Summary of Product Characteristics for
(Glimepiride) 2 Tablet

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Glimepiride 2 Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Name of Ingredients	Quality Standard Reference	Quantity/ tablet	Overage
Glimepiride	BP	2.00 mg	5%
Microcrystalline Cellulose	NF	36.86 mg	-
Lactose Monohydrate	BP	80.00 mg	-
Sodium Starch Glycolate	BP	5.00 mg	-
Maize Starch	BP	28.00 mg	-
Magnesium Stearate	BP	2.00 mg	-
Purified Talc	BP	1.00 mg	-
Orange Red Color	Pharma grade	0.04 mg	-

3. PHARMACEUTICAL FORM

Tablet

Light orange, flat, oblong tablet having a breakline on one face and other face is plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

(Glimepiride) is indicated in type-2 diabetes mellitus when dietary modification has failed in adequate glycemic control.

4.2 Posology and method of administration

Usual Starting Dose:

The usual starting dose of (Glimepiride) as initial therapy is 1-2 mg once daily, administered with breakfast or the first main meal. Those patients who may be more sensitive to hypoglycemic drugs should be started at 1 mg once daily. The maximum starting dose of Swimepiride (Glimepiride) should be not more than 2 mg.

Usual Maintenance Dose:

The usual maintenance dose is 1 to 4 mg once daily. The maximum recommended dose is 8 mg once daily. After reaching a dose of 2 mg, dosage increases should be made in increments of not more than 2 mg at 1-2 week intervals based upon the patient's blood glucose response.

OR AS DIRECTED BY THE PHYSICIAN.

4.3 Contra-indications:

(Glimepiride) is contraindicated in patients with known hypersensitivity to the drug. It is also contraindicated in patients with type 1 diabetes mellitus, diabetic coma, and ketoacidosis.

4.4 Special warnings and precautions for use:

In the initial weeks of treatment, the risk of hypoglycemia may be increased. If such risk is present it may be necessary to adjust the dosage of Glimepiride.

Use in Children & Elderly

Children: Safety and effectiveness in children have not been established.

Elderly: No overall differences in safety or effectiveness were observed between elderly and younger. There are no significant differences in pharmacokinetics between the elderly and adults.

4.5 Interaction with other medicinal products and other forms of interaction:

1. The hypoglycemic action of Glimepiride may be potentiated by certain drugs, include NSAID and other drugs that are highly protein bound such as salicylates, sulfonamides, chloramphenicol, coumarin derivatives, probenecid, monoamine oxidase inhibitors, and beta adrenargic blocking agents.

2. Weakening of the blood sugar lowering effect of Glimepiride may occur with acetazolamide barbiturates, corticosteroids, diazoxide, diuretics, epinephrine and other sympathomimetic agents, laxatives, oestrogens and progestogens, phenothiazines, phenytoin, rifampicin and thyroid hormones.

4.6 Pregnancy and lactation:

Pregnancy: Glimepiride is contraindicated during pregnancy.

Lactation: Glimepiride must not be taken during lactation.

4.7 Effects on the ability to drive and operate machinery:

There is no evidence to suggest that Swimepiride (Glimepiride) may have an effect on a patient's ability to drive or operate machinery.

4.8 Undesirable effect:

Hypoglycemia, gastrointestinal disturbances such as nausea, vomiting, abdominal pain, diarrhea and constipation may occur.

4.9 Overdose:

Overdosage of sulphonylureas, including Glimepiride can produce hypoglycemia. Severe hypoglycemic reactions with coma, or neurological impairments occur infrequently.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Pharmacotherapeutic group: Sulphonylurea group.
ATC code: A10BB12

Mode of action:

(Glimepiride) is an oral hypoglycemic drug belonging to the sulphonylurea group. It stimulates the release of insulin from functioning pancreatic β-cells. It also can increase sensitivity of peripheral tissues to insulin.

In healthy subjects, the time to reach maximal effect (minimum blood glucose concentrations) was approximately 2–3 hours after single oral doses of Swimepiride (Glimepiride).

5.2 Pharmacokinetics properties:

Absorption: Studies with single oral doses of glimepiride in healthy subjects and with multiple oral doses in patients with type 2 diabetes showed peak drug concentrations (C_{max}) 2 to 3 hours post-dose. When glimepiride was given with meals, the mean C_{max} and AUC (area under the curve) were decreased by 8% and 9%, respectively.
Glimepiride does not accumulate in serum following multiple dosing. The pharmacokinetics of glimepiride does not differ between healthy subjects and patients with type 2 diabetes. Clearance of glimepiride after oral administration does not change over the 1 mg to 8 mg dose range, indicating linear pharmacokinetics.
In healthy subjects, the intra- and inter-individual variabilities of glimepiride pharmacokinetic parameters were 15-23% and 24-29%, respectively.

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

Metabolism: Glimepiride is completely metabolized by oxidative biotransformation after either an intravenous or oral dose. The major metabolites are the cyclohexyl hydroxy methyl derivative (M1) and the carboxyl derivative (M2). Cytochrome P450 2C9 is involved in the biotransformation of glimepiride to M1. M1 is further metabolized to M2 by one or several cytosolic enzymes. M2 is inactive.

Excretion: When C-glimepiride was given orally to 3 healthy male subjects, approximately 60% of the total radioactivity was recovered in the urine in 7 days.

5.3 Preclinical safety data:

Studies in rats at doses of up to 5000 parts per million (ppm) in complete feed (approximately 340 times the maximum recommended human dose, based on surface area) for 30 months showed no evidence of carcinogenesis. In mice, administration of glimepiride for 24 months resulted in an increase in benign pancreatic adenoma formation that was dose-related and was thought to be the result of chronic pancreatic stimulation. No adenoma formation in mice was observed at a dose of 320 ppm in complete feed, or 46–54 mg/kg body weight/day. This is at least 28 times the maximum human recommended dose

of 8 mg once daily based on surface area.

Glimepiride was non-mutagenic in a battery of in vitro and in vivo mutagenicity studies (Ames test, somatic cell mutation, chromosomal aberration, unscheduled DNA synthesis, and mouse micronucleus test).

There was no effect of glimepiride on male mouse fertility in animals exposed up to 2500 mg/kg body weight (>1,500 times the maximum recommended human dose based on surface area). Glimepiride had no effect on the fertility of male and female rats administered up to 4000 mg/kg body weight (approximately 4,000 times the maximum recommended human dose based on surface area).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Microcrystalline Cellulose (101)
Lactose Monohydrate
Sodium Starch Glycolate
Maize Starch
Magnesium Stearate
Purified Talc
Orange Red Color

6.2 Incompatibilities

Not incompatibility is observed.

6.3 Shelf-life:

Proposed shelf life (after pack): 24 months

6.4 Special precautions for storage:

Store below 30°C. Protect from light.

6.5 Nature and contents of container

10 tablets are in Alu– PVDC blister pack. 3 blisters in a carton box.

6.6 Instructions for use and handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Name and address of holder of a registration:

Name	**:**	The ACME Laboratories Ltd.
Address	**:**	Court de la ACME, ¼, Mirpur Road, Kallayanpur, Dhaka-1207
Telephone	**:**	+88-02-7730881-2, 7730816-7, 7730142 (Plant); 9004194-6, 9004748 (Business)
Fax	**:**	+88-02-7730141(Plant); +880-2-9016872 (Business)
E-Mail	**:**	plant@acmeglobal.com (Plant), export@acmeglobal.com (Business)

Name	:	SWISS PHARMA NIGERIA LIMITED,
Address	:	5,DOPEMU ROAD AGEGE, Lagos
Tel	:	017745276