SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG PRODUCT

Getryl (Glimepiride) 2mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Glimepiride USP . . . 2mg
For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Grey colored caplet, engraved "GETZ" on one side and a bisect line on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GETRYL (Glimepiride) is indicated as an adjunct to diet and exercise to lower the blood glucose in patients with noninsulin-dependent (Type 2) diabetes mellitus (NIDDM) whose hyperglycemia cannot be controlled by diet and exercise alone.

GETRYL (Glimepiride) may be used concomitantly with metformin when diet, exercise, and GETRYL (Glimepiride) or metformin alone do not result in adequate glycemic control.

GETRYL (Glimepiride) is also indicated for use in combination with insulin to lower blood glucose in patients whose hyperglycemia cannot be controlled by diet and exercise in conjunction with an oral hypoglycemic agent.

4.2 Posology and method of administration

In initiating treatment for noninsulin-dependent diabetes, diet and exercise should be emphasized as the primary form of treatment. There is no fixed dosage regimen for the management of diabetes mellitus with GETRYL (Glimepiride) or any other hypoglycemic agent. The patient's fasting blood glucose and HbA1c must be measured periodically to determine the minimum effective dose for the patient.
Short-term administration of GETRYL (Glimepiride) may be sufficient during periods of transient loss of control in patients usually controlled well on diet and exercise.

Usual Starting Dose:
The usual starting dose of GETRYL (Glimepiride) as initial therapy is 1-2mg once daily, administered with breakfast or the first main meal. Those patients who may be more sensitive to hypoglycemic drugs should be started at 1mg

once daily, and should be titrated carefully. The maximum starting dose of GETRYL (Glimepiride) should be not more than 2mg.

Usual Maintenance Dose:
The usual maintenance dose of GETRYL (Glimepiride) is 1 to 4mg once daily. The maximum recommended dose is 8mg once daily. After reaching a dose of 2mg, dose increases should be made in increments of no more than 2mg at 1-2 week intervals based upon the patient's blood glucose response. Long-term efficacy should be monitored by measurement of HbA1c levels, for example, every 3 to 6 months.

GETRYL (Glimepiride)-Metformin Combination Therapy:
If patients do not respond adequately to the maximal dose of GETRYL (Glimepiride) monotherapy, addition of metformin may be considered. With concomitant GETRYL (Glimepiride) and metformin therapy, the desired control of blood glucose may be obtained by adjusting the dose of each drug.

GETRYL (Glimepiride)-Insulin Combination Therapy:
Combination therapy with GETRYL (Glimepiride) and insulin may also be used in secondary failure patients. The fasting glucose level for instituting combination therapy is in the range of
>150mg/dL in plasma or serum depending on the patient.
The recommended GETRYL (Glimepiride) dose is 8mg once daily administered with the first main meal. After starting with low-dose insulin, upward adjustments of insulin can be done approximately weekly as guided by frequent measurements of fasting blood glucose.

Special population:
In elderly, debilitated, or malnourished patients, or in patients with hepatic insufficiency, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions.

Renal impairment:
In patients with mild to moderate renal impairment, a starting dose of 1mg once daily must not be exceeded. The dose may then be carefully titrated upwards if necessary based on fasting blood glucose levels according to the protocol mentioned above (i.e. in increments of 1mg at intervals of one to two weeks).

4.3 Contraindications

Glimepiride is contraindicated in:
- Patients with known hypersensitivity to the drug.
- Patients with diabetic ketoacidosis, with or without coma. This condition should be treated with insulin.
- Patients and lactating patients
- Pediatric patients
- Acute porphyria

4.4 Special warnings and special precautions for use

The patient's fasting blood glucose and HbA1c must be measured periodically to determine the minimum effective dose for the patient; to detect primary failure, i.e., inadequate lowering of blood glucose at the maximum recommended dose of medication; and to detect secondary failure, i.e., loss of adequate blood glucose lowering response. After an initial period of effectiveness glycosylated hemoglobin levels should be performed to monitor the patient's response to therapy.

Patients with Galactose intolerance, Lapp lactase deficiency or Glucose-galactose malabsorption

Getryl (Glimepiride) Tablets contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption may experience symptoms of intolerance.

Hypoglycemia

All sulfonylurea drugs are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemic episodes.

