Version 3.0, 04/2013

SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

/…/ 30 mg modified-release tablets
/…/ 60 mg modified-release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each modified-release tablet contains 30 mg gliclazide.
Excipient with known effect:
Each modified-release tablet contains 54 mg lactose (as the monohydrate) (see section 4.4)

Each modified-release tablet contains 60 mg gliclazide.
Excipient with known effect:
Each modified-release tablet contains 108 mg lactose (as the monohydrate) (see section 4.4)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified-release tablet.

/…/ 30 mg modified-release tablets are white, oval, biconvex 5 x 11 mm tablets marked "G" on one side.

/…/ 60 mg modified-release tablets are white, oval, biconvex 7 x 15 mm tablets scored on both sides, marked with "G" on one side of the score and "60" on the other side of the score. The tablet can be divided into equal doses.

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.

The daily dose may vary from one half to 2 tablets per day, i.e. 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 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.
The recommended starting dose is 30 mg daily (half a 60 mg 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. The breakability of the /…/ 60 mg modified-release tablet enables flexibility of dosing to be achieved. One /…/ 60 mg modified release tablet corresponds to two /…/ 30 mg modified release tablets.

Switching from gliclazide 80 mg tablets to /.../ 30mg modified-release tablets
1 tablet of gliclazide 80 mg is comparable to 1 tablet of /…/ 30 mg modified-release. Consequently, the switch can be performed provided careful blood monitoring is undertaken.

Switching from gliclazide 80 mg tablets to /.../ 60 mg modified-release tablets
1 tablet of gliclazide 80 mg is comparable to 1 tablet of /…/ 30 mg modified-release (i.e. half a tablet of 60 mg). Consequently, the switch can be performed provided careful blood monitoring is undertaken.

Switching from another oral anti-diabetic agent to /.../
/…/ can be used to replace other oral anti-diabetic agents. The dosage and the half-life of the previous anti-diabetic agent should be taken into account when switching to /…/.

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 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 /…/, 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 anti-diabetic agents
/…/ can be given in combination with biguanides, alpha glucosidase inhibitors or insulin. In patients not adequately controlled with /…/, concomitant insulin therapy can be initiated under close medical supervision.

Special Populations

Older people (over 65 years of age)
/…/ should be prescribed using the same dosing regimen recommended for patients under 65 years of age.

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
There is an increased risk of hypoglycaemia in the following circumstances:
- Undernourished or malnourished patients
- Patients with severe or poorly compensated endocrine disorders (hypopituitarism, hypothyroidism, adrenocorticotrophic insufficiency)
- Following withdrawal of prolonged and/or high dose corticosteroid therapy
- Patients with severe vascular disease (severe coronary heart disease, severe carotid impairment or diffuse vascular disease)

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

Paediatric population
The safety and efficacy of /…/ in children and adolescents has not been established. No data and clinical studies are available in children.

Method of administration

Oral use.

It is recommended that the tablet(s) be swallowed whole without chewing or crushing.

It is recommended that the tablet(s) (whole or half tablet) be swallowed in one piece without chewing or crushing.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Hypersensitivity to other sulphonylureas or sulphonamides
- 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 (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-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 (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 /…/
- Certain endocrine disorders: thyroid disorders, hypopituitarism and adrenal insufficiency
- Concomitant administration of alcohol or 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, along 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 anti-diabetic treatment may be affected by any of the following: Fever, trauma, infection or surgical intervention. In some cases, it may be necessary to administer insulin.

The hypoglycaemic efficacy of any oral anti-diabetic 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.

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

Excipients
/…/ should not be administered to patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

4.5 Interaction with other medicinal products and other forms of interaction

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 (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 anti-diabetic agents (insulins, acarbose, biguanides (e.g. metformin), thiazolidinediones, dipeptidyl peptidase-4 inhibitors, GLP-1 receptor agonists); beta-blockers; fluconazole; angiotensin converting enzyme inhibitors (captopril, enalapril); H2-receptor antagonists; monoamine oxidase inhibitors (MAOIs); sulphonamides; clarithromycin; and non-steroidal anti-inflammatory agents.

