1 Name of the medicinal product:

1.1 Product name: Glycinorm-80
(Gliclazide Tablets BP 80mg**)**

1.2 Strength:
Each tablet contains:
Gliclazide BP……80 mg

1.3 Pharmaceutical dosage form:
Solid dosage form (Tablets)

2. Qualitative and Quantitative Composition:

2.1 Qualitative Declaration:
Gliclazide is chemically described as N-[[Hexahydrocyclopenta[c]pyrrol-2(IH)-y l) -amino] carbony l] -4-methylbenzene sulfonamide

2.2 Quantitative Declaration:
Each tablet contains:
Gliclazide BP……80 mg

3. Pharmaceutical Form:
Glycinorm-80 (Gliclazide Tablets BP 80mg) are white to off white, circular, flat, beveled vedged, uncoated tablets with breakline on one side & 'G 80' embossed on other side.

4. Clinical Particulars:

4.1 Therapeutic Indications:
Glycinorm is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes whose hyperglycaemia cannot be controlled by diet and exercise alone.

4.2 Posology and method of administration:

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 40-80 mg daily and increasing until adequate control is achieved.Asingle dose of gliclazide should not exceed 160mg. When higher doses are required, gliclazide should be taken twice daily and according to the main meals of the day. When patients are transferred to gliclazide from another sulphonylurea antidiabetic medication (with the exception of chlorpropamide), no transition period is required. When transferring patients from chlorpropamide, caution should be exercised during the first 1 to 2 weeks because of the prolonged retention of chlorpropamide in the body. During conversion from insulin therapy to gliclazide therapy, no gradual dosage adjustment is required for patients using less than 20 USP Units of insulin daily. For patients using 20 or more USPunits daily, a 25 to 30% reduction in insulin every day or every second day with gradual dosage adjustment is advisable. Hospitalization for some patients on a higher insulin dosage may be required for uneventful conversion.

4.3 Contraindications:

· Known hypersensitivity to gliclazide or to any of the excipients, other sulphonylureas, sulphonamides

· Juvenile onset diabetes

· Diabetes complicated by ketosis and acidosis

· Diabetic pre-coma and coma

· Severe renal or hepatic insufficiency

· Diabetics undergoing surgery, after severe trauma or during infections

· Pregnancy

4.4 Special warning and precautions for use:

i. Hypoglycaemia

All sulphonylurea drugs are capable of producing moderate or severe hypoglycaemia, 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

· 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 According To The Blood Glucose Response And To The 24- Urinary Glucose During The First Days Oftreatment

· *Dosage adjustments may be necessary:*

· On The Occurrence Of Mild Symptoms Of Hypoglycaemia (Sweating, Pallor, Hunger Pangs, Tachycardia, Sensation Of Malaise). Suchfindings 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)

· 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 Increase Progressively The Dosage Of Gliclazide And If This Is Insufficient, To Discontinue The Treatment With Gliclazide And To administer insulin . As with other Sulphonylureas, Hypoglycaemia Will Occur If The Patients' Dietary Intake Is Reduced Or If They Are Receiving A Larger Dose Of Gliclazide Then Required

ii. Renal or hepatic impairment

Care should be exercised in patients with hepatic and/or renal impairment and a small starting dose should be used with careful patient monitoring

4.5 Drug interactions

Care should be taken when giving gliclazide with drugs which are known to alter the diabetic state or potentiate the drug's action.