Debilitated patients, malnourished patients and patients with adrenal, pituitary, renal or hepatic insufficiency are particularly susceptible to the hypoglycemic action of sulfonylureas and should therefore be carefully monitored. The dosage of glimepiride should be carefully adjusted in these patients.

Hepatic insufficiency may cause increased serum concentrations of glimepiride and may diminish gluconeogenic capacity, both of which increase the risk of severe hypoglycemic reactions.

Alcohol ingestion, severe or prolonged exercise, deficient caloric intake or use of more than one antidiabetic agent may predispose patients to the development of hypoglycemia.

Loss of control of blood glucose

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 add insulin in combination with glimepiride or even use insulin monotherapy.

4.5 Interaction with other medicaments

Glimepiride belongs to sulfonylureas (anti-diabetic) class of drugs and may have the following interactions.

- Hypoglycemic effect of anti-diabetics enhanced by alcohol.
- Hypoglycemic effect of anti-diabetics possibly enhanced by anabolic steroids, MAOIs & testosterone.
- Warning signs of hypoglycemia (such as tremor) with anti-diabetics may be masked when given with beta-blockers.
- Hypoglycemic effect of anti-diabetics possibly antagonized by corticosteroids, diazoxide, loop diuretics, thiazide diuretics, estrogens & progestogens.
- The hypoglycemic effect of sulfonylureas may be possibly potentiated by nonsteroidal anti-inflammatory drugs, coumarins, ACE inhibitors & tetracyclines.

- Effects of sulfonylureas enhanced by cimetidine, MAOIs & sulfinpyrazone.
- Effects of sulfonylureas rarely enhanced by trimethoprim & sulphonamide.
- Plasma concentration of sulfonylureas increased by fluconazole & miconazole.
- Requirements for sulfonylureas possibly reduced by octreotide.

4.6 Pregnancy and Lactation

Pregnancy

Risk related to glimepiride

There are no adequate data from the use of glimepiride in pregnant women. Animal studies have shown reproductive toxicity which likely was related to the pharmacologic action (hypoglycemia) of glimepiride.

Consequently, glimepiride should not be used during the whole pregnancy.

In case of treatment by glimepiride, if the patient plans to become pregnant or if a pregnancy is discovered, the treatment should be switched as soon as possible to insulin therapy.

Lactation

The excretion in human milk is unknown. Glimepiride is excreted in rat milk. As other sulfonylureas are excreted in human milk and because there is a risk of hypoglycemia in nursing infants, breast-feeding is advised against during treatment with glimepiride.

4.7 Effects on ability to drive and use machine

No studies on the effects on the ability to drive and use machines have been performed.

The patient's ability to concentrate and react may be impaired as a result of hypoglycemia or hyperglycemia or, for example, as a result of visual impairment. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning symptoms of hypoglycemia or have frequent episodes of hypoglycemia. It should be considered whether it is advisable to drive or operate machinery in these circumstances.

4.8 Undesirable effects

Glimepiride is generally well tolerated. However following are the side effects reported during treatment with glimepiride.

Hypoglycemia: Hypoglycemia is the greatest potential risk with all sulfonylureas.

Visual reactions: There may be temporary visual impairment (e.g., changes in accommodation and/or blurred vision) due to the change in blood glucose levels, especially at the start of treatment.

Gastrointestinal reactions: Occasionally gastrointestinal symptoms such as nausea, vomiting, sensations of pressure or fullness in the epigastrium, abdominal pain and diarrhea may occur.

Haematologic reactions: Rarely, thrombocytopenia and in isolated cases, leucopenia may develop. In isolated instances, thrombocytopenic purpura, agranulocytosis, pancytopenia due to myelo-suppression, eosinophilia, hemolytic anemia, aplastic anemia, erythrocytopenia and granulocytopenia may occur.

Dermatologic reactions: Occasionally, allergic or pseudo-allergic skin reactions (e.g., pruritus, erythema, urticaria, erythematous and maculo-papular and bullous skin eruptions or psoriasiform drug eruption) may occur in patients treated with sulfonylureas.

Hepatic reactions: Increased liver enzymes (AST, ALT), abnormal liver function, cholestasis, cholestatic hepatitis, granulomatous hepatitis, bilirubinemia anemia and liver failure have been reported with sulfonylureas in isolated cases.

Electrolyte disturbance: In isolated cases, hyponatremia has been reported in patients receiving glimepiride and other sulfonylureas, most often in patients who are on other medications or have medical conditions known to cause hyponatremia or to increase release of antidiuretic hormone.

