a family history of or know you have the hereditary condition glucose-6-phosphate dehydrogenase (G6PD) deficiency (abnormality of red blood cells), lowering of the hemoglobin level and breakdown of red blood cells (hemolytic anemia) can occur. Contact your doctor before taking this medicinal product.

Children and adolescents
Diamicron 30 mg is not recommended for use in children due to a lack of data.

Other medicines and Diamicron 30 mg
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
The blood sugar lowering effect of gliclazide may be strengthened and signs of low blood sugar levels may occur when one of the following medicines is taken:

- other medicines used to treat high blood sugar (oral antidiabetics, GLP-1 receptor agonists or insulin),
- antibiotics (~~e.g. sulphonamides~~sulfonamides, clarithromycin),
- medicines to treat high blood pressure or heart failure (beta blockers, ACE-inhibitors such as captopril, or enalapril),
- medicines to treat fungal infections (miconazole, fluconazole),
- medicines to treat ulcers in the stomach or duodenum (H_2 receptor antagonists),
- medicines to treat depression (monoamine oxidase inhibitors),
- painkiller or antirheumatics (phenylbutazone, ibuprofen),
- medicines containing alcohol.

The blood glucose lowering effect of gliclazide may be weakened and raised blood sugar levels may occur when one of the following medicines is taken:
- medicines to treat disorders of the central nervous system (chlorpromazine),
- medicines reducing inflammation (corticosteroids),
- medicines to treat asthma or used during labour (intravenous salbutamol, ritodrine and terbutaline),
- medicines to treat breast disorders, heavy menstrual bleeding and endometriosis (danazol)~~.~~,
- St John's Wort -*Hypericum perforatum*-preparations.

Blood glucose disturbance (low blood sugar and high blood sugar) can occur when a medicine belonging to a class of antibiotics called fluoroquinolones is taken at the same time than Diamicron 30mg, especially in elderly patients.

Diamicron 30 mg may increase the effects of medicines which reduce blood clotting (~~e.g.~~ warfarin).

Consult your doctor before you start taking another medicinal product. If you go into hospital tell the medical staff you are taking Diamicron 30 mg.

~~Taking~~ Diamicron 30 mg with food, drink and alcohol
Diamicron 30 mg can be taken with food and non-alcoholic drinks.
Drinking alcohol is not recommended as it can alter the control of your diabetes in an unpredictable manner.

Pregnancy and breastfeeding
Diamicron 30 mg is not recommended for use during pregnancy. If you are pregnant~~ or breast feeding~~, think you may be pregnant or are planning to have a baby, ask~~while taking this medicine,inform~~ your doctor for advice before taking this medicine.~~so that he may prescribe a more suitable treatment for you~~

You must not take Diamicron 30 mg while you are breastfeeding.

Driving and using machines
Your ability to concentrate or react may be impaired if your blood sugar is too low (hypoglycaemia), or too high (hyperglycaemia) or if you develop visual problems as a result of such conditions. Bear in mind that you could endanger yourself or others (~~e.g.~~for instance when driving a car or using machines). Please ask your doctor whether you can drive a car if you:
- have frequent episodes of low blood sugar (hypoglycaemia),
- have few or no warning signals of low blood sugar (hypoglycaemia).

3. How to take Diamicron 30 mg

Dose
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
The dose is determined by the doctor, depending on your blood and possibly urine sugar levels.
Change in external factors (~~e.g.~~ weight reduction, change in life style, stress) or improvements in the blood sugar control may require changed gliclazide doses.
The recommended daily dose is one to four tablets (maximum 120 mg) in a single intake at breakfast time. This depends on the response to treatment.
Diamicron 30 mg is for oral use. Take your tablet(s) with a glass of water at breakfast time (and preferably at the same time each day). Swallow your tablets whole. Do not chew them.
You must always eat a meal after taking your tablet(s).

Formatted: Centered

If a combination therapy of Diamicron 30 mg with metformin, an alpha glucosidase inhibitor, a thiazolidinedione, a dipeptidyl peptidase-4 inhibitor, a GLP-1 receptor agonist or insulin is initiated your doctor will determine the proper dose of each medicine individually for you.

If you notice that your blood sugar levels are high although you are taking the medicine as prescribed, you should contact your doctor or pharmacist .

~~**Routes and method of administration**~~
~~Oral use.~~
~~Swallow your tablets whole. Do not chew them.~~
~~Take your tablet(s) with a glass of water at breakfast time (and preferably at the same time each day).~~
~~You must always eat a meal after taking your tablet(s).~~

If you take more Diamicron 30 mg than you should
If you take too many tablets, contact your doctor or the nearest hospital Accident & Emergency department immediately. The signs of overdose are those of low blood sugar (hypoglycaemia) described in Section 2. The symptoms can be helped by taking sugar (4 to 6 lumps) or sugary drinks straight away, followed by a substantial snack or meal. If the patient is unconscious immediately inform a doctor and call the emergency services. The same should be done if somebody, for instance ~~e.g.~~ a child, has taken the product unintentionally. Unconscious patients must not be given food or drink.
It should be ensured that there is always a pre-informed person that can call a doctor in case of emergency.

