

GLIBENCLAMIDE 2.5MG AND 5MG TABLETS

PL 21880/0113-4

UKPAR

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GLIBENCLAMIDE 2.5MG AND 5MG TABLETS

PL 21880/0113-4

LAY SUMMARY

On 15th February 2012, the MHRA granted Medreich PLC Limited Marketing Authorisations (licences) for Glibenclamide 2.5mg and 5mg Tablets (PL 21880/0113-4).

Glibenclamide 2.5mg and 5mg Tablets contain the active ingredient glibenclamide.

Glibenclamide belongs to a group of medicines known as glucose lowering agents.

Glibenclamide 2.5mg and 5mg Tablets are used to treat patients with non-insulin dependent diabetes where dietary measures alone have not achieved control of diabetes(blood glucose).

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Glibenclamide 2.5mg and 5mg Tablets outweigh the risks; hence these Marketing Authorisations have been granted.

GLIBENCLAMIDE 2.5MG AND 5MG TABLETS

PL 21880/0113-4

SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Marketing Authorisations for the medicinal products Glibenclamide 2.5mg and 5mg Tablets to Medreich PLC on 15th February 2012. These prescription-only medicines (POM) are indicated for the treatment of non-insulin dependent diabetes in patients who respond inadequately to dietary measures alone.

These applications for Glibenclamide 2.5mg and 5mg Tablets are submitted according to Article 10c of Directive 2001/83/EC as amended, cross-referring to Glibenclamide 2.5mg and 5mg Tablets, first approved to Arrow Generics Limited on 18th October 2002 (PL 18909/0036-7). These licences underwent a change of ownership to Aurobindo Pharma Limited on 13th September 2006 (PL 20532/0079-80).

It is considered that the pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring.

A Risk Management Plan (RMP) was not submitted and is not required for applications of this type.

No new data were submitted nor were they necessary for these “informed consent” applications, as the data are identical to that of the previously granted cross-reference products.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 21880/0113-4
PROPRIETARY NAME: Glibenclamide 2.5mg and 5mg Tablets
ACTIVE(S): glibenclamide
COMPANY NAME: Medreich PLC
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: POM

1. INTRODUCTION

These are “informed consent” applications for Glibenclamide 2.5mg and 5mg Tablets (PL 21880/0113-4) submitted under Article 10c of Directive 2001/83/EC as amended. The proposed MA holder is Medreich PLC, 9 Royal Parade, Kew Gardens, Surrey, TW9 3QD, United Kingdom.

The applications cross-refer to Glibenclamide 2.5mg and 5mg Tablets, first approved to Arrow Generics Limited on 18th October 2002 (PL 18909/0036-7). These licences underwent a change of ownership to Aurobindo Pharma Limited on 13th September 2006 (PL 20532/0079-80).

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 NAME(S)

The proposed names of the products are Glibenclamide 2.5mg and 5mg Tablets. The product has been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The products are tablets administered orally that contain 2.5mg and 5mg of glibenclamide as the active ingredient. The finished products are packaged in:

- i) Tablet containers composed of polypropylene (PP) or polyethylene (PE) with PP or PE tamper evident closures.
- ii) Glass containers with plastic tamper evident closures.
- iii) White opaque blisters composed of 250µm unplasticised polyvinyl chloride (UPVC) and 40gsm unplasticised polyvinylidene chloride (UPVDC) sealed with 20µm tempered aluminium foil.

Pack sizes are:

- i) PP/PE tablet containers: 100, 500 and 1000 tablets.
- ii) Glass containers: 100, 500 and 1000 tablets.
- iii) Blisters: 10, 14 and 28 tablets.

The proposed shelf-life is 36 months with the following storage instructions:

PP/PE and glass containers: Do not store above 25°C. Store in original container. Keep the container tightly closed.

Blisters: Do not store above 25°C. Store in the original container. Keep in the outer carton.

This is consistent with the details registered for the cross-reference products.

2.3 Legal status

Prescription-only medicine (POM).

2.4 Marketing authorisation holder/Contact Persons/Company

Medreich PLC, 9 Royal Parade, Kew Gardens, Surrey, TW9 3QD, United Kingdom.

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers

The manufacturing sites are consistent with those registered for the cross-reference products and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The composition is consistent with the details registered for the cross-reference products.

2.7 Manufacturing process

The manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch size for each product is stated.

2.8 Finished product/shelf-life specification

The finished product specifications are in-line with the details registered for the cross-reference products.

2.9 Drug substance specification

The drug substance specification is consistent with the details registered for the cross-reference products.

