GLICLAZIDE 80 MG TABLETS

PL 20395/0046

UKPAR

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GLICLAZIDE 80 MG TABLETS

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted RelonChem Limited a Marketing Authorisation (licence) for the medicinal product Gliclazide 80mg Tablets (Product Licence number: 20395/0046). This medicine is only available with a prescription and is used to treat non-insulin-dependent diabetes mellitus.

Gliclazide 80mg Tablets contain the active ingredient gliclazide, which can control blood sugar levels in patients with non-insulin-dependent diabetes mellitus.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Gliclazide 80mg Tablets outweigh the risks, hence a Marketing Authorisation has been granted.

GLICLAZIDE 80 MG TABLETS

PL 20395/0046

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Gliclazide 80mg Tablets (PL 20395/0046) to RelonChem Limited on 2 October 2006. This product is a prescription only medicine (POM).

The application was submitted as an abridged application according to article 10c of Directive 2001/83/EC, cross-referring to Gliclazide 80 mg Tablets (PL 14682/0003), approved 29 August 2003.

No new data were submitted, nor was it necessary for this simple application, as the data is identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report was generated for it.

PHARMACEUTICAL ASSESSMENT REPORT

INTRODUCTION
An abridged application made under Article 10c of Directive 2001/83/EC, cross-referring to PL 14682/0003 for Gliclazide 80 mg Tablets, first granted to Edmond Pharma srl (Italy) on 29 August 2003.

A letter of access dated 4 October 2004 has been submitted. Appropriate declarations confirm that the applicant has full access to Part III and IV data and have all the necessary Part II data in their possession to support the application. The proposed finished product manufacturers have confirmed their willingness to manufacture the product on the applicant's behalf.

EXPERT REPORTS
Satisfactory Pharmaceutical, Pre-clinical and Clinical Expert statements have been provided by suitably qualified experts to confirm that the chemical, pharmaceutical, biological, clinical and toxico-pharmacological documentation included in the cross-reference product dossier are applicable and relevant to this specified marketing authorisation application.

PRODUCT NAMES
The proposed generic name 'Gliclazide 80 mg Tablets' is acceptable.

MAA FORM
The MAA form submitted with this application is satisfactory.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
The SPC is consistent with current licence details of the cross-reference product and is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)
A full colour mock-up of the PIL artwork has been provided and is satisfactory.

LABELLING
Full colour mock-ups of the blister and carton labelling have been provided and are satisfactory.

TSE
Declarations have been provided from the manufacturers of the lactose monohydrate used in this medicinal product confirming that TSE risk is minimised in line with EMEA/CPMP/571/02.. This is consistent with the approved cross-reference product.

Declarations have been provided from the manufacturers of the magnesium stearate used in this medicinal product confirming that the material used is of vegetable origin. This is

consistent with the approved cross-reference product.

ASSESSOR'S CONCLUSION

Grant of the Marketing Authorisation is recommended.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none is required for an application of this type.

CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none is required for an application of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for this application is consistent with that previously assessed for the cross-reference product and as such has been judged to be satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. The risk benefit ratio is considered to be positive.

GLICLAZIDE 80 MG TABLETS

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STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application on 21 October 2004
2	Following assessment of the application the MHRA requested further information relating to the quality dossier 11 March 2005
3	The applicant responded to the MHRA's requests, providing further information on 22 July 2005
4	Following assessment of the response the MHRA requested further information relating to the quality dossier on 26 July 2006
5	The applicant responded to the MHRA's requests, providing further information on 8 August 2006
6	Following assessment of the response the MHRA requested further information relating to the quality dossier on 9 August 2006
7	The applicant responded to the MHRA's requests, providing further information on 7 September 2006
8	Following assessment of the response the MHRA requested further information relating to the quality dossier on 27 September 2006
9	The applicant responded to the MHRA's requests, providing further information on 28 September 2006
10	The application was determined on 2 October 2006

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Gliclazide 80mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 80mg gliclazide.
For excipients see 6.1.

3 PHARMACEUTICAL FORM
Tablet.
White, round tablet, scored on one side and embossed ‘G03’ on the reverse side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
For the treatment of maturity onset diabetes mellitus.

