PRODUCT NAME: HOBETIC 2MG TABLET (A4-5610)

1-Name of the Medicinal Product:

1.1 Product Name

Hobetic 2mg Tablet

1.2 Strength

Glimepiride 2 mg

1.3 Pharmaceutical Dosage Form

Tablet

2-Quality and Quantitative Composition:

ACTIVE INGREDIENTS	PER TABLET (MG)
Glimepiride	2 mg

For excipients, see 6.1

3-Pharmaceutical Form:

Oblong, green mottled uncoated tablet, bevel edged, flat-faces, break-bar on one face and "hovid" embossed on another face.

4-Clinical Particulars

4.1 Therapeutic indications

Treatment of type 2 (non-insulin dependent) diabetes, adjunct to diet and exercise. Treatment with Hobetic shall only be initiated when sugar level cannot be controlled adequately by diet, physical exercise and weight reduction. Hobetic may also be used in combination with insulin.

Posology and method of administration

Dosage of Hobetic is based on the desired blood sugar level. Minimum effective dose, which is sufficient to achieve the desired metabolic control, shall be administered.

Usual starting dose

Initial dose is 1 to 2 mg once a day, administered with breakfast or the first main meal. If necessary, doses can be gradually titrated based on regular blood sugar monitoring, at intervals of 1-2 weeks.

Usual maintenance

The usual maintenance dose is 1 to 4 mg once daily. The maximum recommended dose is 8 mg once daily. After reaching dose of 2 mg, dosage increases should be made in increment no more than 2 mg at 1-2 weeks intervals based on patient's blood sugar response. Only some patients benefit from daily doses of > 6 mg.

Treatment with Hobetic must be initiated and monitored by doctor. The initial and maintenance doses are set based on regular checks of blood and urine sugar level. Timing and distribution of doses shall take into consideration patient's lifestyle. A dose adjustment must be considered whenever the patient's weight and lifestyle changes or other factors causing an increased susceptibility to hypoglycaemia or to

an excessive increase in blood sugar levels arise.

As the control of diabetes improves, sensitivity to insulin increases; thus glimepiride requirements may fall as treatment proceeds. To avoid excessive hypoglycaemia, a timely reduction or cessation of Hobetic must be considered.

When blood sugar level is not adequately controlled with maximum dose of Hobetic, insulin may be given concomitantly. Dosage of Hobetic should be maintained while low dose insulin may be added. Upward adjustment of insulin can be done approximately weekly as guided by frequent measurements of fasting blood sugar.

4.2 Contraindications

- Hobetic is not suitable for the treatment of type I diabetes mellitus (eg for the treatment of diabetics with history of ketoacidosis), of diabetic ketoacidosis, or of diabetic precoma or coma.
- Hobetic is contraindicated in patients with known hypersensitivity to glimepiride, other sulphonamides or any of the excipients.
- There is insufficient data concerning the use of Hobetic in patients with severe renal or hepatic impairment. A changeover to insulin is indicated.

4.4 Special warning and precautions for use

- The administration of one drug in sulfonylurea class (tolbutamide) has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet or diet plus insulin (based on the study conducted by the University Group Diabetes Program). Although only tolbutamide was included in the study, it is for safety standpoint that this warning be applied to other hypoglycaemic agents as well.
- Proper diet, regular and sufficient exercise and achieving healthy body weight shall be part of the blood sugar control regimen.
- Patients must be well informed about these effects and that of Hobetic. When treatment is initiated, the risk of hypoglycaemia may be higher and necessitates careful monitoring. Factors contributing to hypoglycaemia includes incompliance; improper diet and mealtime; imbalance between physical exercise and carbohydrate intake; alcohol consumption; impaired liver or renal function; uncompensated disorder of endocrine system affecting carbohydrate metabolism or counter-regulation of hypoglycaemia; overdosage or concurrent administration with other medicine. If such risk factors present, it may be necessary to adjust the treatment regimen, including Hobetic dosage.
- Hypoglycaemia (mild) can be treated with immediate intake of carbohydrates (glucose or sugar). Immediate medical attention and in some circumstances, hospitalisation, may be necessary in severe cases.
- Alertness and reactions may be impaired due to hypo- or hyperglycaemia. This may affect the ability to operate machinery or vehicle.

