SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

<Invented name> 90 mg modified-release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each modified-release tablet contains 90 mg gliclazide.

Excipient(s) with known effect
Each modified-release tablet contains 133.1 mg lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified-release tablet

White to almost white, capsule shaped, biconvex tablets with two score lines around the tablet.
The tablet can be divided into equal doses.
Tablet dimension: length 17.0 – 17.5 mm and thickness 4.6 – 5.4 mm

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Non-insulin dependent Diabetes mellitus (Type II) 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 of gliclazide may vary from 30 to 120 mg taken orally in a single intake at breakfast time.
If a dose is forgotten, there must be no increase in the dose taken next day.
As with any hypoglycaemic agent, the dose should be adjusted according to the individual patient's metabolic response (blood glucose, HbA1c).

Initial dose
The recommended starting dose is 30 mg daily (one third of <Invented name> 90 mg modified-release tablet).
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.

One <Invented name> 90 mg modified-release tablet corresponds to one and a half gliclazide 60 mg scored modified-release tablet. <Invented name> 90 mg modified-release tablets can be trisected.

The breakability of the <Invented name> 90 mg modified-release tablets enables flexibility of dosing to be achieved.

<Invented name> 90 mg modified-release tablets can provide the following doses: a 30 mg dose (one third of the <Invented name> 90 mg modified-release tablet), a 60 mg dose (two thirds of the <Invented name> 90 mg modified-release tablet), a 90 mg dose (one <Invented name> 90 mg modified-release tablet) and a 120 mg dose (one <Invented name> 90 mg modified-release tablet and a third of another <Invented name> 90 mg modified-release tablet).

If necessary, the tablet may also be trisected in order to facilitate the intake (e.g. for 90 mg dose; one <Invented name> 90 mg modified-release tablet can be divided into three equal parts for easier swallowing).

Switching from gliclazide 80 mg tablets to <Invented name> modified-release tablets
One tablet of gliclazide 80 mg is comparable to one gliclazide modified-release tablet 30 mg (i.e. one third of the <Invented name> 90 mg modified-release tablet). Consequently, the switch can be performed with careful blood monitoring.

Switchover from another oral antidiabetic medicinal product to <Invented name> 90 mg:
<Invented name> modified-release tablets can be used to replace another oral antidiabetic medicinal product.
The dosage and the half-life of the previous antidiabetic agent should be taken into account when switching to gliclazide modified release tablets.
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 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 <Invented name> modified release tablets, i.e. a starting dose of 30 mg/day, followed by a stepwise increase in dose, depending on the metabolic response.

Combination with other antidiabetic medicines
<Invented name> modified-release tablets can be given in combination with biguanides, alpha-glucosidase inhibitors or insulin. In patients not adequately controlled with <Invented name> modified-release tablets, concomitant insulin therapy can be initiated under close medical supervision.

Special populations

Elderly
<Invented name> modified-release tablets should be prescribed using the same dosing regimen recommended for patients under 65 years of age.

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
- undernourishment or malnourishment,
- severe or poorly compensated endocrine disorders (hypopituitarism, hypothyroidism, adrenocorticotrophic insufficiency),
- withdrawal of a prolonged and/or high-dose corticoid therapy,

– severe vascular disease (serious 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 <Invented name> in children and adolescents have not been established.
No data are available in children.

Method of administration

<Invented name> is to be taken as a single dose at breakfast time.
It is recommended to swallow the tablet or tablet third(s) whole without crushing or chewing.

The tablet can be divided by hand along the score lines. The tablet should not be divided in any other way.

4.3 Contraindications

- Hypersensitivity to gliclazide or to any of the excipients listed in section 6.1, other sulfonylureas or sulphonamides
- Type 1 diabetes
- Diabetic pre-coma and coma, diabetic ketoacidosis
- Severe renal or hepatic insufficiency (in these cases the use of insulin is recommended)
- Treatment with miconazole (see Section 4.5)
- Lactation (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 caloric diets, following prolonged or strenuous exercise, alcohol intake or if a combination of hypoglycaemic agents is being used.

Hypoglycaemia may occur following administration of 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 cooperate
- malnutrition, irregular mealtimes, skipping meals, periods of fasting or dietary changes
- imbalance between physical exercise and of carbohydrates intake
- renal insufficiency
- severe hepatic insufficiency
- overdose of <Invented name> modified-release tablet
- certain endocrine disorders: thyroid disorders, hypopituitarism and adrenal insufficiency
- concomitant administration with 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 risk 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 gliclazide 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.