2.10 TSE Compliance

The excipients used are identical to those in the cross-reference products and declarations have been provided to confirm that none contain material of human origin. A declaration has been provided that confirms that the magnesium stearate contained in this product is sourced from vegetable origin. The milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as those intended for human consumption.

This information is consistent with the cross-reference products.

3. EXPERT REPORTS

The applicant has included quality, non-clinical and clinical expert reports in Module 2 of the applications. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product names. The appearance of the products is identical to the cross-reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPCs)

The SmPCs are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL)/LABELLING**PIL**

The PIL has been prepared in-line with the details registered for the cross-reference products. This PIL is identical to the PIL for Glibenclamide 2.5mg and 5mg Tablets, first approved to Arrow Generics Limited on 18th October 2002 (PL 18909/0036-7). These licences underwent a change of ownership to Aurobindo Pharma Limited on 13th September 2006

(PL 20532/0079-80). Therefore the user testing results for the cross-reference products have been submitted and are satisfactory.

The results of consultations with target patient groups ("user testing") are in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that they contain.

Labelling

The artwork is comparable to the artwork registered for the cross-reference products and complies with statutory requirements. In-line with current legislation, the applicant has included the name of the product in Braille on the packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The data submitted with the applications are acceptable. The grant of these Marketing Authorisations is recommended.

NON-CLINICAL ASSESSMENT

No new non-clinical data have been supplied with these applications and none are required for applications of this type.

A satisfactory justification has been provided for the absence of an Environmental Risk Assessment.

CLINICAL ASSESSMENT

No new clinical data have been supplied with these applications and none are required for applications of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for these applications are consistent with that previously approved for the cross-reference products and, as such, has been judged to be satisfactory.

NON-CLINICAL

No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY

These applications are identical to the previously granted applications, Glibenclamide 2.5mg and 5mg Tablets, first approved to Arrow Generics Limited on 18th October 2002 (PL 18909/0036-7). These licences underwent a change of ownership to Aurobindo Pharma Limited on 13th September 2006 (PL 20532/0079-80).

No new or unexpected safety concerns arise from these applications.

At the time of assessment, the SmPCs, PIL and labelling were satisfactory and consistent with that for the cross-reference products.

RISK BENEFIT ASSESSMENT

The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. Extensive clinical experience with glibenclamide is considered to have demonstrated the therapeutic value of the compound. The risk:benefit balance is therefore considered to be positive.

GLIBENCLAMIDE 2.5MG AND 5MG TABLETS**PL 21880/0113-4****STEPS TAKEN FOR ASSESMENT**

1	The MHRA received the Marketing Authorisation Applications on 1 st November 2010.
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 2 nd December 2010.
3	Following assessment of the application further information was requested regarding the quality section of the dossiers on 12 th January 2011, 13 th April 2011 and 22 nd December 2011.
4	The applicant responded to the MHRA's requests, providing further information on 8 th March 2011, 22 nd December 2011 and 14 th February 2012 for the quality section of the dossiers.
5	The applications were determined on 15 th February 2012.

GLIBENCLAMIDE 2.5MG AND 5MG TABLETS

PL 21880/0113-4

STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS**1 NAME OF THE MEDICINAL PRODUCT**

Glibenclamide 2.5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Glibenclamide 2.5mg

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Tablet for oral use

Glibenclamide 2.5mg Tablets are white, circular tablets marked 'GL 2.5' on one face and plain on the reverse.

4 CLINICAL PARTICULARS**4.1 THERAPEUTIC INDICATIONS**

Glibenclamide is a hypoglycaemic agent indicated in the treatment of noninsulin dependent diabetes in patients who respond inadequately to dietary measures alone.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION***For oral administration.******Treatment of previously untreated diabetes:***

Stabilisation can be started with one 5mg tablet daily with or immediately after breakfast or the first main meal. If control is satisfactory one tablet is continued as the maintenance dose. If control is unsatisfactory, the dose can be adjusted by increments of 2.5 or 5mg at weekly intervals. The total daily dosage rarely exceeds 15mg and increasing the daily dosage above this does not generally produce any additional effect.

The total daily requirement should normally be given as a single dose at breakfast, or with the first main meal. The patient's diet and activity should be taken into account.

Children: Glibenclamide is not recommended for use in children.

Elderly: In debilitated patients or aged patients who may be more liable to hypoglycaemia, treatment should be initiated with one 2.5mg tablet daily.

Changeover from other sulphonylureas:

The changeover to glibenclamide from other drugs with similar mode of action can be carried out without any break in therapy.

