GLICLAZIDE 80 MG TABLETS

PL 06464/2062

UKPAR

TABLE OF CONTENTS

GLICLAZIDE 80 MG TABLETS

PL 06464/2062

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency granted Waymade Plc a Marketing Authorisation (licence) for the medicinal product Gliclazide 80mg Tablets (PL 06464/2062) on 5 July 2006. This product has been granted prescription only status.

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

This application is based on a reference product with a valid UK licence.

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 06464/2062

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted a marketing authorisation for the medicinal product Gliclazide 80mg Tablets (PL 06464/2062) to Waymade Plc on 5 July 2006. This tablet is available by prescription only.

This is a national application for Gliclazide 80mg Tablets, submitted under EC Article 10.1, cross-referring to a reference product with a valid UK licence.

No new data was 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 PAR was generated for it.

PHARMACEUTICAL ASSESSMENT

Introduction

Legal Basis
This is a simple abridged application for Gliclazide 80mg Tablets. The reference product has a valid Marketing Authorisation in the UK.

Letters of Access
A satisfactory letter of access is provided, dated 29 March 2004, from the reference product's Marketing Authorisation Holder. Confirmation that the manufacturer is prepared to manufacture the product on the applicant's behalf is supplied, dated 1 April 2004.

The applicant also provided satisfactory confirmation that they have access to all the data supporting the application and that Part II of the data is in their possession in a letter dated 19 July 2004.

Reference Product
There are no outstanding variations or renewal issues.

Expert Reports
The pharmaceutical expert report is written by a manager from the reference product's Marketing Authorisation holder. She has relevant experience and confirms that the product will have the same qualitative and quantitative composition as the reference product and that manufacture and QC will also be the same. The report is acceptable.

The clinical expert report is written by a medical advisor with relevant experience. He confirms that the details are in agreement with those specified in the licence application. The report is acceptable.

Product Name and Appearance
The generic name is acceptable.

Summary of Product Characteristics

The SPC is exactly the same as the cross referral. No amendments are necessary.

Patient Information leaflet

The PIL is acceptable, almost identical to the cross referral and in-line with the SPC.

Labelling
Labelling is acceptable.

MAA Form
The MAA form is satisfactory.

TSE
Magnesium Stearate is the only TSE risk material. A letter stating that it is of vegetable origin has been supplied.

Recommendation
A product license may be granted for this product.

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

PL 06464/2062

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application on 19 July 2004
2	Following assessment of the application the MHRA requested further information relating to the quality dossier on 15 February 2005
3	The applicant responded to the MHRA's requests, providing further information on the quality dossier on 3 March 2005
4	Following assessment of the application the MHRA requested further information relating to the quality dossier on 8 May 2006
5	The applicant responded to the MHRA's requests, providing further information on the quality dossier on 21 June 2006
6	The application was determined on 5 July 2006

SUMMARY OF PRODUCT CHARACTERISTICS

Gliclazide 80 mg Tablets (PL 06464/2062) has the following product summary:

1. NAME OF THE MEDICINAL PRODUCT

Gliclazide 80 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 80 mg 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 320 mg taken orally. The dose should be adjusted according to the individual patient’s response, commencing with 40 – 80 mg daily (½ - 1 tablet) and increasing until adequate control is achieved.

A single dose should not exceed 160 mg (2 tablets). When higher doses are required, Gliclazide 80 mg tablets should be taken twice daily according to the main meals of the day.

In obese patients or those not showing adequate response to Gliclazide 80 mg 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, as with other sulphonylureas, is not indicated for the treatment of juvenile onset diabetes mellitus.

4.3. Contraindications

Gliclazide 80 mg 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
- Diabetics 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 sulphonylureas drugs are capable of producing moderate to severe hypoglycaemia. As with other sulphonylureas, hypoglycaemia will occur if the patient's dietary intake is reduced or if they are receiving a larger dose of Gliclazide 80 mg 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 80 mg tablets according to the blood glucose response and to the 24 hour urinary glucose during the first days of treatment.

Dosage adjustment 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 adjustment 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 stabilized 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 80 mg tablets and if this is insufficient, to discontinue the treatment and to administer insulin.

4.5. Interactions with other medicinal products and other forms of interaction

Care should be taken with giving Gliclazide 80 mg tablets with drugs which are known to alter the diabetic state or potentiate the drug's action. The hypoglycaemic effect of Gliclazide 80 mg tablets may be potentiated by phenylbutazone, salicylates, sulphonamides, coumarin derivatives, MAOIs, 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 "Contraindications".
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, this type of adverse reaction can be avoided if Gliclazide 80 mg tablets are taken during a meal.

Skin reactions including rash, pruritus, erythema, bullous eruption; blood dyscrasias including anaemia, leucopenia, thrombocytopenia and granulocytopenia 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 patient's blood sugar until the effect of the drug has ceased.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Sulfonamides, urea derivatives
ATC code: A10BB

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 the 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 metabolized 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
Pregelatinized 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 25°C.