4.2 Posology and method of administration
Adults: The total daily dose may vary from 40 to 320mg taken orally. The dose should be adjusted according to the individual patient’s response, commencing with 40 - 80mg daily (1/2 - 1 tablets) and increasing until adequate control is achieved.
A single dose should not exceed 160mg (2 tablets). When higher doses are required Gliclazide 80mg Tablets should be taken twice daily and according to the main meals of the day.
In obese patients or those not showing adequate response to Gliclazide 80mg Tablets alone additional therapy may be required.
Elderly: Plasma clearance of gliclazide is not altered in the elderly and steady state plasma levels can therefore be expected to be similar to those in adults under 65 years. Clinical experience in the elderly to date shows that gliclazide is effective and well tolerated. Care should be exercised, however, when prescribing sulphonylureas in the elderly due to a possible age-related increased risk of hypoglycaemia.
Children: Gliclazide 80mg, as with other sulphonylureas, is not indicated for the treatment of juvenile onset diabetes mellitus.

4.3 Contraindications
Gliclazide 80mg tablets are contraindicated in:
- juvenile onset diabetes
- diabetes complicated by ketosis and acidosis
- pregnancy
- diabetics undergoing surgery after severe trauma or during infections
- patients known to have hypersensitivity to other sulphonylureas and related drugs

- diabetic pre-coma and coma
- severe renal or hepatic insufficiency

4.4 Special warnings and precautions for use

Care should be exercised in patients with hepatic and/or renal impairment and a small starting dose should be used with careful patient monitoring.
All sulphonylurea drugs are capable of producing moderate or severe hypoglycaemia. As with other sulphonylureas, hypoglycaemia will occur if the patients dietary intake is reduced or if they are receiving a larger dose of Gliclazide 80mg tablets than required, particularly in the following conditions:
- in patients controlled by diet alone
- in cases of accidental overdose
- when calorie or glucose intake is deficient
- in patients with hepatic and/or renal impairment. However in long term clinical trials, patients with renal insufficiency have been treated satisfactorily using gliclazide at reduced doses. In order to reduce the risk of hypoglycaemia it is therefore recommended:
- to initiate treatment for non-insulin dependent diabetics by diet alone if this is possible;
- to take into account the age of the patient: blood sugar levels not strictly controlled by diet alone might be acceptable in the elderly.
- to adjust the dose of Gliclazide 80mg tablets according to the blood glucose response and to the 24 hour urinary glucose during the first days of treatment.
Dosage adjustments may be necessary:
- on the occurrence of mild symptoms of hypoglycaemia (sweating, pallor, hunger pangs, tachycardia, sensation of malaise). Such findings should be treated with oral glucose and adjustments made in drug dosage and/or meal patterns;
- on the occurrence of severe hypoglycaemic reactions (coma or neurological impairment, see overdose);
- loss of control of blood glucose (hyperglycaemia). When a patient stabilised on any diabetic regimen is exposed to stress such as fever, trauma, infection or surgery, a loss of control may occur. At such times it may be necessary to progressively increase the dosage of Gliclazide 80mg tablets and if this is insufficient, to discontinue the treatment and administer insulin.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Care should be taken when giving Gliclazide 80mg tablets with drugs which are known to alter the diabetic state or potentiate the drugs action. The hypoglycaemic effect of Gliclazide 80mg Tablets may be potentiated by phenylbutazone, salicylates, sulphonamides, coumarin derivatives, MAOI's, beta adrenergic blocking agents, tetracycline compounds, chloramphenicol, clofibrate, disopyramide, miconazole (oral forms) and cimetidine.
It may be diminished by corticosteroids, oral contraceptives, thiazide diuretics, phenothiazine derivatives, thyroid hormones and abuse of laxatives.

4.6 Pregnancy and lactation

Pregnancy: See contra-indications.
Nursing mothers: It has not yet been established whether gliclazide is transferred to human milk. However, other sulphonylureas have been found in milk and there is no evidence to suggest that gliclazide differs from the group in this respect.

4.7 Effects on ability to drive and use machines

Patients should be informed that their concentration may be affected if their diabetes is not satisfactorily controlled, especially at the beginning of treatment (see other special warnings and precautions).