Treatment is commenced with the equivalent dose of glibenclamide without exceeding an initial dose of 10mg. If response is inadequate, the dose can be raised in a stepwise fashion to 15mg daily. One 5mg tablet of glibenclamide is approximately equivalent to 1g tolbutamide or glymidine, 250mg chlorpropamide or tolazamide, 500mg acetohexamide, 25mg glibornuride or 5mg glipizide.

Changeover from biguanides: The biguanide should be withdrawn and glibenclamide treatment started with one 2.5mg tablet. The dosage should then be adjusted by increments of 2.5mg to achieve control.

Combination with biguanides: If adequate control is not possible with diet and 15mg of glibenclamide, control may be established by combined administration of glibenclamide and a biguanide derivative.

Changeover from insulin:

While it is appreciated that most patients who are on insulin therapy will continue to need it, there may be a few patients, particularly those on low daily doses, who will remain stabilised if transferred from insulin to glibenclamide.

4.3 CONTRAINDICATIONS

- i) Those patients who have or have ever had diabetic ketoacidosis.
- ii) Insulin dependent diabetes mellitus.
- iii) Severe impairment of renal, hepatic, thyroid or adrenocortical function.
- iv) Circumstances of unusual stress such as surgery, severe infection and trauma.
- v) Hypersensitivity to glibenclamide.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Care is necessary in elderly, debilitated or malnourished patients who are particularly susceptible to the hypoglycaemic effects of sulphonylureas, and during excessive exercise as hypoglycaemia may be provoked.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

The hypoglycaemic effect of glibenclamide may be increased by: antiinfective agents (eg: chloramphenicol, fluconazole, miconazole, sulphonamides including co-trimoxazole), anti-inflammatory/analgesic agents (e.g.: phenylbutazone, salicylates), dicoumarin anticoagulants and heparin, lipid regulating agents (e.g. clofibrate), some antidepressants (monoamine oxidase inhibitors, doxepin, nortriptyline), ACE-inhibitors captopril, enalapril, H2-blockers, cimetidine, ranitidine, fenfluramine, methyl dopa and sulphinyprazone, necessitating dosage reduction.

The hypoglycaemic effect of glibenclamide may be diminished by rifampicin, thiazide diuretics and beta-blockers, necessitating dosage increase. Beta-blockers may mask some of the symptoms of hypoglycaemia. Alcohol may interact with the sulphonylureas, provoking facial flushing, and has a variable effect on blood sugar levels.

4.6 FERTILITY, PREGNANCY AND LACTATION

There is no specific information on glibenclamide in pregnancy – insulin therapy is usually substituted. Glibenclamide may be secreted in breast milk and caution should be exercised when prescribing for nursing mothers, as there is a possibility of causing hypoglycaemia in the infant.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None (unless there is a risk of hypoglycaemia).

4.8 UNDESIRABLE EFFECTS

Hypoglycaemia occurs with all hypoglycaemic agents. Gastrointestinal disturbances (e.g.: nausea, vomiting, heartburn, anorexia, diarrhoea, metallic taste) are usually mild and dose dependant. Increased appetite and weight gain may occur, also rashes (usually hypersensitivity reactions), pruritus and photosensitivity. Severe manifestations of hypersensitivity include cholestatic jaundice, leucopenia, thrombocytopenia, aplastic anaemia, agranulocytosis, haemolytic anaemia, erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis and erythema nodosum. Infrequently a syndrome of inappropriate secretion of antidiuretic hormone may be induced.

4.9 OVERDOSE

In acute poisoning the stomach should be emptied by emesis or lavage.

Hypoglycaemia should be treated urgently in the conscious patient with oral glucose. If the patient is comatose glucose should be administered as an intravenous infusion. Alternatively glucagon, administered in a dose of 1mg subcutaneously or intramuscularly may be used. The patient should be observed over several days in case hypoglycaemia recurs.

5 PHARMACOLOGICAL PROPERTIES**5.1 PHARMACODYNAMIC PROPERTIES**

Glibenclamide is an orally active hypoglycaemic agent, which acts by stimulating insulin secretion.
ATC Code: A10BB01

5.2 PHARMACOKINETIC PROPERTIES

Glibenclamide is rapidly absorbed and is extensively bound to plasma proteins, but is not readily displaced by acidic drugs. It is excreted as metabolites in the urine and bile.

5.3 PRECLINICAL SAFETY DATA

There are no pre-clinical data of any relevance to the prescriber, which are additional to those already included in other sections.

6 PHARMACEUTICAL PARTICULARS**6.1 LIST OF EXCIPIENTS**

Lactose monohydrate
Maize Starch
Povidone K30
Magnesium stearate

6.2 INCOMPATIBILITIES

None.

