NORLIM Tablets

(Glimepiride Tablets USP)

نورلم گولیاں

(گلی میپیرائیڈ یو ایس پی)

COMPOSITION:
Each tablet contains:
Glimepiride USP ... 1mg, 2mg, 3mg & 4mg.
[USP Specs.]

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

PHARMACOLOGY:
Mechanism of action: Glimepiride is an orally active hypoglycaemic substance belonging to the sulphonylurea group. It may be used in non-insulin dependent (type 2) 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 extrapancreatic effects also postulated for other sulfonylureas.

PHARMACOKINETICS:
Absorption: The bioavailability of glimepiride after oral administration is complete. Food intake has no relevant influence on absorption, only the absorption rate is slightly diminished. Maximum serum concentrations (C_{max}) are reached approx. 2.5 hours after oral intake (mean 0.3 µg/ml during multiple dosing of 4mg/daily) and there is a linear relationship between dose and both C_{max} and AUC (area under the time concentration curve).
Distribution: Glimepiride has a very low distribution volume (approx. 8.8 litres), which is roughly equal to the albumin distribution space, high protein binding (>99%) and a low clearance (approx. 48 ml/min).
Biotransformation and elimination: Mean dominant serum half-life, which is of relevance for the serum concentrations under multiple-dose conditions, is about 5 to 8 hours. After high doses, slightly longer half-lives were noted. After a single dose of radiolabelled glimepiride, 58% of the radioactivity was recovered in the urine, and 35% in the faeces. No unchanged substance was detected in the urine. Two metabolites most probably resulting from hepatic metabolism (major enzyme is CYP2C9) were identified both in urine and faeces: the hydroxy derivative and the carboxy derivative. After oral administration of glimepiride, the terminal half-lives of these metabolites were 3 to 6 and 5 to 6 hours respectively.
Special populations: Pharmacokinetics were similar in males and females, as well as in young and elderly (above 65 years) patients. Renal elimination of the two metabolites was impaired. Overall, no additional risk of accumulation is to be assumed in such patients. Pharmacokinetics in five non-diabetic patients after bile duct surgery were similar to those in healthy persons.
Paediatric population: A fed study investigating the pharmacokinetics, safety, and tolerability of a 1mg single dose of glimepiride in 30 paediatric patients (4 children aged 10-12 years and 26 children aged 12-17 years) with type 2 diabetes showed mean $AUC_{(0\text{-last})}$, C_{max} and $t_{1/2}$ similar to that previously observed in adults.

DOSAGE AND ADMINISTRATION:
For oral administration: The basis for successful treatment of diabetes is a good diet, regular physical activity, as well as routine checks of blood and urine. Tablets or insulin cannot compensate if the patient does not keep to the recommended diet. The dosage 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 dosage should be used for maintenance therapy. For the different dosage regimens appropriate strengths are available. If control is unsatisfactory, the dosage should be increased, based on the glycaemic 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 dosage 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 metformin, concomitant glimepiride therapy can be initiated. In patients not adequately controlled with the maximum daily dose of glimepiride, concomitant insulin therapy can be initiated if necessary. 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.
Method of administration: Tablets should be swallowed without chewing with some liquid.

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. Nausea, vomiting and epigastric pain may occur. The hypoglycaemia may in general be accompanied by neurological symptoms like restlessness, tremor, visual disturbances, co-ordination problems, sleepiness, coma and convulsions.

CONTRAINDICATIONS:
Glimepiride is contraindicated in patients with the following conditions: Hypersensitivity to glimepiride, other sulfonylureas or sulfonamides or to any of the excipients, insulin dependent diabetes, diabetic coma, ketoacidosis, severe renal or hepatic function disorders. In case of severe renal or hepatic function disorders, a change over to insulin is required.

WARNING & PRECAUTION:
Norlim Tablets is contraindicated in patients with a history of a hypersensitivity reaction to: Glimepiride or any of the product's ingredients, Sulfonamide derivatives: Patients who

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have developed an allergic reaction to sulfonamide derivatives may develop an allergic reaction to **Norlim Tablets**. Do not use **Norlim Tablets** in patients who have a history of an allergic reaction to sulfonamide derivatives. Reported hypersensitivity reactions include cutaneous eruptions with or without pruritus as well as more serious reactions (e.g. anaphylaxis, angioedema, Stevens-Johnson Syndrome, dyspnea).