The hypoglycaemic effect of gliclazide may be potentiated by phenylbutazone, salicylates, sulphonamides, non-steroidal anti-inflammatory drugs, coumarin derivatives, MAOIs, beta adrenergic receptor blocking agents, tetracycline compounds, chloramphenicol, clofibrate, disopyramide, miconazole (oral forms) and cimetidine. It may be diminished by corticosteroids, oral contraceptives, phenothiazine derivatives, thyroid hormones and abuse of laxatives. The hypoglycaemic action of sulphonylureas may be opposed by the induction of hepatic enzymes which metabolize the drug, causing lower plasma concentrations and less hypoglycaemic effect. Common inducers include rifampicin, barbiturates, phenytoin and alcohol or by drugs that inhibit the release or action of insulin e.g. thiazide diuretics, diazoxide, glucocorticoids, estrogens or sympathomimetic drugs. Early symptoms of hypoglycaemia such as tremor, sweating, and tachycardia may be masked by beta-adrenoreceptor blocking drugs,such as propranolol , al lowing severe hypoglycemic episodes. If beta adrenoreceptor blocking drugs are required, the more selective types such as metoprolol or atenolol are preferred in the diabetic patients.

Drug food interactions

Food delays absorption of gliclazide; may be best taken 30 minutes before or with a meal.

4.6 Pregnancy and lactation:

Glycinorm is contraindicated in pregnancy. It has not been established whether gliclazide is transferred to human milk. However, othersulphonylureas have been found in milk and there from the group in this respect.

Usage in paediatrics

There are no data and clinical studies available in children

Usage in geriatrics

Plasma clearance of gliclazide is not altered in the elderly and steady state plasma levels can therefore be expected to be similar to those inadults 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.

Some elderly patients may be more sensitive to the drug, but the plasma clearance is not altered so that increased plasma levels are unlikely. All sulphonylureas should be used with caution in the elderly because of the greater likelihood of their missing meals and the more severe outcome of significant hypoglycemia.

4.7 Effect on ability to drive and use machine:

Patients should be made aware of the symptoms of hypoglycaemia and should be careful if driving or operating machinery, especially at the beginning of the treatment.

4.8 Adverse Effects:

· Hypoglycaemia

· Abnormalites of hepatic function are not uncommon during gliclazide therapy. There are rare reports of hepatic failure, hepatitis and jaundice following treatment with gliclazide · Mild gastrointestinal disturbances including nausea, dyspepsia, diarrhoea, constipation have been reported but this type of adverse reaction can be avoided if gliclazide is taken during a meal

· Skin reactions including rash, pruritus, erythema, bullous eruption; blood dyscrasia including anemia , lukopenia , 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 of overdose would be hypoglycaemia. The treatment is gastric lavage and correction of the hypoglycaemia by appropriate means with continual monitoring of the patient's blood sugar until the effect of the drug has ceased.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties:

Gliclazide reduces blood glucose levels by stimulating insulin secretion from the beta cells of the islets of Langerhans. 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. In addition to these metabolic properties, gliclazide has haemovascular properties. 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, hromboxane B) 2

· An action on the vascular endothelium fibrinolytic activity with an increase in tPAactivity

5.2 Pharmacokinetic properties:

Gliclazide is well absorbed. Food delays absorption of gliclazide; may be best taken 30 minutes before or with a meal. Plasma protein binding is approximately 95%. Gliclazide is mainly metabolised in the liver and excreted in the urine: less than 5% of the dose is excreted unchanged in the urine. No active metabolites have been detected in plasma. Its half life in man is approximately 10-12 hours. No clinical significant changes in pharmacokinetic parameters have been observed in elderly patients.

5.3 Preclinical safety data:

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6. Pharmaceutical Particulars:

6.1 List of excipients:

Microcrystalline Cellulose (Avicel pH 101), Lactose, Polyvinyl Pyrrolidone Povidone K 30), Purified Talc, Crosscarmellose Sodium, Magnesium Stearate

6.2 Incompatibilities:

Not applicable

6.3 Shelf – life:

36 months

6.4 Special precautions for storage:

Store below 30°C. Store in dry condition.