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

Combination which is not recommended

- *Danazol:* has a diabetogenic effect. 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 anti-diabetic 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 anti-diabetic active substance during and after treatment with the neuroleptic agent.
- *Glucocorticoids (systemic and local route: intra-articular, cutaneous and rectal preparations) and tetracosactrin:* increase 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 anti-diabetic active substance during and after treatment with glucocorticoids.
- *Ritodrine, salbutamol and terbutaline (I.V. administration):* increased blood glucose levels due to beta-2 agonist effects. Emphasise the importance of monitoring blood glucose levels. If necessary, switch to insulin.

3) Combination which must be taken into account

- *Anticoagulant therapy (e.g. warfarin):* Sulphonylureas 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 with the use of gliclazide during pregnancy in humans, although there is some data available for other sulphonylureas.

In animal studies, gliclazide is not teratogenic.

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 known whether gliclazide or its metabolites are excreted in breast milk. Given the risk of neonatal hypoglycaemia, the product is contra-indicated in breast-feeding mothers.

4.7 Effects on ability to drive and use machines

/…/ has no known 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 and with other sulphonylureas, the following undesirable effects have to be mentioned.

Hypoglycaemia
As for other sulphonylureas, treatment with gliclazide can cause hypoglycaemia, if meal times 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 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 is required.

Other undesirable effects
Gastrointestinal disturbances, including abdominal pain, nausea, vomiting, dyspepsia, diarrhoea and constipation have been reported. These can be avoided or minimised if gliclazide is taken with a meal.

The following undesirable effects have been more rarely reported.

Skin and subcutaneous tissue disorders
Rash, pruritus, urticaria, angioedema, erythema, maculopapular rashes, and bullous reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis)

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 gliclazide.

Hepato-biliary disorders
Raised hepatic enzyme levels (AST, ALT, alkaline phosphatase) and 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
The following adverse events have been described for other sulphonylureas: 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 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 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: Blood glucose lowering drugs, excl. insulins: Sulfonylureas, ATC code: A10BB09

Gliclazide is a hypoglycaemic, sulphonylurea, oral anti-diabetic active substance differing from other related compounds by an N-containing heterocyclic ring with an endocyclic bond.

Mechanism of action

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 /…/ 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

Older people
No clinically significant changes in 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 foetal body weight was observed in animals receiving doses 25 fold higher than the maximum recommended dose in humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Hypromellose
Cellulose, microcrystalline
Silica, colloidal anhydrous
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Do not store above 25ºC.

6.5 Nature and contents of container

PVC/PVDC/Al blisters.
PVC/PVDC/PVC/Al blisters.
White HDPE containers closed with LDPE caps (for Duma) or PP caps (for Duma Twist-off).

Pack sizes:

[DK/H/2376/001-002/DC]
Blisters: 10, 14, 28, 30, 56, 60, 90, 120, 180 modified-release tablets.
Containers: 90, 120, 180 modified-release tablets.

[DK/H/2377/001-002/DC]
Blisters: 10, 14, 30, 60, 90, 120 modified-release tablets.
Containers: 90, 100, 120 modified-release tablets.

[DK/H/2399/001-002/DC]
Blisters: 10, 14, 28, 30, 56, 60, 90, 120, 180 modified-release tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7. MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

<[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}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

<[To be completed nationally]>

<Detailed information on this medicinal product is available on the website of {name of MS/Agency}>

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON
LABEL FOR CONTAINER

1. NAME OF THE MEDICINAL PRODUCT

/…/ 30 mg modified-release tablets
/…/ 60 mg modified-release tablets

Gliclazide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each modified-release tablet contains 30 mg gliclazide.
Each modified-release tablet contains 60 mg gliclazide.

