Package leaflet: Information for the patient

Diacronal MR 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 Diacronal MR is and what it is used for

Diacronal MR is a medicine that reduces blood sugar levels (antidiabetic medicine taken orally, belonging to the sulphonylurea group).

Diacronal MR 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 Diacronal MR

Do not take Diacronal MR
- 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 substance group (sulphonylureas) or to other related medicines (hypoglycaemic sulphonamides);
- if you have insulin-dependent diabetes (type I);
- if you have ketone bodies and sugar in your urine (this may mean that you have diabetic ketoacidosis), a diabetic precoma or coma;
- if you have severe kidney or liver disease;
- if you are taking medicines to treat fungal infections (miconazole, see section "Taking Diacronal MR with other medicines");
- if you are breast feeding (see section "Pregnancy and breast-feeding").

Warnings and precautions
Talk to your doctor or pharmacist before taking Diacronal MR.
You should observe the treatment plan prescribed by your doctor to achieve the recommended blood sugar levels. This means, apart from the 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. Therefore, it is vital that you are carefully monitored by your doctor.

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 renal function or liver function is severely decreased.

If you have low blood sugar you may have the following symptoms:
headache, increased 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 heartbeat, high blood pressure and 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, possibly resulting in coma. The clinical picture of a severe reduced blood sugar level may resemble that of a stroke.

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).
It may also happen when you suffer from certain disorders of the endocrine system (e.g. certain disorders of thyroid function and anterior pituitary or adrenocortical insufficiency).

If you are in stress-situations (e.g. accident, surgical procedure, 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 Diacronal MR"), or in special stress situations. Symptoms 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
Diacronal MR is not recommended for use in children due to a lack of data.

Other medicines and Diacronal MR
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 Diacronal MR, especially in elderly patients.

Diacronal MR 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 Diacronal MR.

Diacronal MR with food, drink and alcohol
Diacronal MR 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
Diacronal MR 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 so that he may prescribe a more suitable treatment for you.

You must not take Diacronal MR 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 fewer or no warning signals of low blood sugar (hypoglycaemia).

Diacronal MR 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 Diacronal MR

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 one 30 mg modified-release tablet up to two 60 mg modified-release tablets (maximum 120 mg) in a single intake at breakfast. This depends on the response to treatment.

If a combination therapy of Diacronal MR 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
Swallow the tablet(s) whole 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 every day).
You must always eat a meal after taking your tablet(s).

If you take more Diacronal MR than you should
If you have taken 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 Diacronal MR
It is important that you take the medicine every day as regular treatment works better.
However, if you forget to take a dose of Diacronal MR 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 Diacronal MR
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.

Common (may affect up to 1 in 10 people):

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.

Uncommon (may affect up to 1 in 100 people):

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

Rare (may affect up to 1 in 1,000 people):

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 diseases
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 Diacronal MR, 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 disease
There have been isolated reports of abnormal liver function tests, 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 very rarely (may affect up to 1 in 10,000 people):
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 HPRA Pharmacovigilance, Website: www.hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Diacronal MR

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 Diacronal MR contains
- The active substance is gliclazide. Each modified-release tablet contains 60 mg gliclazide.
- The other ingredients are hypromellose, lactose monohydrate, colloidal anhydrous silica and magnesium stearate. See section 2 “Diacronal MR contains lactose”.

What Diacronal MR looks like and contents of the pack
White to almost white, oval, biconvex tablet, 13 mm long and with a thickness of 3.5 mm to 4.9 mm.

Diacronal MR is available in boxes of 14, 15, 28, 30, 56, 60, 84, 90, 120 or 180 modified-release tablets in blisters.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

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:

Estonia, Poland, Italy, United Kingdom	Gliclazide Krka
Germany	Glibemat
Spain	Gliclazida Krka
Ireland	Diacronal MR
Portugal	Gliclazida TAD

This leaflet was last revised in