Keep out of reach and sight of children

6.5 Nature and contents of container:

Glycinorm-80 (Gliclazide Tablets BP 80mg) is packaged in clear PVDC coated PVC / Aluminium blister pack. 3 such blister strips, each containing 10 tablets in a printed showbox with a leaflet.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

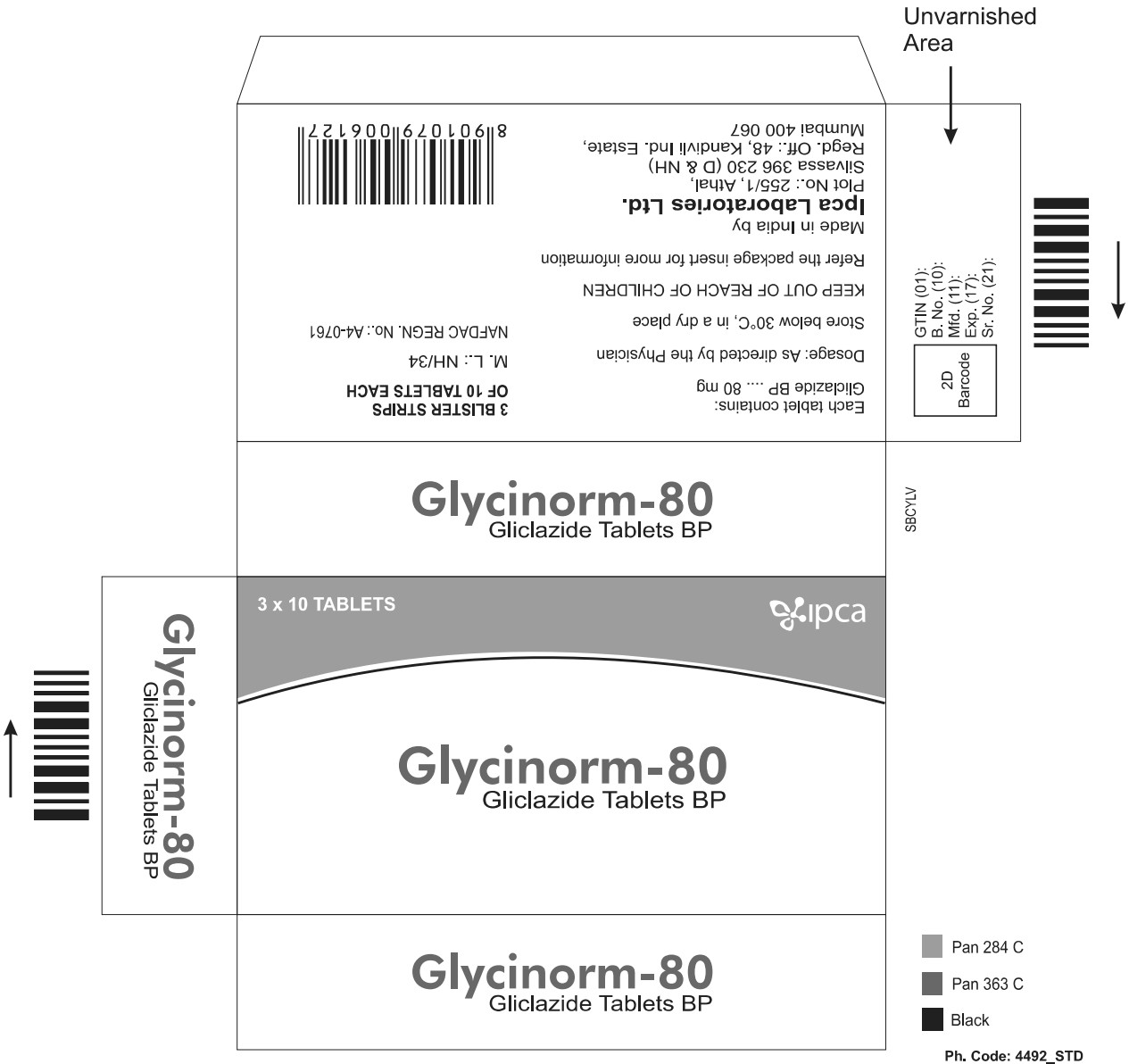
Ipca Pharma Nig Ltd.
No, 3, llupeju Bye Pass,
(Olajire House)
llupeju Lagos,
ipcaharma@yahoo.com