6.5. Nature and contents of container

The tablets are packed into polyvinyl chloride (PVC)/aluminium foil blister packs. Boxes of 28 and 60 tablets are available. Not all pack sizes may be marketed.

6.6. Instruction for use and handling (, and disposal)

No special instruction. Tablets to be taken as directed by a physician.

7. MARKETING AUTHORISATION HOLDER

Waymade Plc trading as Sovereign Medical
Sovereign House
Miles Gray Road
Basildon
Essex
SS14 3FR
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 06464/2062

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/07/2006

10 DATE OF REVISION OF THE TEXT

05/07/2006

PATIENT INFORMATION LEAFLET

797-5279

Patient Information Leaflet

Gliclazide 80 mg Tablets

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 80 mg Tablets

What is in the tablet?
Gliclazide 80 mg Tablets are white round tablets embossed with 'G03' on one side. Each tablet contains 80 mg gliclazide.

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

Gliclazide 80 mg tablets are available in packs containing 28 or 60 tablets.

Marketing Authorisation holder:
Waymade plc trading as Sovereign Medical, Sovereign House, Miles Gray Road, Basildon, Essex, SS14 3FR

Manufacturer responsible for release:
Waymade plc, Sovereign House, Miles Gray Road, Basildon, Essex, SS14 3FR

What are Gliclazide 80 mg tablets used for?
Your doctor has diagnosed that you have too much sugar in your blood (diabetes mellitus). Gliclazide 80 mg tablets are used to treat diabetes mellitus in adults. Gliclazide 80 mg 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 80 mg 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. anticoagulants)
- Contraception (pill or mini pill)
- Depression or any emotional problem
- Ulcer

Your doctor may need to change your dose of Gliclazide 80 mg 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 80 mg tablets should be taken immediately after food, either with breakfast or the main meal of the day.
If you forget 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 80 mg 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 80 mg 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 80 mg 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 degrees C.
Do not use your medicine after the expiry date shown on the label.
Keep your medicine in a safe place, where children cannot get at it.
If your doctor tells you to stop your treatment, return any left over tablets to your pharmacist.

SOVEREIGN MEDICAL

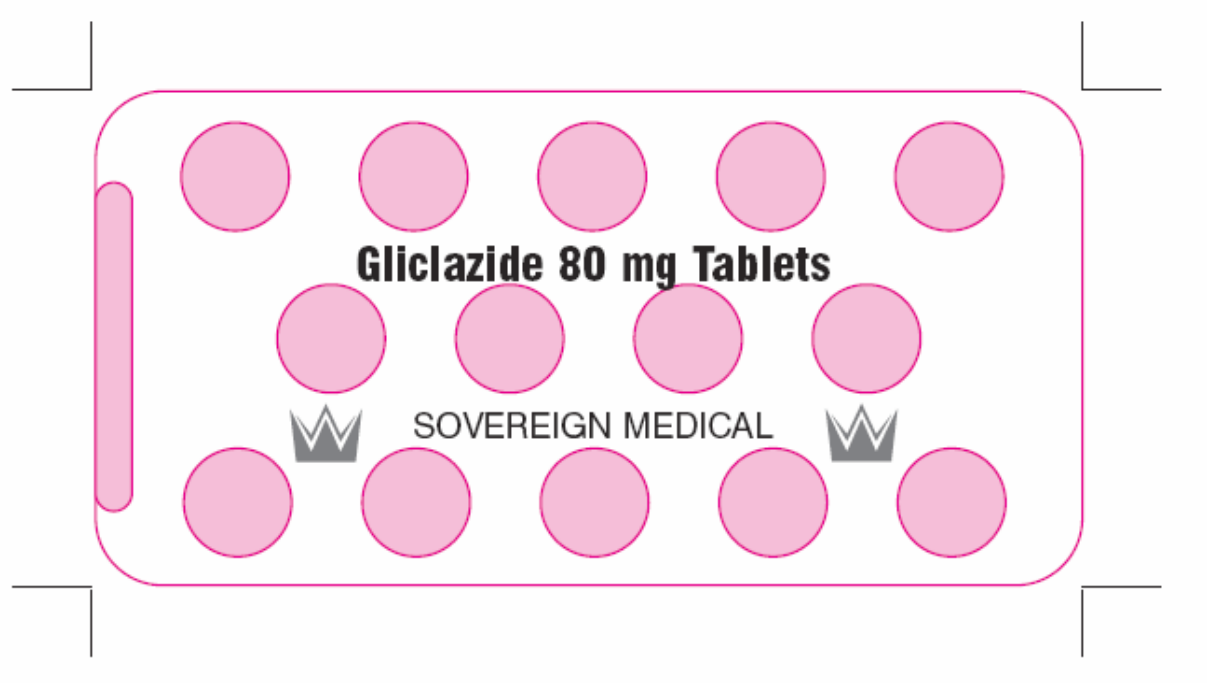
Date of preparation: February 2005

LABELLING

Carton (28 tablets):

Carton (60 tablets):

Blister (28 tablets):



Blister (60 tablets):