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Polyethylene/polypropylene and glass containers: Do not store above 25° C. Store in the original container. Keep the container tightly closed.

Blister strips: Do not store above 25° C. Store in the original container. Keep in the outer carton.

6.5 NATURE AND CONTENTS OF CONTAINER

Polypropylene or polyethylene tablet container with polypropylene or polyethylene tamper evident closure containing 100, 500 or 1000 tablets

Glass container with plastic tamper evident closure containing 100, 500 or 1000 tablets.

White opaque blister (250µm UPVC 40gsm UPVDC) sealed with 20µm tempered aluminium foil. Tablets are packed in multiples of strips of 10, 14 or 28 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

None

7 MARKETING AUTHORISATION HOLDER

Medreich Plc
9 Royal Parade,
Kew Gardens,
Surrey,
TW9 3QD

8 MARKETING AUTHORISATION NUMBER(S)

PL 21880/0113

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/02/2012

10 DATE OF REVISION OF THE TEXT

15/02/2012

1 NAME OF THE MEDICINAL PRODUCT

Glibenclamide 5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Glibenclamide 5mg

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Tablet for oral use

Glibenclamide 5mg Tablets are white, dragee shaped tablets marked 'GL' and '5' on either side of a break-line on one face and plain on the reverse.

4 CLINICAL PARTICULARS**4.1 THERAPEUTIC INDICATIONS**

Glibenclamide is a hypoglycaemic agent indicated in the treatment of noninsulin dependent diabetes in patients who respond inadequately to dietary measures alone.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION***For oral administration.******Treatment of previously untreated diabetes:***

Stabilisation can be started with one 5mg tablet daily with or immediately after breakfast or the first main meal. If control is satisfactory one tablet is continued as the maintenance dose. If control is unsatisfactory, the dose can be adjusted by increments of 2.5 or 5mg at weekly intervals. The total daily dosage rarely exceeds 15mg and increasing the daily dosage above this does not generally produce any additional effect.

The total daily requirement should normally be given as a single dose at breakfast, or with the first main meal. The patient's diet and activity should be taken into account.

Children: Glibenclamide is not recommended for use in children.

Elderly: In debilitated patients or aged patients who may be more liable to hypoglycaemia, treatment should be initiated with one 2.5mg tablet daily.

Changeover from other sulphonylureas:

The changeover to glibenclamide from other drugs with similar mode of action can be carried out without any break in therapy.

Treatment is commenced with the equivalent dose of glibenclamide without exceeding an initial dose of 10mg. If response is inadequate, the dose can be raised in a stepwise fashion to 15mg daily. One 5mg tablet of glibenclamide is approximately equivalent to 1g tolbutamine or glymidine, 250mg chlorpropamide or tolazamide, 500mg acetohexamide, 25mg glibornuride or 5mg glipizide.

Changeover from biguanides: The biguanide should be withdrawn and glibenclamide treatment started with one 2.5mg tablet. The dosage should then be adjusted by increments of 2.5mg to achieve control.

Combination with biguanides: If adequate control is not possible with diet and 15mg of glibenclamide, control may be established by combined administration of glibenclamide and a biguanide derivative.

Changeover from insulin:

While it is appreciated that most patients who are on insulin therapy will continue to need it, there may be a few patients, particularly those on low daily doses, who will remain stabilised if transferred from insulin to glibenclamide.

4.3 CONTRAINDICATIONS

- i) Those patients who have or have ever had diabetic ketoacidosis.
- ii) Insulin dependent diabetes mellitus.
- iii) Severe impairment of renal, hepatic, thyroid or adrenocortical function.
- iv) Circumstances of unusual stress such as surgery, severe infection and trauma.
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4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Care is necessary in elderly, debilitated or malnourished patients who are particularly susceptible to the hypoglycaemic effects of sulphonylureas, and during excessive exercise as hypoglycaemia may be provoked.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

The hypoglycaemic effect of glibenclamide may be increased by: antiinfective agents (eg: chloramphenicol, fluconazole, miconazole, sulphonamides including co-trimoxazole), anti-inflammatory/analgesic agents (e.g.: phenylbutazone, salicylates), dicoumarin anticoagulants and heparin, lipid regulating agents (e.g. clofibrate), some antidepressants (monoamine oxidase inhibitors, doxepin, nortriptyline), ACE-inhibitors captopril, enalapril, H2-blockers, cimetidine, ranitidine, fenfluramine, methyl dopa and sulphapyrazone, necessitating dosage reduction.