8. DRUG PRODUCT MANUFACTURER

Ipca Laboratories Limited,
Plot No. 255/1, Village-Athal,
Silvassa 396230, Union Territory of Dadra & Nagar
Haveli and Daman & Diu, India

9. NAFDAC REGISTRATION NUMBER (S)

A4-0761



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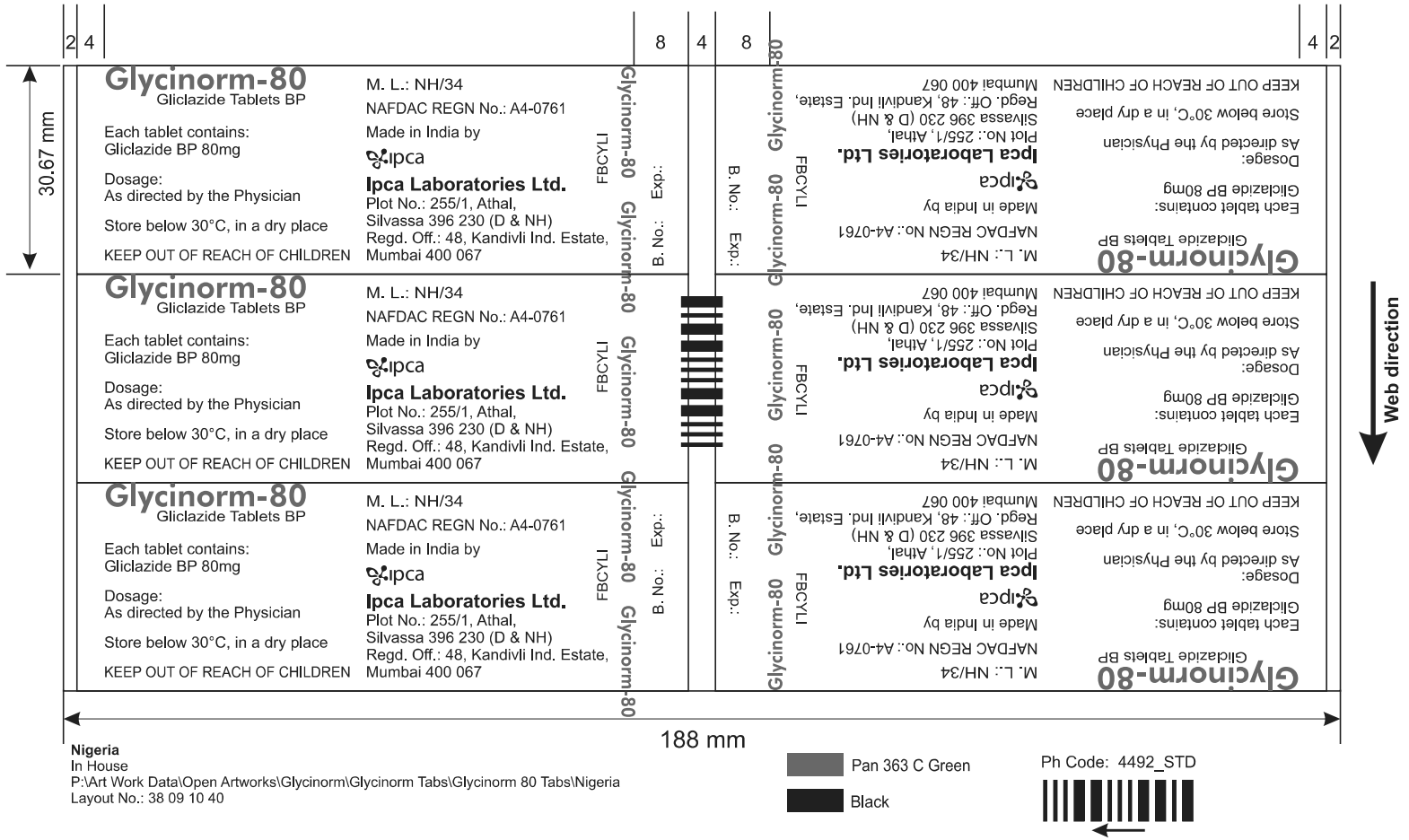
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4 2
30.67 mm
Glycinorm-80
Gliclazide Tablets BP
Each tablet contains:
Gliclazide BP 80mg
Dosage:
As directed by the Physician
Store below 30°C, in a dry place
KEEP OUT OF REACH OF CHILDREN
M. L.: NH/34
NAFDAC REGN No.: A4-0761
Made in India by
Ipca Laboratories Ltd.
Plot No.: 255/1, Athal,
Silvassa 396 230 (D & NH)
Regd. Off.: 48, Kandivli Ind. Estate,
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For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Glycinorm