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

Other ingredients
<Invented name> modified release tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

1) The following medicines can increase the risk of hypoglycaemia:

Contraindicated 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 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. It may be necessary to adjust the dose of the antidiabetic active substance during and after treatment with the anti-inflammatory agent.

Alcohol: increases in the hypoglycaemic reaction (by inhibiting compensatory reactions) that can lead to the onset of hypoglycaemic coma. Alcohol or medicinal products containing alcohol should be avoided.

Combinations requiring precautions for use
Potentiation of the blood glucose lowering effect and thus in some instances hypoglycaemia may also occur when one of the following medicinal products is taken:
other antidiabetics (insulins, acarbose, metformin, thiazolidinediones, dipeptidylpeptidase-4 inhibitors, GLP-1 receptor agonists), beta blockers, fluconazole, ACE inhibitors (captopril, enalapril), H_2-receptor antagonists, MAO inhibitors, sulfonamides, clarithromycin and non-steroidal anti-inflammatory agents.

2) <u>The following medicinal products may cause an increase in blood glucose levels:</u>

Combination which is not recommended
Danazol: diabetogenic effect of danazol.
If the use of this active substance cannot be avoided the patient must be warned and informed of the importance of urine and blood glucose monitoring. It may be necessary to adjust the dose of the antidiabetic active substance during and after treatment with danazol.

Combinations requiring precautions during use
Chlorpromazine (neuroleptic agent): High doses (>100 mg per day of chlorpromazine) increase in blood glucose levels (reduction of insulin release).
Warn the patient and emphasize 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 the glucocorticoids). Warn the patient and emphasize 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 sugar level due to beta-2-agonist effects. The patient must be informed of the importance of blood glucose monitoring. A switch to insulin treatment may be necessary.

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.

<u>The following products may cause dysglycaemia</u>
Combinations requiring precautions during use
- **Fluoroquinolones**: in case of a concomitant use of gliclazide 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 has to be taken into account:
Anticoagulant therapy (e.g. warfarin, etc.):
Sulfonylureas may lead to potentiation of anticoagulation during concurrent treatment. Adjustment of the dose of the anticoagulant may be necessary.

4.6 Fertility, pregnancy and lactation

Pregnancy
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 sulfonylureas.

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 unknown whether gliclazide or its metabolites are excreted in human milk. Given the risk of neonatal hypoglycaemia the product is contraindicated 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

<Invented name> 90 mg modified-release tablet has no or negligible influence on the ability to drive and use machines. However, patients must 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.

Description of selected adverse reactions

Hypoglycaemia
The most frequent adverse reaction with gliclazide is hypoglycaemia
As with other sulfonylureas, treatment with <Invented name> modified-release tablets can commonly cause hypoglycaemia if meals are taken irregularly, and, in particular, if they 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 the intake of carbohydrates (sugar). However, artificial sweeteners have no effect. Experience with other 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.

Other undesirable effects

Gastrointestinal disorders
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 autoimmune bullous disorders), 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 and granulocytopenia. These are generally reversible upon discontinuation of the medication.

Hepatobiliary 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 sulfonylureas, the following undesirable effects have been observed: cases of erythrocytopenia, agranulocytosis, haemolytic anaemia, pancytopenia, allergic vasculitis, hyponatremia, 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

Symptoms
An overdose of 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.

Management
If a 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 a 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 closely monitored 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: Drugs used in diabetes; sulfonylureas; ATC code: A10BB09.

Mechanism of action
Gliclazide is a hypoglycaemic sulfonylurea oral antidiabetic 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 partial inhibition of platelet aggregation and adhesion with a decrease in the markers of platelet activation (beta thromboglobulin, thromboxane B_2);
- 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 <Invented name> modified-release tablets 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 is 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 relevant changes in the pharmacokinetic parameters have been observed in elderly patients.