The hypoglycaemic effect of glibenclamide may be diminished by rifampicin, thiazide diuretics and beta-blockers, necessitating dosage increase. Beta-blockers may mask some of the symptoms of hypoglycaemia. Alcohol may interact with the sulphonylureas, provoking facial flushing, and has a variable effect on blood sugar levels.

4.6 FERTILITY, PREGNANCY AND LACTATION

There is no specific information on glibenclamide in pregnancy – insulin therapy is usually substituted. Glibenclamide may be secreted in breast milk and caution should be exercised when prescribing for nursing mothers, as there is a possibility of causing hypoglycaemia in the infant.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None (unless there is a risk of hypoglycaemia).

4.8 UNDESIRABLE EFFECTS

Hypoglycaemia occurs with all hypoglycaemic agents. Gastrointestinal disturbances (e.g.: nausea, vomiting, heartburn, anorexia, diarrhoea, metallic taste) are usually mild and dose dependant. Increased appetite and weight gain may occur, also rashes (usually hypersensitivity reactions), pruritus and photosensitivity. Severe manifestations of hypersensitivity include cholestatic jaundice, leucopenia, thrombocytopenia, aplastic anaemia, agranulocytosis, haemolytic anaemia, erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis and erythema nodosum. Infrequently a syndrome of inappropriate secretion of antidiuretic hormone may be induced.

4.9 OVERDOSE

In acute poisoning the stomach should be emptied by emesis or lavage.

Hypoglycaemia should be treated urgently in the conscious patient with oral glucose. If the patient is comatose glucose should be administered as an intravenous infusion. Alternatively glucagon, administered in a dose of 1mg subcutaneously or intramuscularly may be used. The patient should be observed over several days in case hypoglycaemia recurs.

5 PHARMACOLOGICAL PROPERTIES**5.1 PHARMACODYNAMIC PROPERTIES**

Glibenclamide is an orally active hypoglycaemic agent, which acts by stimulating insulin secretion.
ATC Code: A10BB01

5.2 PHARMACOKINETIC PROPERTIES

Glibenclamide is rapidly absorbed and is extensively bound to plasma proteins, but is not readily displaced by acidic drugs. It is excreted as metabolites in the urine and bile.

5.3 PRECLINICAL SAFETY DATA

There are no pre-clinical data of any relevance to the prescriber, which are additional to those already included in other sections.

6 PHARMACEUTICAL PARTICULARS**6.1 LIST OF EXCIPIENTS**

Lactose monohydrate
Maize Starch
Povidone K30
Magnesium stearate

6.2 INCOMPATIBILITIES

None.

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Polyethylene/polypropylene and glass containers: Do not store above 25° C. Store in the original container. Keep the container tightly closed.

Blister strips: Do not store above 25° C. Store in the original container. Keep in the outer carton.

6.5 NATURE AND CONTENTS OF CONTAINER

Polypropylene or polyethylene tablet container with polypropylene or polyethylene tamper evident closure containing 100, 500 or 1000 tablets

Glass container with plastic tamper evident closure containing 100, 500 or 1000 tablets.

White opaque blister (250µm UPVC 40gsm UPVDC) sealed with 20µm tempered aluminium foil. Tablets are packed in multiples of strips of 10, 14 or 28 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

None

7 MARKETING AUTHORISATION HOLDER

Medreich Plc
9 Royal Parade,
Kew Gardens,
Surrey,
TW9 3QD

8 MARKETING AUTHORISATION NUMBER(S)

PL 21880/0114

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/02/2012

10 DATE OF REVISION OF THE TEXT

15/02/2012

PACKAGE LEAFLET: INFORMATION FOR THE USER

Glibenclamide 2.5mg Tablets
Glibenclamide 5mg Tablets
 (glibenclamide)

Read all of this leaflet carefully before you start taking this medicine.

- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Glibenclamide Tablets are and what they are used for
2. Before you take Glibenclamide Tablets
3. How to take Glibenclamide Tablets
4. Possible side effects
5. How to store Glibenclamide Tablets
6. Further information

1. WHAT GLIBENCLAMIDE TABLETS ARE AND WHAT THEY ARE USED FOR

Glibenclamide belongs to a group of medicines known as oral hypoglycaemics which are used to treat diabetics of the non insulin dependent type which does not respond to dietary measures and which generally only occurs in adults.