GLICLAZIDE TABLETS BP

DESCRIPTION

Gliclazide is an oral antidiabetic agent, belonging to sulphonylurea group and differing from other related compounds by the addition of an azabicyclo-octane ring. It is a second generation sulphonylurea drug that has hypoglycaemic and potentially useful hemobiological properties. It has chemical formula N-[[Hexahydrocyclopenta [c]pyrrol-2(1H)-yl)-amino]carbonyl]-4-methylbenzene sulfonamide. Its empirical formula is $C_{15}H_{21}N_3O_3S$.

COMPOSITION

GLYCINORM-40

Each tablet contains:
Gliclazide BP.....40 mg

GLYCINORM-80

Each tablet contains:
Gliclazide BP.....80 mg

PHARMACOLOGY

Gliclazide reduces blood glucose levels by stimulating insulin secretion from the beta cells of the islets of Langerhans. 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.

In addition to these metabolic properties, gliclazide has haemovascular properties.

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

PHARMACOKINETICS

Gliclazide is well absorbed. Food delays absorption of gliclazide; may be best taken 30 minutes before or with a meal.

Plasma protein binding is approximately 95%.

Gliclazide is mainly metabolised in the liver and excreted in the urine: less than 5% of the dose is excreted unchanged in the urine. No active metabolites have been detected in plasma.

Its half life in man is approximately 10-12 hours.

No clinically significant changes in pharmacokinetic parameters have been observed in elderly patients.

INDICATIONS

Glycinorm is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes whose hyperglycaemia cannot be controlled by diet and exercise alone.

CONTRAINDICATIONS

- Known hypersensitivity to gliclazide or to any of the excipients, other sulphonylureas, sulphonamides
- Juvenile onset diabetes
- Diabetes complicated by ketosis and acidosis
- Diabetic pre-coma and coma
- Severe renal or hepatic insufficiency
- Diabetics undergoing surgery, after severe trauma or during infections
- Pregnancy

PRECAUTIONS AND WARNINGS

i. Hypoglycaemia

All sulphonylurea drugs are capable of producing moderate or severe hypoglycaemia, 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
- 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 according to the blood glucose response and to the 24-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)
- 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 increase progressively the dosage of gliclazide and if this is insufficient, to discontinue the treatment with gliclazide and to administer insulin. As with other sulphonylureas, hypoglycaemia will occur if the patients' dietary intake is reduced or if they are receiving a larger dose of gliclazide then required

ii. Renal or hepatic impairment

Care should be exercised in patients with hepatic and/or renal impairment and a small starting dose should be used with careful patient monitoring

Effects on ability to drive and use machines

Patients should be made aware of the symptoms of hypoglycaemia and should be careful if driving or operating machinery, especially at the beginning of the treatment.

Usage in pregnancy and lactation

Glycinorm is contraindicated in pregnancy.