3. LIST OF EXCIPIENTS

Contains lactose (as the monohydrate) (see leaflet for further information).

4. PHARMACEUTICAL FORM AND CONTENTS

[DK/H/2376/001-002/DC]
Blisters: 10, 14, 28, 30, 56, 60, 90, 120 or 180 modified-release tablets.
Containers: 90, 120 or 180 modified-release tablets.

[DK/H/2377/001-002/DC]
Blisters: 10, 14, 30, 60, 90 or 120 modified-release tablets.
Containers: 90, 100 or 120 modified-release tablets.

[DK/H/2399/001-002/DC]
Blisters: 10, 14, 28, 30, 56, 60, 90, 120, 180 modified-release tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Swallow your whole tablet(s) in one piece.
Swallow your half tablet or whole tablet(s) in one piece.
Do not chew or crush.
Read the package leaflet before 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:

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.

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]>

{Name and Address}
<{tel}>
<{fax}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

<[To be completed nationally]>

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

/…/ 30 mg modified-release tablets
/…/ 60 mg modified-release tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

/…/ 30 mg modified-release tablets
/…/ 60 mg modified-release tablets

Gliclazide

2. NAME OF THE MARKETING AUTHORISATION HOLDER

<[To be completed nationally]>

{Name}

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. OTHER

PACKAGE LEAFLET

Package leaflet: Information for the patient

/…/ 30 mg modified-release tablets
/…/ 60 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 /…/ is and what it is used for

/…/ is a medicine that reduces blood sugar levels (oral anti-diabetic medicine belonging to the sulphonylurea group).

/…/ 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 /…/

Do not take /…/:
- 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 (sulphonylureas) , or to other related medicines (hypoglycaemic sulphonamides)
- 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 section ‘Other medicines and /…/’)
- if you are breastfeeding (see Section ‘Pregnancy and breastfeeding’).

Warnings and precautions
Talk to your doctor or pharmacist before taking /…/.

You should observe the treatment plan prescribed by your doctor to achieve proper blood sugar levels. This means, apart from regular tablet intake, you 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. It may also be useful to monitor your own blood sugar levels, although only following instruction from your doctor.

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 recently stopped taking corticosteroids (medicines that reduce inflammation) following prolonged and /or high dose use.
- if you have a severe blood circulation disorder, such as coronary heart disease, severe carotid artery impairment or diffuse vascular disease.

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. 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 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. 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 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.

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 haemoglobin level and breakdown of red blood cells (haemolytic anaemia) can occur. Contact your doctor before taking this medicinal product.

Children and adolescents
/…/ is not recommended for use in children and adolescents due to a lack of data.

Other medicines and /…/
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 anti-diabetics or insulin)
- Antibiotics (e.g. sulphonamides or clarithromycin)
- Medicines to treat high blood pressure or heart failure (beta blockers, ACE-inhibitors such as captopril or enalpril)
- Medicines to treat fungal infections (e.g. miconazole, fluconazole – see section 'Do not take /…/')
- Medicines to treat ulcers in the stomach or duodenum (H_2 receptor antagonists)
- Medicines to treat depression (monamine oxidase inhibitors)
- Painkillers or antirheumatics (phenylbutazone, ibuprofen)
- Medicines containing alcohol

The blood glucose lowering effect of gliclazide may be weakened and raised blood sugar may occur when one of the following medicines is taken:
- Medicines to treat disorders of the central nervous system (chlorpromazine)
- Medicines reducing inflammation (corticosteroids or tetracosactrin)
- Medicines to treat asthma or used during labour (intravenous salbutamol, ritodrine and terbutaline)
- Medicines to treat breast disorders, heavy menstrual bleeding and endometriosis (danazol)

/…/ 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 to into hospital tell the medical staff you are taking /…/.

/…/ with food, drink and alcohol
/…/ 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 breast-feeding
Pregnancy
/…/ 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 your doctor or pharmacist for advice before taking this medicine.