2. BEFORE YOU TAKE GLIBENCLAMIDE TABLETS**Do not take Glibenclamide Tablets**

- If you are allergic (hypersensitive) to glibenclamide or any of the ingredients in the tablet (see Section 6 and end of Section 2).
- if you suffer from insulin-dependent diabetes mellitus
- If you are having an operation, or have a severe infection, or are suffering from extreme stress or trauma.
- If you have ketoacidosis (a complication of diabetes with ketones in the urine).
- If you have any problem with your liver or kidneys.
- If you have severe thyroid or adrenal gland problems

Take special care with Glibenclamide Tablets

- If you are run-down or elderly
- if you are malnourished,
- During excessive exercise or unusual stress as these can cause blood sugar levels to get too low, known as "hypoglycaemia". Early warning symptoms of low blood sugar include faintness, sweating, trembling, confusion or headache. You will need to eat and drink something sugary quickly.

Taking other medicines

The dose of Glibenclamide may need to be reduced if you are taking the following:

- drugs which are used to treat infections e.g. *fluconazole, sulphonamides*
- some pain killers e.g. aspirin,
- some agents used to thin the blood e.g. *heparin*
- some drugs for high cholesterol in the blood e.g. *clofibrate*
- some anti-depressants e.g. *doxepine, nortriptyline*
- drugs for high blood pressure and heart failure e.g. *captopril, enalapril*
- drugs for stomach ulcers and dyspepsia e.g. *cimetidine, ranitidine*
- drugs for obesity and gout e.g. fenfluramine; Sulphinpyrazone

The dose of Glibenclamide may need to be increased if you are taking the following:

- rifampicin.
- diuretic drugs e.g. thiazide
- beta-blocker drugs such as propranolol

Some product purchased at the chemists may have a high sugar content which may raise blood sugar levels.

Taking Glibenclamide Tablets with food and drink:

Glibenclamide should be taken with or immediately after food.

Drinking alcohol is not recommended as it can alter the control of your diabetes in an unpredictable manner.

Pregnancy and breast-feeding

Tell your doctor if you are pregnant, planning to become pregnant or breast-feeding. Do not breastfeed whilst on Glibenclamide Tablets without advice from your doctor.

Effects on the ability to drive and use machines:

Low blood sugar may occur at the beginning of the treatment while your doctor is trying to find the dose that best suits you. If you experience the symptoms of low blood sugar (hypoglycaemia) – **sweating, trembling, weakness, double vision, palpitations, confusion**, you should not drive or operate machinery.

When your blood sugar is stabilized you may drive or operate machinery.

Important information about some of the ingredients of Glibenclamide Tablets

Lactose - if you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE GLIBENCLAMIDE TABLETS

Always take Glibenclamide Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The usual starting dose for Glibenclamide is 2.5 - 5mg orally once a day with or immediately after breakfast or the first main meal of the day.

Children: Glibenclamide is not recommended for used in children

Elderly: treatment should be initiated with one 2.5mg daily.

Your doctor will inform you on your specific dosage needs if you are changing over from other medicines which you have been taking for this condition or if glibenclamide must be used together with another medicine to keep your illness in control.

You should continue to take these tablets for as long as your doctor tells you to.

If you take more Glibenclamide than you should

If you or someone else accidentally takes too many Glibenclamide Tablets seek immediate medical help by contacting your doctor or nearest hospital casualty department. Take the carton and any remaining tablets you have with you.

If you forget to take Glibenclamide Tablets

If you forget to take a dose, do not worry, just wait until it is time for your next dose.

Do not take a double dose to make up for a forgotten tablet.

If you stop taking Glibenclamide Tablets

If you stop taking Glibenclamide Tablets tell your doctor as soon as possible, as your diabetes will not be controlled. If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines Glibenclamide Tablets can cause some side-effects although not everybody gets them.

You may suffer an **allergic** reaction, symptoms of which include rash, itching, difficulty in breathing or swelling of the face, lips, throat or tongue. If this happens to you, **stop taking** the Tablets immediately and seek medical help.

The following have also been reported:

Common side effects (affecting between 1 in 10 and 1 in 100 people):

- low blood sugar
- changes in taste sensation
- constipation
- diarrhea
- dizziness
- frequent urination or increased amounts of urine
- gas in stomach
- heartburn
- nausea, vomiting
- stomach pain or discomfort
- unusual weight gain

Uncommon side effects (affecting between 1 in 100 and 1 in 1000 people):

- itching and/or rash
- peeling of skin
- reddening of skin

Rare side effects (affecting between 1 in 1000 and 1 in 10000 people)

- inflammation of the liver
- yellowing of eyes or skin
- shortness of breath

- leucopenia (abnormally low white blood cell count)
- sore throat
- unusual bleeding or bruising
- unusual tiredness

Very Rare side effects (affecting 1 in 10,000 people)

- increased sensitivity to skin to the sun

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE GLIBENCLAMIDE TABLETS

Keep out of the reach and sight of children.