4.5 Interaction with other medicinal products and other forms of interactions

Antacids, Sucralfate, Metal Cations

- Concurrent use with one of the following medicines may enhance blood sugar-lowering effect, thus, in some instances, hypoglycaemia may occur; insulin and other oral antidiabetics, ACE inhibitors, allopurinol, coumarin derivatives, chloramphenicol, anabolic steroids and male sex hormones, fenfluramine, disopyramide, fibrates, MAO inhibitors, fluoxetine, guanethidine, ifosfamide, miconazole, para-aminosalicytic acid, pentoxifyline (high-dose parenteral),

trofosfamide, triqualine, tetracyclines, sulphonamides, salicylates, sulfinpyrazone, quinolones, probenecid, oxyphenbutazone, azapropazone, phenylbutazone.

- Acute or chronic alcohol intake may enhance or reduce the blood sugar-lowering action of Hobetic unpredictably.
- Concurrent use with one of the following medicines may reduce blood sugar-lowering effect, thus may risk hyperglycaemia; thyroid hormones, oestrogens and progestrogens, phenothiazines, phenytoin, rifampicin, nicotinic acid (in high doses), acetazolamide, barbiturates, corticosteroids, diazoxide, diuretics, epinephrine (adrenaline) and other sympathomimetic agents, glucagon, laxatives (after protracted use).
- Use with clonidine or reserpine may cause increase or reduce blood sugar-lowering effect.
- Beta-adrenergic blocking agents, including ophthalmics (if significant absorption occurs): May affect control of normal physiological response to a fall in blood sugar, such as a blocked catecholamine-mediated response to hypoglycaemia (glycogenolysis and mobilization of glucose), thereby increasing the risk of hypoglycaemic reaction. On the other hand, beta-adrenergic blocking agents may decrease the hypoglycaemic effects of sulfonylureas to some extent by inhibition of insulin secretion, modification of carbohydrate metabolism and increased peripheral insulin resistance, leading to hyperglycaemia, thus adjustment in dose may be required.
- The effect of coumarin derivatives may be enhanced or weakened.

4.6 Pregnancy and lactation

Hobetic must not be taken during pregnancy to avoid risk or harm to the child. Patient planning a pregnancy must inform physician. Hobetic should be discontinued in nursing mothers as ingestion of glimepiride in the breast may harm the child.

4.7 Effects on ability to drive and use machine

NOT APPLICABLE

4.8 Undesirable effects

Hypoglycaemia may occur and prolonged, as a result of the blood sugar-lowering action of glimepiride. Symptoms that may be observed are headache, nausea, vomiting, lassitude, excessive hunger, sleepiness, restlessness, disordered sleep, aggressiveness, impaired concentration, alertness and reactions, depression, confusion, slurred speech, aphasia, visual disturbances, tremor, pareses, sensory disturbances, dizziness, helplessness, loss of self control, delirium, cerebral convulsions, somnolence and loss of consciousness up to and including coma, shallow respiration and bradycardia.

In addition, the following signs of adrenergic counter-regulation may be manifested: cold sweats, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris and cardiac arrhythmias. The symptoms of hypoglycaemia usually subside when it is corrected.

Blurred vision and/or changes in accommodation may be more pronounced when therapy is initiated and are thought to be caused by changes in blood glucose concentration.

Gastrointestinal tract: followings may occur: nausea, vomiting, sensation of fullness

in the epigastrium, abdominal pain and diarrhoea.

In rare cases, liver enzyme may be elevated. In isolated cases, impairment of liver function and hepatitis may develop.

Blood: severe changes in the blood may occur. Rarely, thrombocytopenia, and in isolated cases, leucopenia, haemolytic anaemia or erythrocytopenia, granulocytopenia, agranulocytosis and pancytopenia may develop

Others: Allergic or pseudoallergic reactions may occasionally occur (itching, urticaria or rashes). Such reactions are mild but may become serious and accompanied by dyspnoea and a fall in blood pressure, sometimes progressing to shock. If urticaria occurs, consult physician immediately.

Allergic vasculitis, hypersensitivity of the skin to light and a decrease in serum sodium may occur in isolated cases.

Since some adverse reactions may in certain circumstances become life-threatening, if sudden or severe reactions occur, it is crucial to immediately consult physician.

4.9 Overdose

Overdose of Hobetic can produce severe and sometimes life-threatening hypoglycaemia. Immediate hospitalisation may be necessary in cases of significant overdose with severe reactions.