4.8 Undesirable effects

Hypoglycaemia (see special warnings and precautions).
Abnormalities of hepatic function are not uncommon during gliclazide therapy. There are rare reports of hepatic failure, hepatitis and jaundice following treatment with gliclazide.
Mild gastro-intestinal disturbances including nausea, dyspepsia, diarrhoea and constipation have been reported, but this type of adverse reaction can be avoided if Gliclazide 80mg tablets are taken during a meal.
Skin reactions including rash, pruritis, erythema, bullous eruption; blood dyscrasia including anaemia, leucopaenia, thrombocytopaenia and granulocytopaenia have been observed during treatment with gliclazide but are not known to be directly attributable to the drug.

4.9 Overdose

The symptom to be expected with an overdose would be hypoglycaemia. The treatment is gastric lavage and correction of the hypoglycaemia by appropriate means with continued monitoring of the patients blood sugar until the effect of the drug has ceased

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Gliclazide is a hypoglycaemic sulphonylurea differing from other related compounds by the addition of an azabicyclo octane ring. Oral sulphonylureas act by stimulating the release of insulin from beta cells but they may also have long-term extrapancreatic effects that reduce hepatic glucose production and increase the number of peripheral insulin receptors. Sulphonylureas are effective only in individuals with functional beta cells.
In man, apart from having a similar hypoglycaemic effect to other sulphonylureas, gliclazide has been shown to reduce platelet adhesiveness and aggregation and increase fibrinolytic activity. These factors are thought to be implicated in the pathogenesis of long term complications of diabetes mellitus.

5.2 Pharmacokinetic properties

The drug is well absorbed and its half life in man is approximately 10 - 12 hours. Gliclazide is metabolised in the liver to inactive metabolites; less than 5% of the dose is excreted unchanged in the urine. Although there is a dose-dependent relationship between gliclazide and plasma concentrations, no clear correlation with hypoglycaemic activity

exists.

5.3 Preclinical safety data
No further relevant information.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Lactose monohydrate
Silicon dioxide
Pregelatinised Maize Starch
Talc
Magnesium Stearate

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
Do not store above 25ºC.

6.5 Nature and contents of container
The tablets are packaged into white, opaque polyvinyl chloride (PVC)/aluminium foil blister packs. Boxes of 28 and 60 tablets are available. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special instructions. Tablets to be taken as directed by a physician.

7 MARKETING AUTHORISATION HOLDER
Relonchem Limited,
27 Old Gloucester Street,
London,
WC1 3XX

8 MARKETING AUTHORISATION NUMBER(S)
PL 20395/0046

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02/10/2006

10 DATE OF REVISION OF THE TEXT

02/10/2006

PATIENT INFORMATION LEAFLET

Gliclazide 80mg Tablets

RelonChem

Patient Information Leaflet

Please read this leaflet carefully before taking your medicine. This leaflet contains a summary of information available on the product. If you have any questions or are not sure about anything, ask your doctor or pharmacist. Keep this leaflet, you may want to read it again.

The name of your medicine is:

Gliclazide 80mg Tablets.

What is in the tablet?

Gliclazide 80mg tablets are white, flat faced, round tablets, embossed with 'G03' on one side and scored on the reverse. Each tablet contains 80mg gliclazide.

The tablets also contain the inactive ingredients lactose, silicon dioxide, pregelatinized maize starch, talc, magnesium stearate.

Tablets are packaged into white, opaque polyvinyl chloride (PVC)/aluminium foil blister packs. Gliclazide 80mg Tablets are available in two different pack sizes containing 28 tablets or 60 tablets.

The Marketing Authorisation holder is:
Relonchem Limited
27 Old Gloucester Street,
London WC1 3XX.

The marketing authorisation number is PL 20395/0046 and the product is a prescription only medicine (POM).

The tablets are manufactured by:
Edmond Pharma
131 Via dei Giovi,
20037 Paderno Dugnano
Milan, Italy

What are Gliclazide 80mg tablets used for?

Your doctor has diagnosed that you have too much sugar in your blood (diabetes mellitus). Gliclazide 80mg tablets are used to treat diabetes mellitus in adults. Gliclazide 80mg tablets contain gliclazide which is a hypoglycaemic sulphonylurea. Sulphonylureas act by stimulating the release of insulin from beta cells and so lower the amount of sugar in your blood.