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

The expiry date refers to the last day of the month.

These tablets should not be stored above 25°C and should be kept in their original container to protect them from light and moisture.

Medicines should not be disposed of via wastewater or household water. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

6. FURTHER INFORMATION

What Glibenclamide Tablets contain

The active substance is glibenclamide.

The 2.5mg tablet contains 2.5mg of glibenclamide and the 5.0mg tablet contains 5.0mg glibenclamide.

The other ingredients are lactose, maize starch, povidone K30 and magnesium stearate.

What Glibenclamide Tablets look like and the contents of the pack

Glibenclamide 2.5mg Tablets are white circular tablets marked 'GL 2.5' on one face and plain on the reverse. They are available in blister packs of 10, 14, 28, 100, 500 and 1000 tablets.

Glibenclamide 5mg Tablets are white, dragee shaped tablets marked 'GL' and '5' either side of a breakline on one face and plain on the reverse. They are available in blister packs of 28, 100, 500 and 1000 tablets.

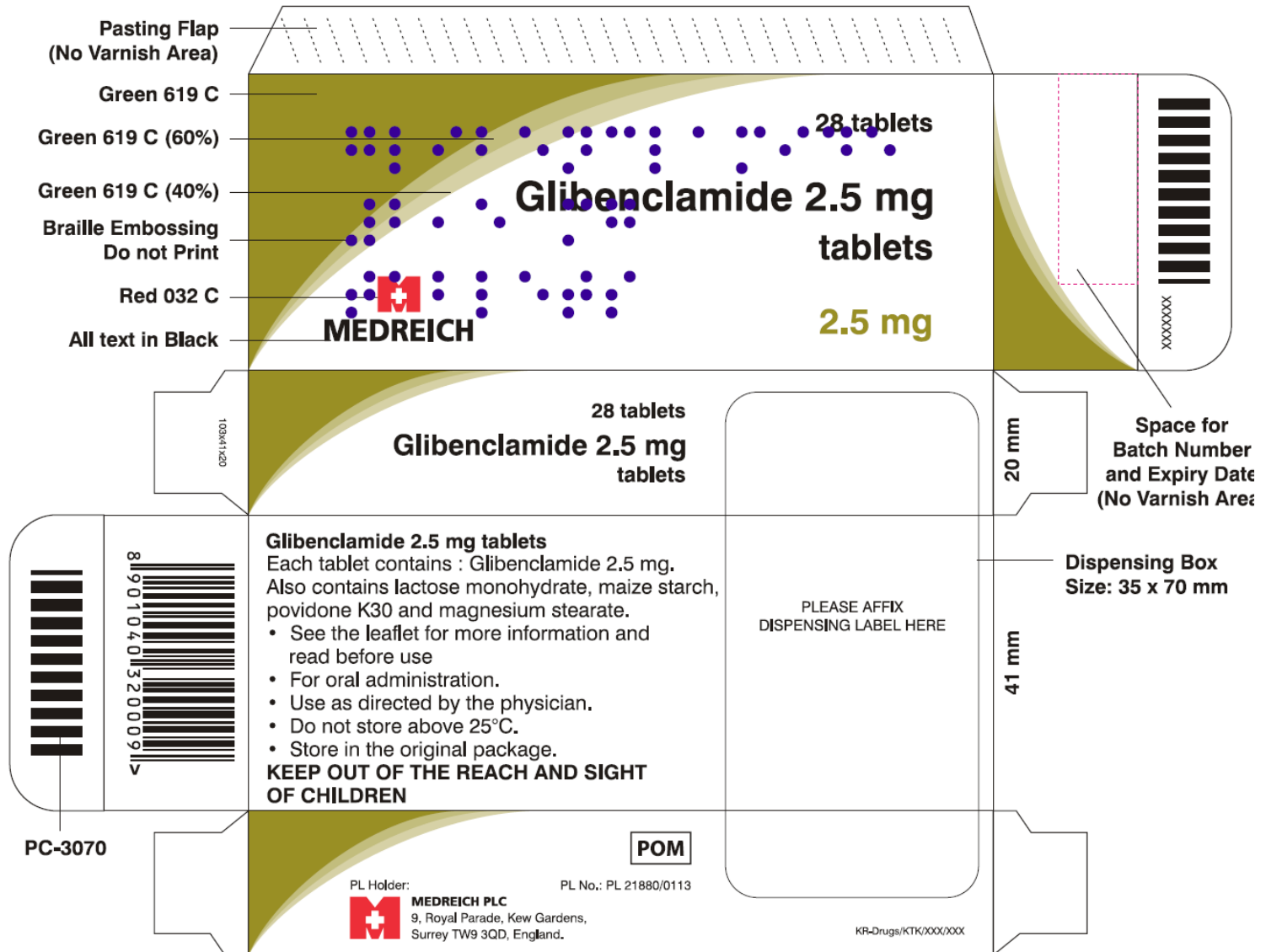
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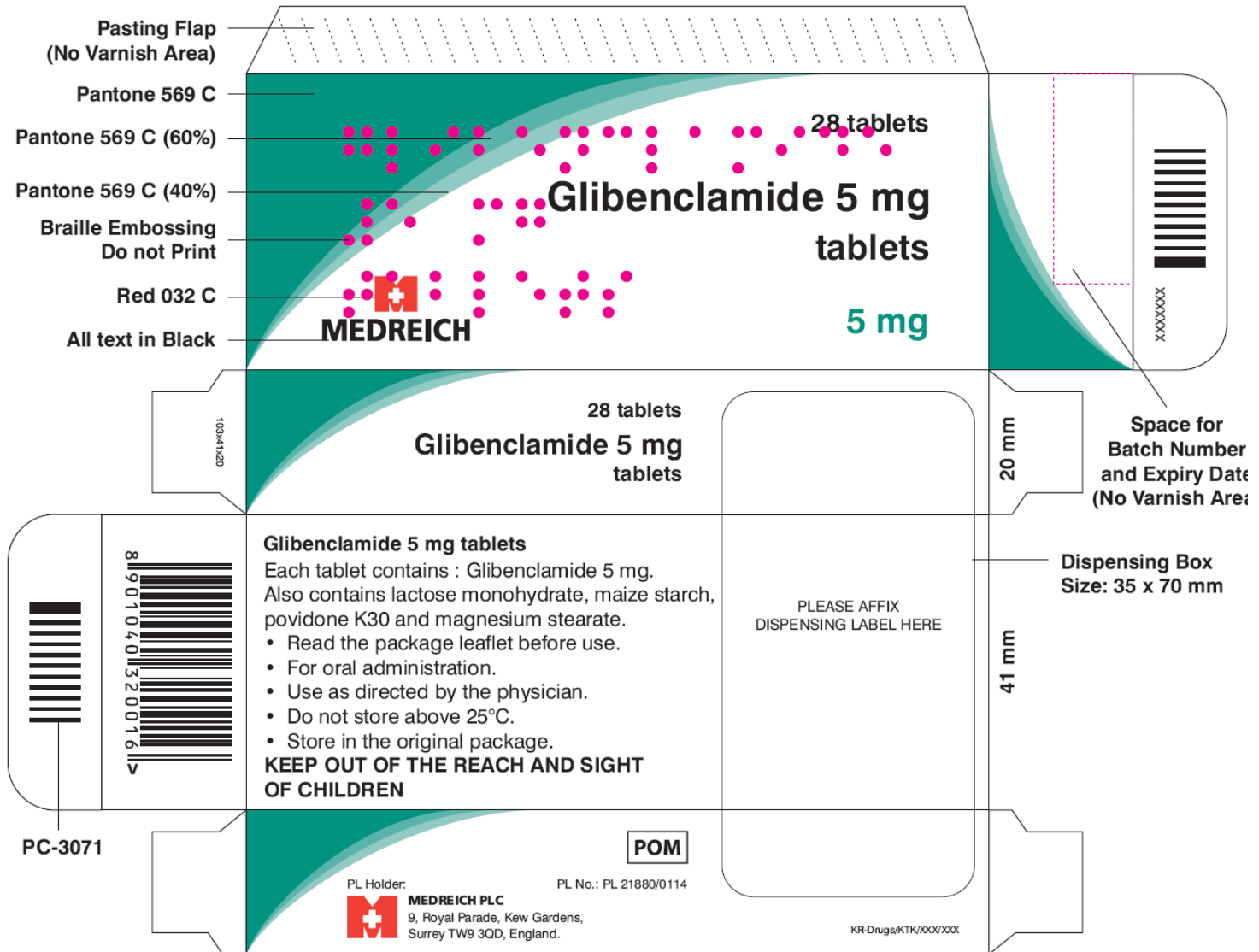
Medreich Plc,
9 Royal Parade, Kew Gardens,
Surrey, TW9 3QD,
United Kingdom

Manufacturer

Milpharm Limited
Ares Odyssey Business Park
West End Road
South Ruislip HA4 6QD
United Kingdom

This leaflet was last approved in {10/2010}.





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