It has not been established whether gliclazide is transferred to human milk. However, other sulphonylureas have been found in milk and there from the group in this respect.

Usage in paediatrics

There are no data and clinical studies available in children.

Usage in geriatrics

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.

Some elderly patients may be more sensitive to the drug, but the plasma clearance is not altered so that increased plasma levels are unlikely. All sulphonylureas should be used with caution in the elderly because of the greater likelihood of their missing meals and the more severe outcome of significant hypoglycemia.

Drug interactions

Care should be taken when giving gliclazide with drugs which are known to alter the diabetic state or potentiate the drug's action.

The hypoglycaemic effect of gliclazide may be potentiated by phenylbutazone, salicylates, sulphonamides, non-steroidal anti-inflammatory drugs, coumarin derivatives, MAOIs, beta adrenergic receptor blocking agents, tetracycline compounds, chloramphenicol, clofibrate, disopyramide, miconazole (oral forms) and cimetidine.

It may be diminished by corticosteroids, oral contraceptives, phenothiazine derivatives, thyroid hormones and abuse of laxatives.

The hypoglycaemic action of sulphonylureas may be opposed by the induction of hepatic enzymes which metabolize the drug, causing lower plasma concentrations and less hypoglycaemic effect. Common inducers include rifampicin, barbiturates, phenytoin and alcohol or by drugs that inhibit the release or action of insulin e.g. thiazide diuretics, diazoxide, glucocorticoids, estrogens or sympathomimetic drugs. Early symptoms of hypoglycaemia such as tremor, sweating, and tachycardia may be masked by beta-adrenoreceptor blocking drugs, such as propranolol, allowing severe hypoglycemic episodes. If beta adrenoreceptor blocking drugs are required, the more selective types such as metoprolol or atenolol are preferred in the diabetic patients.

Drug food interactions

Food delays absorption of gliclazide; may be best taken 30 minutes before or with a meal.

ADVERSE DRUG REACTIONS

- Hypoglycaemia
- Abnormalites of hepatic function are not uncommon during gliclazide therapy. There are rare reports of hepatic failure, hepatitis and jaundice following treatment with gliclazide
- Mild gastrointestinal disturbances including nausea, dyspepsia, diarrhoea, constipation have been reported but this type of adverse reaction can be avoided if gliclazide is taken during a meal
- Skin reactions including rash, pruritus, erythema, bullous eruption; blood dyscrasia including anaemia, leukopenia, thrombocytopenia and granulocytopenia have been observed during treatment with gliclazide but are not known to be directly attributable to the drug.

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

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 40-80 mg daily and increasing until adequate control is achieved. A single dose of gliclazide should not exceed 160mg.

When higher doses are required, gliclazide should be taken twice daily and according to the main meals of the day.

When patients are transferred to gliclazide from another sulphonylurea antidiabetic medication (with the exception of chlorpropamide), no transition period is required. When transferring patients from chlorpropamide, caution should be exercised during the first 1 to 2 weeks because of the prolonged retention of chlorpropamide in the body.

During conversion from insulin therapy to gliclazide therapy, no gradual dosage adjustment is required for patients using less than 20 USP Units of insulin daily. For patients using 20 or more USP units daily, a 25 to 30% reduction in insulin every day or every second day with gradual dosage adjustment is advisable. Hospitalization for some patients on a higher insulin dosage may be required for uneventful conversion.

PRESENTATION

GLYCINORM-40: Blister pack of 10 tablets
GLYCINORM-80: Blister pack of 10 tablets

STORAGE

Store below 30°C, in a dry place
KEEP OUT OF REACH OF CHILDREN

IBCYRA

Made in India by

ipca

Ipca Laboratories Ltd.

Regd. Off.: 48, Kandivli Ind. Estate,
Mumbai 400 067

IBCYRA

Size: 120 x 150 mm

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In House
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Ph Code: 4492_STD