Before taking your medicine:

Tell your doctor if:

- You have liver or kidney problems
- You are allergic to sulphonylureas or related drugs or are allergic to any of the ingredients in the tablets
- You are pregnant or thinking of becoming pregnant
- You are to have an operation
- You are suffering from any type of infection
- You are under the age of 14
- You suffer from diabetes and have faulty fat metabolism.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Are you taking other medicines?

Other medicines that you may be taking and Gliclazide 80mg Tablets may affect each other's action. For this reason it is important to tell your doctor or pharmacist about ALL the medicines you are taking, such as those for the following conditions:

- High Blood pressure
- Heart problems such as angina or heart failure
- High Cholesterol Levels
- Thyroid problems
- Rheumatism, arthritis
- Gout
- Blood conditions (medicines to thin your blood, i.e. anti coagulants)
- Contraception (pill or mini pill)
- Depression or any emotional problem
- Ulcer

Your doctor may need to change your dose of Gliclazide 80mg Tablets if you are taking any other medication.

Driving or operating machinery

If you experience the symptoms of low blood sugar (hypoglycaemia) you should not drive or operate machinery.

Low blood sugar may occur at the beginning of treatment while your doctor is trying to find the dose that best suits you. Your doctor will give you further advice. If your blood sugar is stabilised you may drive or operate machinery.

How to take your medicine

Always take the number of tablets your doctor has asked you to take. At first this may be half or one tablet a day.

Your doctor may increase your dose if your blood sugar level does not come down enough. You should not take more than your doctor tells you.

Gliclazide 80mg tablets should be taken immediately after food, either with breakfast or the first main meal of the day.

If you forgot to take your tablets wait until your next scheduled time to take them and then take them as normal.

If you take too many tablets seek help from your doctor or pharmacist immediately.

Side effects of your medicine

Like all medicines, Gliclazide 80mg Tablets may cause some side effects. Light-headedness, a pounding heart, clamminess or sweaty palms may mean that your blood sugar level is too low and the dose of Gliclazide 80mg Tablets is not right for you. If you think this is happening to you, contact your doctor or pharmacist immediately.

You may experience some other side effects, for example tummy upset, slight sickness, diarrhoea or constipation, but these can be avoided if you take your medicine during a meal.

Your skin may feel itchy or develop a rash. You may bruise or bleed more easily. Very rarely you may become anaemic and/or the number of white blood cells may decrease. Please tell your doctor if you notice any of these effects.

Rarely, people have become jaundiced (yellowing of the skin) or developed liver problems such as hepatitis during treatment with Gliclazide 80mg Tablets. If you notice this, tell your doctor immediately.

If you develop any other problems that you believe to be due to your medicine please tell your doctor or pharmacist.

How to store your medicine

Do not store above 25°C.

Do not use your medicine after the expiry date shown on the label.

Keep out of the sight and reach of children.

If your doctor tells you to stop your treatment, return any left overtablets to your pharmacist.

Date of revision of leaflet: August 2006.

LABELLING


Gliclazide 80mg Tablets
RelonChem
28 Tablets
PL 20395/0046 POM
Keep out of the sight and reach of children.
Do not store above 25°C.
Please read the enclosed leaflet carefully.
Take by mouth as directed by your doctor.
See leaflet for further information.
Also contains Lactose.
Each tablet contains 80mg Gliclazide.
Batch No:
Expiry Date:
Product Licence Holder: Relonchem Limited
27 Old Gloucester Street, London WC1 3XX
Gliclazide 80mg Tablets
28 Tablets


Gliclazide 80mg Tablets
RelonChem
60 Tablets
PL 20395/0046 POM
Keep out of the sight and reach of children.
Each tablet contains 80mg Gliclazide.
Also contains Lactose.
See leaflet for further information.
Take by mouth as directed by your doctor.
Please read the enclosed leaflet carefully.
Do not store above 25°C.
Batch No:
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Product Licence Holder: Relonchem Limited
27 Old Gloucester Street, London WC1 3XX
Gliclazide 80mg Tablets
60 Tablets


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Gliclazide 80mg Tablets
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