DRUG INTERACTIONS:
If glimepiride is taken simultaneously with certain other medicinal products, both undesired increases and decreases in the hypoglycaemic action of glimepiride can occur. For this reason, other medicinal products should only be taken with the knowledge (or at the prescription) of the doctor. Glimepiride is metabolized by cytochrome P450 2C9 (CYP2C9). Its metabolism is known to be influenced by concomitant administration of CYP2C9 inducers (e.g. rifampicin) or inhibitors (e.g. fluconazole).
Potentiation of the blood-glucose-lowering effect and, thus in some instances hypoglycaemia may occur when one of the following medicinal products is taken, for example: phenylbutazone, azapropazone and oxyfenbutazone, insulin and oral antidiabetic products, such as metformin, salicylates and p-amino-salicylic acid, anabolic steroids and male sex hormones, chloramphenicol, certain long acting sulfonamides, tetracyclines, quinolone antibiotics and clarithromycin, coumarin anticoagulants, fenfluramine, disopyramide, fibrates, ACE inhibitors, fluoxetine, MAO-inhibitors, allopurinol, probenecid sulfinpyrazone, sympatholytics, cyclophosphamide, trophosphamide and iphosphamides, miconazole, fluconazole, pentoxifylline (high dose parenteral), tritoqualine.
Weakening of the blood-glucose-lowering effect and, thus raised blood glucose levels may occur when one of the following medicinal products is taken for example: oestrogens and progestogens, saluretics, thiazide diuretics, thyroid stimulating agents, glucocorticoids, phenothiazine derivatives, chlorpromazine, adrenaline and sympathicomimetics, nicotinic acid (high dosages) and nicotinic acid derivatives, laxatives (long term use), phenytoin, diazoxide, glucagon, barbiturates and rifampicin, acetazolamide, H2 antagonists, β-blockers, clonidine and reserpine may lead to either potentiation or weakening of the blood-glucose-lowering effect.
Under the influence of sympatholytic medicinal products such as beta-blockers, clonidine, guanethidine and reserpine, the signs of adrenergic counter-regulation to hypoglycaemia may be reduced or absent.
Alcohol intake may potentiate or weaken the hypoglycaemic action of glimepiride in an unpredictable fashion.
Glimepiride may either potentiate or weaken the effects of coumarin derivatives.
Colesevelam binds to glimepiride and reduces glimepiride absorption from the gastro-intestinal tract. No interaction was observed when glimepiride was taken at least 4 hours before colesevelam. Therefore, glimepiride should be administered at least 4 hours prior to colesevelam.

SIDE EFFECTS:
Blood and lymphatic system disorders:
Rare: thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, erythropenia, haemolytic anaemia and pancytopenia, which are in general reversible upon discontinuation of medication.
Not known: severe thrombocytopenia with platelet count less than 10,000/µl and thrombocytopenic purpura.
Immune system disorders:
Very rare: leukocytoclastic vasculitis, mild hypersensitivity reactions that may develop into serious reactions with dyspnoea, fall in blood pressure and sometimes shock.
Not known: cross-allergenicity with sulfonylureas, sulfonamides or related substances is possible.
Metabolism and nutrition disorders:
Rare: hypoglycaemia.
These hypoglycaemic reactions mostly occur immediately, may be severe and are not always easy to correct. The occurrence of such reactions depends, as with other hypoglycaemic therapies, on individual factors such as dietary habits and dosage.
Eye disorders:
Not known: visual disturbances, transient, may occur especially on initiation of treatment, due to changes in blood glucose levels.
Gastrointestinal disorders:
Very rare: nausea, vomiting, diarrhoea, abdominal distension, abdominal discomfort and abdominal pain, which seldom lead to discontinuation of therapy.
Hepato-biliary disorders:
Very rare: hepatic function abnormal (e.g. with cholestasis and jaundice), hepatitis and hepatic failure.
Not known: hepatic enzymes increased.
Skin and subcutaneous tissue disorders:
Not known: hypersensitivity reactions of the skin may occur as pruritus, rash, urticaria and photosensitivity.

INSTRUCTIONS:
Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION:
Norlim Tablets 1mg, 2mg, 3mg & 4mg available in blister Pack of 10's x 2.

ہدایات: ۳۰ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured By:
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PHARMA
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