

# Glimicot-M4 Forte

## Composition :

Glimepiride: 4mg + Metformin 1000 mg

## Indications :

For management of Overt Type II Diabetes Mellitus

## Mechanism Of Action :

Glimepiride stimulates the insulin release from pancreatic  $\beta$ -cells and reduces glucose output from the liver. It also increases insulin sensitivity at peripheral target sites.

Metformin is a biguanide with antihyperglycemic effects, lowering both basal and postprandial plasma glucose. It decreases hepatic glucose production by inhibiting gluconeogenesis and glycogenolytic; delays intestinal absorption of glucose; and enhances insulin sensitivity by increasing peripheral glucose uptake and utilisation.

## Pharmacokinetic's :

### Glimepiride :

Duration : 24hr.

concentration : 2-3 hr.

Absorption : Completely absorbed from the GI tract. Time to peak plasma

Distribution : Volume of distribution: 8.8 L. Plasma protein binding: >99.5%.

Metabolism : Extensively metabolised in the liver via oxidation by CYP2C9 isoenzyme to 2 main metabolites.

Excretion : Via urine (approx. 60%) and faeces (40%). Half-life: Approx. 9 hr.

### Metformin :

Absorption : Slowly and incompletely absorbed from the GI tract. Absolute bioavailability: Approx. 50-60% (fasting); reduced if taken w/ food. Time to peak plasma concentration: 2-3 hr (immediate-release); 4-8 hr (extended-release).

Distribution : It crosses the placenta and distributed in breast milk (small amounts).

Volume of distribution:  $654 \pm 358$  L.

Plasma protein binding : Negligible.

Metabolism : Not metabolised

Excretion : Via urine (90% as unchanged drug). Elimination half-life: Approx. 2-6 hr.

## Side Effects :

Glimepiride : Potentially Fatal: Severe hypoglycaemia. Dizziness, headache, nausea, increased serum ALT, flu-like symptoms, accidental injury, dyspnoea, fall in BP, shock, thrombocytopenia and thrombocytopenic purpura.

Metformin : Anorexia, nausea, vomiting, diarrhoea, abdominal pain, taste disturbance, hepatitis. Rarely, decreased vit B12 absorption, erythema, pruritus and urticaria. Potentially Fatal: Lactic acidosis.

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## **Precaution :**

**Glimepiride** : Patient with G6PD deficiency, autonomic neuropathy, thyroid or adrenocortical insufficiency. Patient exposed to stress (e.g. fever, trauma, infection, surgery). Mild to moderate hepatic or renal impairment. Elderly, debilitated and malnourished patients.

Pregnancy and lactation: Patient Counselling Adhere to diet and exercise regimen.

Monitoring Parameters: Monitor blood glucose, glycosylated Hb level, signs and symptoms of hypoglycaemia.

**Metformin** : Patient with CHF requiring drug therapy, cardiac or resp failure, recent MI, shock. Patient exposed to stress-related states (e.g. fever, trauma, infection, surgery). Hepatic impairment. Elderly.

Pregnancy and lactation

Monitoring Parameters: Monitor renal function regularly. Hematologic parameters (e.g. Hb, haematocrit, erythrocyte indices) should be evaluated prior to initiation of therapy and at least annually during treatment.

## **Dosage :**

**Glimepiride** : Type 2 diabetes mellitus

Adult: Initially, 1-2 mg daily. May be increased in increments of 1-2 mg at intervals of 1-2 wk. Maintenance: 4 mg daily. Max: 6 mg daily. Elderly: Initially, 1 mg once daily.

Renal impairment: Severe: Contraindicated.

Hepatic impairment: Severe: Contraindicated.

## **Metformin** :

Adult: Conventional preparation: Initially, 500 mg twice a day or Thrice a day, or 850 mg 1-2 times daily, may increase gradually to 2000-3000 mg daily at intervals of at least 1 wk.

Modified-release preparation: Initially, 500 mg once daily, may increase in increments of 500 mg at intervals of at least 1 wk. to max 2000 mg once daily at night. If glycaemic control is not sufficient, dose may be divided to give 1000 mg twice a day. Doses >2000 mg daily, admin the conventional preparation.

Child:  $\geq 10$  yr. Initially, 500 mg 1-2 times daily or 850 mg once daily, may increase gradually to max 2000 mg daily in 2 or 3 divided doses at intervals of at least 1 wk.