

GLUCO OFF® Film Coated Tablets



Composition:

Each GLUCO OFF 2.5 Film Coated Tablet contains: Metformin Hydrochloride 500 mg and Glyburide 2.5 mg.

Each GLUCO OFF 5 Film Coated Tablet contains:

Metformin Hydrochloride 500 mg and Glyburide 5 mg.

Mechanism of Action:

GLUCO OFF combines Glyburide and Metformin Hydrochloride, two antihyperglycemic agents with complementary mechanisms of action, to improve glycemic control in patients with type 2 diabetes. Glyburide appears to lower blood glucose acutely by stimulating the release of insulin from the pancreas.

Metformin works by decreasing hepatic glucose production, decreasing intestinal absorption of glucose, and improving insulin sensitivity.

Pharmacokinetics:

After an oral dose of GLUCO OFF, maximum plasma concentration (C_{max}) is reached in 2.5 hours (t_{max}). Metformin absorption is saturable and incomplete. Plasma protein binding is negligible. Metformin is excreted unchanged in the urine. The elimination half-life is approximately 6.5 hours.

Single-dose studies Glyburide demonstrate significant absorption of Glyburide within 1-hour, peak drug levels at about 4 hours. Glyburide is extensively bound to serum proteins. Glyburide is excreted as metabolites in the bile and urine, approximately 50% by each route. The terminal half-life is about 10 hours.

Indications:

GLUCO OFF is indicated for the management of type II diabetes mellitus when diet, exercise and single drug therapy do not result in adequate glycemic control.

Contraindications:

- Hypersensitivity to the active substances or to any of the Excipients.
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.
- Type 1 diabetes (insulin-dependent diabetes).
- Severe renal failure (GFR <30 mL/min).
- Acute conditions that can affect kidney function such as: dehydration and shock.
- Concomitant administration of bosentan.
- Alcoholism (acute, chronic).

Warnings & Precautions:

- Rare lactic acidosis may occur due to Metformin accumulation.
- The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet / diet plus insulin.
- GLUCO OFF contains a sulphonylurea (Glyburide), it exposes the patient to a risk of onset of hypoglycaemic episodes.

Pregnancy & Lactations:

Pregnancy: GLUCO OFF must not be taken during pregnancy. The patient must change over to insulin during pregnancy.
Lactation: In view of the risk of neonatal hypoglycaemia, GLUCO OFF is contraindicated in the event of breast-feeding.

Driving & Using Machines:

Patients should be alerted to the symptoms of hypoglycaemia and should be advised to exercise caution when driving or using machines.

Drug Interactions:

Bosentan: Increased liver enzymes.

Inducers or inhibitors of CYP 2C9: Glyburide is mainly metabolized by CYP 2C9.

Cyclosporine: Glyburide may increase cyclosporine plasma

concentration and potentially lead to its increased toxicity.

Insulin and other, oral antidiabetics: Increased risk of hypoglycaemia.

Alcohol: Alcohol intoxication is associated with an increased risk of lactic acidosis.

Corticosteroids, beta2-stimulators and diuretics, owing hyperglycemic activity: More frequent blood glucose monitoring may be required. If necessary, adjust the Metformin dosage.

Inhibitors of OCT1 (such as Verapamil) may reduce efficacy of Metformin.

Inducers of OCT1 (such as Rifampicin) may increase absorption and efficacy of Metformin.

Inhibitors of OCT2 (such as Cimetidine, Trimethoprim, Isavuconazole) may decrease the renal elimination of Metformin and thus lead to an increase in Metformin plasma concentration.

Side Effects:

The most noticeable side effects were hypoglycaemia, headache, fullness, nausea, vomiting, diarrhea, abdominal pain, loss of appetite and taste disturbance.

Very rare: Lactic acidosis, hemolytic anemia, thrombopenia, agranulocytosis, decrease of vitamin B12 absorption, erythema, urticaria and hepatitis.

Dosage & Administration:

Adults: Initial dose: One GLUCO OFF 2.5 tablet should be administered as once daily with meals. After several days the dose should be adjusted based on blood glucose measurements. For once daily administration maximum 2 tablets of GLUCO OFF 5 can be given. For higher doses it may be necessary to divide the administration into 2 doses. Up to 4 tablets of GLUCO OFF 5 can be given per day.

Renal impairment: Depending on the glomerular clearance rate, the dose is as follows:

Glyburide (Maximum daily)	Metformin (Maximum daily)	GFR (mL/ min)
20 mg (higher daily doses of 20 mg are not recommended because they are more effective only in exceptional cases)	3000 mg Dose reduction may be considered in relation to declining renal function 2000 mg The starting dose is at most half of the maximum dose. 1000 mg The starting dose is at most half of the maximum dose.	60- 89 45- 59 30- 44
GLUCO OFF is contraindicated		<30

Geriatric population: Patients aged 65 years and older: starting and maintenance doses of Glyburid must be carefully adjusted to reduce the risk of hypoglycaemia.

Overdose: Overdose may precipitate hypoglycaemia due to the presence of the sulphonylurea. High overdose of Metformin or concomitant risks may lead to lactic acidosis. Lactic acidosis is a medical emergency and must be treated in hospital. The most effective method to remove lactate and Metformin is haemodialysis. Since Glyburide is extensively bound to proteins, it is not eliminated by dialysis.

Storage: Store at a temperature below 25°C. Keep out of reach of children.

Packaging: GLUCO OFF (2.5-5) Carton Box contains 20 or 30 Film Coated Tablets in two or three blisters.

A medication is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medication.
- The doctor and the pharmacist experts in medicine, it's benefits and risks.
- Do not expect the same prescription without consulting your doctor.
KEEP THE MEDICATIONS OUT OF REACH OF CHILDREN
Council of Arab Health Ministries - Union of Arab Pharmacies

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