Treatment of overdose:
Glucose administration is the basis for treatment of hypoglycaemia. Mild hypoglycaemia symptoms without loss of consciousness or neurologic findings should be treated aggressively with oral glucose and adjustments in drug dosage and/or meal patterns and physical activity.

Severe hypoglycaemia reactions with coma, seizure, or other neurological impairment, may be treated with glucagon (intramuscular or subcutanous) or concentrated glucose solution (intravenous). If life-threatening amount ingested, detoxification (gastric lavage or activated charcoal) will be necessary.

Close monitoring and administration of carbohydrates should continue as hypoglycaemia may recur after apparent clinical recovery

5-Pharmacological Properties :

5.1 Pharmacodynamic properties

Glimepiride is a sulfonylurea antidiabetic agent that is used to reduce blood glucose in type 2 diabetes patients by directly stimulating release of insulin from functioning beta cells of pancreatic islet tissue. In addition, glimepiride has extrapancreatic effects that increase the insulin sensitivity in target tissues. However, as with other sulfonylurea, the mechanism by which glimepiride lowers blood sugar during long term administration has not been clearly established.

Good metabolic control over 24 hours can be achieved with single dose of Hobetic. In patients with insufficient response to the maximum dose, combination therapy with oral antidiabetic containing metformin or with insulin improves metabolic control.

5.2 Pharmacokinetic properties

Absorption: After oral administration, glimepiride is rapidly and well absorbed from GI tract. Peak drug levels (Cmax) are achieved between 2 to 3 hours. When glimepiride was given with meals, the mean Tmax (time to reach Cmax) was slightly elevated and mean Cmax and area under the curve (AUC) were slightly decreased (by 8% and 9%, respectively).

Distribution: After intravenous (IV) dosing in normal subjects, the volume of distribution (Vd) was 8.8L (113mL/kg), and total body clearance (CL) was 47.8mL/min. Protein binding was greater than 99.5%.

Metabolism: Glimepiride is completely metabolised by oxidative biotransformation after either an IV or oral dose. The major metabolites are the cyclohexyl hydroxy methyl derivative (M1) and the carboxyl derivative (M2). Cytochrome P450 II C9 has been shown to be involved in the biotransformation of glimepiride to M1. M1 is further metabolised to M2 by one or several cytosolic enzymes. M1, butnot M2, possess 1 /3 of the pharmacological activity as compared to its parent in the animal model; however, whether the sugar lowering effect of M1 is clinically meaningful is not clear.

Excretion: When 14C-glimepiride was given orally, approximately 60% of the total radioactivity was recovered in the urine in 7 days and M1 (predominant) and M2 accounted for 80 - 90% of the recovered urine. Approximately 40% of the total radioactivity was recovered in faeces and M1 and M2 (predominant) accounted for 70% of that recovered in faeces. No parent drug was recovered in urine and faeces. After IV dosing in patients, no significant biliary excretion of glimepiride or its M1 metabolite has been observed.

6-Pharmaceutical Particulars:

6.1 List of excipients

a) Lactose Monohydrate
b) Microcrystalline cellulose
c) Sodium Starch Glycolate
d) Iron Oxide Yellow
e) Dispersed Blue
f) Talc
g) Sodium Lauryl Sulfate
h) Magnesium Stearate
i) Colloidal Silicon Dioxide

6.2 Incompatibilities

NOT APPLICABLE

6.3 Shelf life

3 years from date of manufacture

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture.

6.5 Nature and contents of container

PRODUCT NAME: HOBETIC 2MG TABLET (A4-5610)

Immediate Container/Packaging

Primary Packaging

1	Material description	:	Rigid PVC film
	Colour of film	:	Glass clear transparent
2	Material description	:	Hobetic 2mg aluminium foil
	Specification	:	Foil property: Silver plain hard tempered 20 micron aluminium foil with 6276 primer on bright and heat seal on dull surface. 3-4 gsm.

Outer Container / Secondary Packaging

Type: Unit box, Package Insert & Plain Carton for Hobetic 2 mg Tablet.

6.6 Special precautions for disposal

NOT APPLICABLE

7-Applicant

Marketing Authorization Holder:

Name : HOVID Bhd.
Address : 121, Jalan Tunku Abdul Rahman,
(Jalan Kuala Kangsar)
30010 Ipoh, Perak, Malaysia

Production Site : HOVID BHD.,
Lot 56442, 7 ½ miles, Jalan Ipoh/Chemor,
31200 Chemor, Perak, Malaysia.

8-Date of revision : December 2024