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

Hypromellose
Lactose monohydrate
Silica, colloidal anhydrous
Magnesium stearate

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

1.3.1	Gliclazide
SPC, Labeling and Package Leaflet	DE

DE/H/892/003
Pack sizes: 10 x 1, 20 x 1, 30 x 1, 60 x 1 or 90 x1 tablet in perforated unit dose blisters (OPA/Alu/PVC foil//Alu peel-off foil)
Pack sizes: 10 x 1, 20 x 1, 30 x 1, 60 x 1 or 90 x 1 tablet in perforated unit dose blisters (OPA/Alu/PVC foil//PET/Alu peel-off foil)
DE/H/894/003
Pack sizes: 10 x 1, 30 x 1, 40 x 1 or 60 x 1 tablet in perforated unit dose blisters (OPA/Alu/PVC foil//Alu peel-off foil)
Pack sizes: 10 x 1, 30 x 1, 40 x 1 or 60 x 1 tablet in perforated unit dose blisters (OPA/Alu/PVC foil//PET/Alu peel-off foil)

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]

Detailed information on this medicinal product is available on the website of {name of MS Agency (link)}

1.3.1	Gliclazide
SPC, Labeling and Package Leaflet	DE

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

<Invented name> 90 mg modified-release tablets

gliclazide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each modified-release tablet contains 90 mg gliclazide.

3. LIST OF EXCIPIENTS

Also contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Modified-release tablet

DE/H/892/003
10 x 1 modified-release tablet
20 x 1 modified-release tablet
30 x 1 modified-release tablet
60 x 1 modified-release tablet
90 x 1 modified-release tablet

DE/H/894/003
10 x 1 modified-release tablet
30 x 1 modified-release tablet
40 x 1 modified-release tablet
60 x 1 modified-release tablet

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Swallow your tablet or third(s) of a tablet in one piece. Do not chew or crush.
Read the package leaflet before use.

Oral use

1. Hold the blister at the edges, bend along the perforations and separate one blister cell from the rest of the blister by gently tearing along the perforations around it.
2. Pull up the edge of the foil and peel the foil off completely.
3. Tip the tablet out onto your hand.

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

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]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

1.3.1	Gliclazide
SPC, Labeling and Package Leaflet	DE

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

<Invented name> 90 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
<NN>

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

<Invented name> 90 mg modified-release tablets

gliclazide

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

1. Bend and tear.
2. Peel.

PACKAGE LEAFLET

Package leaflet: Information for the user

<Invented name> 90 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 <Invented name> is and what it is used for

<Invented name> is a medicine that reduces blood sugar levels (oral antidiabetic medicine belonging to the sulfonylurea group).

<Invented name> 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 <Invented name>

Do not take <Invented name>
- if you are allergic to gliclazide or any of the other ingredients of this medicine (listed in section 6), or to other medicines of the same group (sulfonylureas) or to other related medicines (hypoglycaemic sulfonamides);
- if you have insulin-dependent diabetes (type 1);
- if you have ketone bodies and sugar in your urine (this may mean that you have diabetic ketoacidosis), 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 section "Other medicines and <Invented name>");
- if you are breast feeding (see section "Pregnancy and breast-feeding").

Warnings and precautions
Talk to your doctor or pharmacist before taking <Invented name>.

You should observe the treatment plan prescribed by your doctor to achieve proper blood sugar levels. This means, apart from regular tablet intake, 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 without an appropriate increase in carbohydrate intake,
- 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 the 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 and 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 the 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. 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 (e.g. those acting on the central nervous system and beta-blockers).

If you are in stress-situations (e.g. accident, surgical operations, fever, etc.) your doctor may temporarily switch you to insulin therapy.

Symptoms of high blood sugar level (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 <Invented name>"), 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.

Cases of acute porphyria have been described with some other sulfonylurea drugs, in patients who have porphyria (inherited genetic disorders with accumulation in the body of porphyrins or porphyrin precursors).

Children and adolescents
<Invented name> is not recommended for use in children due to a lack of data.

Other medicines and <Invented name>
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 levels (oral antidiabetics, GLP-1 receptor agonists or insulin),
- antibiotics (e.g. 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 (H2 receptor antagonists),
- medicines to treat depression (monoamine oxidase inhibitors),
- painkillers 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 inflammations (corticosteroids)
- medicines to treat asthma or used during labour (intravenous salbutamol, ritodrine, 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 <Invented name>, especially in elderly patients.

<Invented name> may increase the effect 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 that you are taking <Invented name>.