Breastfeeding
You must not take /…/ 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. 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).

/…/ contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take /…/

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Dosage
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 starting dose is 30 mg.

For 30 mg tablets: The usual dose is one to four tablets (maximum 120 mg) in a single intake at breakfast time. This depends on the response to treatment.

For 60 mg tablets: The tablet can be divided into equal doses. The usual dose is half to two tablets (maximum 120 mg) in a single intake at breakfast time. This depends on the response to treatment.

If a combination therapy of /…/ with metformin, an alpha glucosidase inhibitor or insulin is initiated your doctor will determine the proper dose of each medicine individually for you.

Please talk to your doctor or pharmacist if you have the impression that /…/ is acting too strongly or not strongly enough.

Methods and routes of administration
Oral use.
For 30 mg tablets: Swallow your whole tablet(s) in one piece.
For 60 mg tablets: Swallow your half tablet or whole tablet(s) in one piece.
Do not chew or crush.
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 /…/ 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, 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 /…/
It is important to take your medicine every day as regular treatment works better.

However, if you forget to take a dose of /…/, take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If your doctor switches you from gliclazide 80 mg tablets or from other anti-diabetics to /…/
Your doctor will decide your initial dose and monitor you more closely for a short time.

If you stop taking /…/
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).

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 most commonly observed side effect is low blood sugar (hypoglycaemia). For symptoms and signs see 'Warnings and precautions' in section 2. 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 and 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.

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.

Digestive disorders
Stomach pain or discomfort, nausea, vomiting, indigestion, diarrhoea, and constipation. These effects are reduced when /…/ is taken with a meal as recommended, see section 3 'How to take /…/.

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.

The following adverse events have been observed with other sulphonylureas: Severe changes in the number of blood cells and allergic inflammation of the wall of blood vessels; reduction in blood sodium (hyponatraemia); and symptoms of liver impairment (e.g. jaundice), which in most cases disappeared after withdrawal of the sulphonylurea, 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 /…/

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

Do not store above 25ºC.

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

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 /…/ contains

- The active substance is gliclazide. One tablet contains either 30 mg or 60 mg of gliclazide, in a modified-release formulation.
- The other ingredients are: lactose monohydrate, hypromellose, microcrystalline cellulose, colloidal, anhydrous silica, magnesium stearate.

What /…/ looks like and contents of the pack

/…/ 30 mg modified-release tablets are white, oval, biconvex 5 x 11 mm tablets marked "G" on one side.
/…/ 60 mg modified-release tablets are white, oval, biconvex 7 x 15 mm tablets scored on both sides, marked with "G" on one side of the score and "60" on the other side of the score.

Pack sizes:

[DK/H/2376/001-002/DC]
Blisters: 10, 14, 28, 30, 56, 60, 90, 120, 180 modified-release tablets.
Containers: 90, 120, 180 modified-release tablets.

[DK/H/2377/001-002/DC]
Blisters: 10, 14, 30, 60, 90, 120 modified-release tablets.
Containers: 90, 100, 120 modified-release tablets.

[DK/H/2399/001-002/DC]
Blisters: 10, 14, 28, 30, 56, 60, 90, 120, 180 modified-release tablets.

Not all pack sizes may be available

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

<[To be completed nationally]>

{Name and address}
<{tel}>

<{fax}>
<{e-mail}>

Manufacturer:

Actavis ehf.
Reykjavikurvegur 78
IS-220 Hafnarfjörður
Iceland

and

Balkanpharma-Dupnitsa AD
3 Samokovsko Shosse Str.,
Dupnitza 2600
Bulgaria

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

<{Name of the Member State}> <{Name of the medicinal product}>
<{Name of the Member State}> <{Name of the medicinal product}>

<[To be completed nationally]>

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

<[To be completed nationally]>

<Detailed information on this medicine is available on the web site of {MA/Agency}>