If you forget to take Diamicron 30 mg
It is important to take your medicine every day as regular treatment works better.
However, if you forget to take a dose of Diamicron 30 mg, take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Diamicron 30 mg
As the treatment for diabetes is usually life long, you should discuss with your doctor before stopping this medicinal product. Stopping could cause high blood sugar (hyperglycaemia) which increases the risk of developing complications of diabetes.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines this medicine can cause side effects, although not everybody gets them.

The most commonly observed side effect is low blood sugar (hypoglycaemia). For symptoms and signs see Section "Warnings and precautions".
If left untreated these symptoms could progress to drowsiness, loss of consciousness or possibly coma. If an episode of low blood sugar is severe or prolonged, even if it is temporarily controlled by eating sugar, you should seek immediate medical attention.

Liver disorders
There have been isolated reports of abnormal liver function, which can cause yellow skin and eyes. If you get this, see your doctor immediately. The symptoms generally disappear if the medicine is stopped. Your doctor will decide whether to stop your treatment.

Skin disorders
Skin reactions such as rash, redness, itching, hives, angioedema (rapid swelling of tissues such as eyelids, face, lips, mouth, tongue or throat that may result in breathing difficulty) have been reported. The rash may progress to widespread blistering or peeling of the skin.
Exceptionally, signs of severe hypersensitivity reactions (DRESS) have been reported: initially as flu-like symptoms and a rash on the face then an extended rash with a high temperature.

Blood disorders
Decrease in the number of cells in the blood (for instance ~~e.g.~~ platelets, red and white blood cells) which may cause paleness, prolonged bleeding, bruising, sore throat and fever have been reported. These symptoms usually vanish when the treatment is discontinued.

Digestive disorders
Abdominal pain, nausea, vomiting, indigestion, diarrhoea, and constipation. These effects are reduced when Diamicron 30 mg is taken with a meal as recommended.

Eye disorders
Your vision may be affected for a short time especially at the start of treatment. This effect is due to changes in blood sugar levels.

As for other ~~sulphonylureas~~sulfonylureas, the following adverse events have been observed: cases of severe changes in the number of blood cells and allergic inflammation of the wall of blood vessels, reduction in blood sodium (hyponatraemia), symptoms of liver impairment (for instance ~~e.g.~~ jaundice) which in most cases disappeared after withdrawal of the ~~sulphonylureas~~sulfonylureas, but may lead to life-threatening liver failure in isolated cases.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Diamicron 30 mg

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the blister strip after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Diamicron 30 mg contains
The active substance is gliclazide. Each tablet contains 30 mg of gliclazide, in a modified release formulation.
The other ingredients are: calcium hydrogen phosphate dihydrate, maltodextrin, hypromellose, magnesium stearate, anhydrous colloidal silica.

What Diamicron 30 mg looks like and contents of the pack
Diamicron 30 mg is a white oblong modified release tablet, engraved on both faces, 'DIA 30' on one face and  on the other. The tablets are available in blister packed in cartons of 7, 10, 14, 20, 28, 30, 56, 60, 84, 90, 100, 112, 120, 180 or 500 tablets.
Not all pack sizes may be available.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

[To be completed nationally].
For RMS (France):
Les Laboratoires Servier
50, rue Carnot
92284 Suresnes cedex– France

Manufacturers

Les Laboratoires Servier Industrie
905 route de Saran
45520 Gidy - France

or

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

or

ANPHARM Przedsiębiorstwo Farmaceutyczne S.A.
Ul. Annopol 6B
03-236 Warszawa - Poland

or

IBERFAR Indústria Farmacêutica SA.
rua Consiglieri Pedroso (IBERFAR), n° 123,
2734-501 Queluz de Baixo - Portugal

or

Qualiti (Burnley) Limited
Talbot Street, Briercliffe
Burnley,
Lancashire BB10 2JY - United Kingdom

or

LABORATORIOS SERVIER S.L.
Avd. de los Madroños, 33
28043 Madrid - Spain

This medicinal product is authorised in the Member States of the EEA under the following names

Austria	DIAMICRON® MR 30 mg
Belgium	UNI DIAMICRON®
Cyprus	DIAMICRON® MR 30 mg
Czech Republic	DIAPREL® MR
Denmark	DIAMICRON UNO® 30 mg
Estonia	DIAPREL® MR
France (RMS)	DIAMICRON® 30 mg
Germany	DIAMICRON® UNO 30 mg
Greece	DIAMICRON® MR
Hungary	DIAPREL® MR
Iceland	DIAMICRON UNO® 30 mg
Ireland	DIAMICRON® MR 30 mg
Italy	DIAMICRON® 30mg
~~Latvia~~	~~DIAPREL® MR~~
Lithuania	DIAPREL® MR
Luxembourg	DIAMICRON® 30 mg
Malta	DIAMICRON® MR
Netherlands	DIAMICRON® MR 30 mg
Poland	DIAMICRON® 30 mg
Portugal	DIAMICRON® LM 30 mg
Slovakia	DIAPREL® MR
Slovenia	DIAPREL® MR
Spain	DIAMICRON 30 mg
United Kingdom	DIAMICRON® 30 mg MR

This leaflet was last revised in {MM/YYYY}.