AMARYL® Abridged Prescribing Information

1-NAME AND PRESENTATION: Amaryl tablets contain 1mg, 2mg, 3mg, 4mg or 6mg glimepiride.

2. THERAPEUTIC INDICATIONS: Amaryl is indicated for the treatment of type 2 diabetes mellitus, when diet, physical exercise and weight reduction alone are not adequate.

3. POSOLOGY AND METHOD OF ADMINISTRATION: Dose is determined by the results of blood and urinary glucose determinations. The starting dose is 1 mg glimepiride per day.
If good control is achieved this dose should be used for maintenance therapy. For the different dose regimens appropriate strengths are available.
If control is unsatisfactory the dose should be increased, based on the glycemic control, in a stepwise manner with an interval of about 1 to 2 weeks between each step, to 2, 3 or 4 mg glimepiride per day. A dose of more than 4 mg glimepiride per day gives better results only in exceptional cases.
The maximum recommended dose is 6 mg glimepiride per day. In patients not adequately controlled with the maximum daily dose of Amaryl, concomitant insulin therapy can be initiated if necessary. While maintaining the glimepiride dose, insulin treatment is started at low dose and titrated up depending on the desired level of metabolic control. The combination therapy should be initiated under close medical supervision.
Normally a single daily dose of glimepiride is sufficient. It is recommended that this dose be taken shortly before or during a substantial breakfast or - if none is taken - shortly before or during the first main meal.
If a dose is forgotten, this should not be corrected by increasing the next dose.

4. **CONTRA-INDICATIONS**: Diabetes mellitus type I, diabetic coma, ketoacidosis, severe renal or hepatic function disorders, hypersensitivity to glimepiride, other sulphonylureas or sulphonamides or excipients in the tablet.

5. SPECIAL WARNINGS AND PRECAUTIONS FOR USE: Amaryl must be taken shortly before or during meal. Treatment with Amaryl requires regular monitoring of glucose levels in blood and urine. HbA1c dosage is recommended. Regular hepatic and haematological monitoring are required. In stress-situations (e.g. Accidents, acute operations, infections with fever, etc.) a temporary switch to insulin may be indicated. In case of severe renal or hepatic function disorders, a change over to insulin is required.

6. DRUG INTERACTIONS: Glimepiride is metabolized by cytochrome P450 2C9 (CYP2C9). This should be taken into account when it is co-administered with inducers (e.g. rifampicin) or inhibitors (e.g. fluconazole) of CYP 2C9. See full SmPC for others.

7. PREGNANCY AND LACTATION: 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.
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 hypoglycaemia in nursing infants, breast-feeding is advised against during treatment with glimepiride.

8. EFFECTS ON ABILITY TO DRIVE: Patients should be advised to take precautions to avoid hypoglycaemia whilst driving.

9. UNDESIRABLE EFFECTS: hypoglycaemic reactions, transient visual disturbances, elevation of liver enzyme. For other uncommon, rare and very rare effects.

10. OVERDOSAGE: After ingestion of an overdosage, hypoglycaemia 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 and it could cause nausea, vomiting, restlessness, tremor and visual disturbance. Treatment primarily consists of preventing absorption by inducing vomiting and then drinking water or lemonade with activated charcoal (adsorbent) and sodium-sulphate (laxative). If large quantities have been ingested, gastric lavage is indicated, followed by activated charcoal and sodium-sulphate. In case of (severe) overdose hospitalisation in an intensive care department is indicated. Start the administration of glucose as soon as possible.

11.PHARMACODYNAMIC PROPERTIES: Glimepiride is an orally active hypoglycaemic substance belonging to the sulfonylurea group. It may be used in non-insulin dependent diabetes mellitus. Glimepiride acts mainly by stimulating insulin release from pancreatic beta cells.

As with other sulfonylureas this effect is based on an increase of responsiveness of the pancreatic beta cells to the physiological glucose stimulus. In addition, glimepiride seems to have pronounced extra pancreatic effects also postulated for other sulfonylureas. Insulin release
Sulfonylureas regulate insulin secretion by closing the ATP-sensitive potassium channel in the beta cell membrane. Closing the potassium channel induces depolarization of the beta cell and results - by opening of calcium channels - in an increased influx of calcium into the cell. This leads to insulin release through exocytosis. Glimepiride binds with a high exchange rate to a beta cell membrane protein which is associated with the ATP-sensitive potassium channel, but which is different from the usual sulfonylurea binding site. Extrapancreatic activity the extra pancreatic effects are for example an improvement of the sensitivity of the peripheral tissue for insulin and a decrease of the insulin uptake by the liver. The uptake of glucose from blood into peripheral muscle and fat tissues occurs via special transport proteins, located in the cell's membrane. The transport of glucose in these tissues is the rate limiting step in the use of glucose. Glimepiride increases very rapidly the number of active glucose transport molecules in the plasma membranes of muscle and fat cells, resulting in stimulated glucose uptake.

12. MARKETING AUTHORISATION HOLDER : Sanofi Aventis Deutschland GmbH, Bruningstrasse 50, D – 65926 Frankfurt am main, Frankfurt, Germany. Abbreviated Prescribing Information based on the EU SmPC as of April 2017. Always refer to the full Summary of Product Characteristics (SmPC) before prescribing.