<Invented name> with food, drink and alcohol
<Invented name> 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, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor so that he may prescribe a more suitable treatment for you.

<Invented name> is not recommended for use during pregnancy.
You must not take <Invented name> while you are breast-feeding.

Driving and using machines
Your ability to concentrate or react may be impaired if your blood sugar level 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. 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 levels (hypoglycaemia),
- have few or no warning signals of low blood sugar (hypoglycaemia).

<Invented name> contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take <Invented name>

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 your 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 blood sugar may require changed gliclazide doses.

The recommended dose is 30 mg up to 120 mg modified-release tablets of gliclazide in a single intake at breakfast. This depends on the response to treatment.
The tablets can be divided into three equal parts to provide any of the following doses:
a 30 mg dose (take one third of a tablet), a 60 mg dose (take two thirds of a tablet), a 90 mg dose (take one whole tablet) and a 120 mg dose (take one whole tablet and a third of another tablet).
You can also divide the tablet into three equal parts for easier swallowing.

If a combination therapy of <Invented name> modified-release tablet 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.

Method of use

Oral use

To take a tablet out of the packaging:

1. Hold the blister at the edges, bend along the perforations and separate one blister cell from the rest of the blister by gently tearing along the perforations around it.
2. Pull up the edge of the foil and peel the foil off completely.
3. Tip the tablet out onto your hand.

How to divide your <Invented name> tablet:
The tablet is marked with two score lines so it can be divided into three equal parts.

4. Divide the tablet by hand along the score lines. Hold the tablet between your thumb and index finger close to the score line for your dose of the tablet as shown in the picture 4. Do not divide the tablet in any other way.

Swallow your tablet or third(s) of a tablet in one piece with a glass of water at breakfast time (and preferably at the same time every day).

Do not chew or crush. You must always eat a meal after taking this medicine.

If you take more <Invented name> than you should
If you take too many tablets, contact your doctor or the nearest hospital Accident & Emergency department immediately. The signs of an overdose and those of low blood sugar (hypoglycaemia) are 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 or call the emergency services. The same should be done if somebody, 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 <Invented name>
It is important that you take the medicine every day as regular treatment works better.
However, if you forget to take a dose of <Invented name> take the next dose at the usual time. Do not take a double dose to make up for the forgotten dose.

If you stop taking <Invented name>
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 levels (hyperglycaemia) which increases the risk of developing complications of diabetes.

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

4. Possible side effects

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

The assessment of side effects is based on their frequency.

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.

Digestive disorders
Abdominal pain, nausea, vomiting, indigestion, diarrhoea and constipation. These effects are reduced when <Invented name> modified release tablet is taken with meals as recommended.

Blood disorders
Decrease in the number of cells in the blood (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.

Skin disorders
Skin reactions such as rash, redness, itching, hives, blisters, 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.
If you develop this, stop taking <Invented name>, seek urgent advice from a doctor and tell him that you are taking this medicine.
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.

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.

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 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 (e. g. jaundice) which in most cases disappeared after withdrawal of the sulfonylurea, 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 <Invented name>

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 blister and carton after EXP. The

expiry date refers to the last day of that month.

This medicine 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 <Invented name> contains
- The active substance is gliclazide. Each modified-release tablet contains 90 mg gliclazide.
- The other ingredients are hypromellose, lactose monohydrate, colloidal anhydrous silica and magnesium stearate. See section 2 "<Invented name> contains lactose".

What <Invented name> looks like and contents of the pack
White to almost white, capsule shaped, biconvex tablets with two score lines around the tablet.
The tablet can be divided into equal doses.
Tablet dimension: length 17.0 – 17.5 mm and thickness 4.6 – 5.4 mm

DE/H/892/003
<Invented name> is available in boxes of 10 x 1, 20 x 1, 30 x 1, 60 x 1 or 90 x 1 modified-release tablet in perforated unit dose blisters.

DE/H/894/003
<Invented name> is available in boxes of 10 x 1, 30 x 1, 40 x 1 or 60 x 1 modified-release tablet in perforated unit dose blisters.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
[To be completed nationally]

Manufacturer
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

This medicinal product is authorised in the Member States of the EEA under the following names:
[To be completed nationally]

This leaflet was last revised in
[To be completed nationally]

Detailed information on this medicine is available on the website of {name of MS Agency (link)}