Other: Isolated cases of allergic vasculitis have been reported with sulfonylureas.

Reporting of Suspected Adverse Reactions

Healthcare professionals are requested to report any Suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org'

4.9 OVERDOSE

Symptoms

After ingestion of an overdosage hypoglycemia may occur, lasting from 12 to 72 hours, and may recur after an initial recovery. Symptoms may not be present for up to 24 hours after ingestion. In general observation in hospital is recommended. Nausea, vomiting and epigastric pain may occur. The hypoglycemia may in general be accompanied by neurological symptoms like restlessness, tremor, visual disturbances, co-ordination problems, sleepiness, coma and convulsions.

Management

Treatment primarily consists of preventing absorption by inducing vomiting and then drinking water with activated charcoal (adsorbent) and sodium-sulfate (laxative). If large quantities have been ingested, gastric lavage is indicated, followed by activated charcoal and sodium-sulfate. In case of (severe) overdosage hospitalization in an intensive care department is indicated. Start the administration of glucose as soon as possible, if necessary by a bolus intravenous injection of 50 ml of a 50% solution, followed by an infusion of a 10% solution with strict monitoring of blood glucose. Further treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Blood glucose lowering drugs, excl. insulins: sulfonylureas

ATC-code: A10BB12

Mechanism of action

The primary mechanism of action of glimepiride appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells. In addition, extra pancreatic effects (e.g., reduction of basal hepatic glucose production and increased peripheral tissue sensitivity to insulin and glucose uptake) may also play role in the activity of glimepiride.
However, as with other sulfonylureas, the mechanism by which glimepiride lowers blood glucose during long-term administration has not been clearly established.

5.2 Pharmacokinetic properties

After oral administration glimepiride is completely absorbed from the GI tract. The oral bioavailability is approximately 100%. Peak plasma concentrations occur in 2-3 hours. More than 99% of the drug is bound to plasma proteins. Glimepiride is completely metabolized by oxidative biotransformation into two main metabolites, a hydroxy derivative and a carboxy derivative.

The elimination half-life ($t1/2$) after multiple doses is about 5 hours. Approximately 60% of dose is eliminated in the urine and 40% in the feces.

Special population
Renal Insufficiency
A single-dose clinical study of glimepiride showed that glimepiride serum levels decreased as renal function decreased. However, metabolites serum levels (mean AUC values) increased. The apparent terminal half-life ($t1/2$) for glimepiride did not change, while the half-lives for metabolites increased as renal function decreased. Mean urinary excretion of metabolites as percent of dose, however, decreased.

5.3 Preclinical safety data

Preclinical effects observed occurred at exposures sufficiently in excess of the maximum human exposure as to indicate little relevance to clinical use, or were due to the pharmacodynamic action (hypoglycemia) of the compound. This finding is based on conventional safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenicity, and reproduction toxicity studies. In the latter (covering embryotoxicity, teratogenicity and developmental toxicity), adverse effects observed were considered to be secondary to the hypoglycemic effects induced by the compound in dams and in offspring.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate, Sodium Starch Glycolate, Povidone K-25 (PVP K-25), Microcrystalline Cellulose 102 Premium (Avicel PH-102), Grey Dry Mix O/S (1526/2820) and Magnesium Stearate.

6.2 Incompatibilities

None

6.3 Shelf-life

3 Years
The expiration dates refer to the product correctly stored in the required conditions.

6.4 Special precautions for storage

Store below 30℃
Protect from sunlight &
moisture. Keep out of reach of
children.

6.5 Nature and contents of container

Getryl (Glimepiride) 2mg Tablets are available in Alu-Alu Blister Pack of 2 x 10 (20's) tablets along with the package insert.

6.6 Special precautions for disposal

No special requirements.

6.7 Instructions for use/handling

- To be sold on prescription of a registered medical practitioner only.
- Keep out of the reach of children.

7. MARKETING AUTHORISATION HOLDER

Getz Pharma (Private) Limited
29-30/27, Korangi Industrial Area Karachi 74900,
Pakistan Tel: (92-21) 111-111-511
Fax: (92-21) 5057592

8. MARKETING AUTHORIZATION NUMBER

16612

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

Date of re-registration: 28/02/2026

10. DATE OF REVISION OF THE TEXT

February 28, 2026