METFORMIN HCl

PANFOR SR-500
PANFOR SR-1000

Oral Hypoglycemic

FORMULATION :

Each PANFOR SR-500 sustained - release tablet contains
Metformin HCl, BP 500 mg
Each PANFOR SR-1000 sustained-release tablet contains
Metformin HCl, BP 1 g

CLINICAL PHARMACOLOGY :

Metformin hydrochloride is an antihyperglycemic agent which improves glucose tolerance in NIDDM (type 2 diabetes mellitus) subjects, lowering both basal and postprandial plasma glucose. Its pharmacological mechanisms of action are different from those of sulfonylureas. Metformin decrease hepatic glucose production and improves insulin sensitivity (increases peripheral glucose uptake and utilization). Unlike sulfonylureas, Metformin does not produce hypoglycemia in either diabetic or nondiabetic subjects, and does not cause hyperinsulinemia. With Metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin levels may actually decrease.

PHARMACOKINETICS :

Absorption and Bioavailability : Following a single oral dose of sustained-release Metformin, C_{max} is achieved with a median value of 7 hours and a range of 4 hours to 8 hours. After repeated administration of a sustained-release formulation, Metformin does not accumulate in plasma. Although the extent of absorption of sustained-release Metformin is increased by approximately 50 % when given with food, there is no effect of food on C_{max} and T_{max} of Metformin.

Distribution

The apparent volume of distribution (V/F) of Metformin following single oral dose of 850 mg is 654±375 L. Metformin is negligibly bound to plasma proteins. At usual clinical doses and dosing schedules, steady state plasma concentrations of Metformin are reached within 24-48 hours and are generally < 1mg/ml

Metabolism and Elimination

Metformin is excreted unchanged in the urine, and does not undergo hepatic metabolism or biliary excretion. Renal clearance is approximately 3.5 times greater than creatinine clearance, which indicates that tubular secretion is the major route of Metformin elimination. Following oral administration, approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination half-life of approximately 17.6 hours.

SPECIAL POPULATIONS

Patients with type 2 diabetes and Gender : There are no reported differences in pharmacokinetics of Metformin hydrochloride between patients with type 2 diabetes and normal subjects when analyzed according to gender.

Renal insufficiency :

In patients with decreased renal function (based on measured creatinine clearance), the plasma and blood half life of Metformin hydrochloride is prolonged and the renal clearance is decreased in proportion to the decrease in creatinine clearance. This increased level may lead to condition of lactic acidosis.

Hepatic insufficiency :

No pharmacokinetic studies of Metformin hydrochloride have been conducted in patients with hepatic insufficiency.

Geriatrics : Reported data from controlled pharmacokinetic studies of Metformin hydrochloride in healthy elderly subjects suggest that total plasma clearance is decreased, the half-life is prolonged and Cmax is increased, compared to healthy young subjects. From this data, it appears that the change in Metformin hydrochloride pharmacokinetics with aging is primarily accounted for by a change in renal function.

Pediatrics : No pharmacokinetic studies of Metformin hydrochloride in pediatric patients have been conducted.

INDICATION :

Metformin hydrochloride (PANFOR SR) is used for treatment of non-insulin dependent diabetes mellitus (NIDDM) or type 2 DM, particularly in obese and juvenile diabetics in whom diet alone has failed as monotherapy. Metformin could also be used in *combination with insulin or with other oral antidiabetics such as* glitazones and sulfonylureas. Glitazone could be used in combination with Metformin when glycemic control is poor during monotherapy and maximum tolerated dose (preferable) of Metformin has been tried. The combination of glitazone plus Metformin is preferred over glitazone plus sulfonylurea especially for obese patients. Metformin could also be used as adjunct to diet and exercise to improve glycemic control in patients with type II diabetes.

DOSAGE AND ADMINISTRATION :

Dosage of **Metformin hydrochloride (PANFOR SR)** must be individualized on the basis of both effectiveness and tolerance in patients. The maximum recommended daily dose of 2000 mg should not be exceeded.

The drug should be started at a low dose, with gradual dose escalation, both to reduce gastrointestinal side effects and to permit identification of the minimum dose required for adequate glycemic control of the patient.

During treatment initiation and dose titration, fasting plasma glucose should be used to determine the therapeutic response to the drug and identify the minimum effective dose for the patient. Thereafter, glycosylated hemoglobin should be measured at intervals of approximately three months. The therapeutic goal should be to decrease both fasting plasma glucose and glycosylated hemoglobin levels to normal or near normal by using the lowest effective dose.

Short-term administration of the drug may be sufficient during periods of transient loss of blood glucose control in patients usually well-controlled on diet alone.

The usual starting dose of **Metformin hydrochloride (PANFOR SR)** is 500 mg once daily with the evening meal. Dosage increase should be made in increments of 500 mg weekly, up to a maximum of 2000 mg once daily with the evening meal. If glycemic control is not achieved on 2000 mg once daily, trial of 1000 mg twice daily should be considered.

The tablet should be swallowed whole and not to be chewed. The tablet should be taken after meals, or as prescribed by a physician.

CONTRAINDICATIONS :

Renal or hepatic failure, alcoholism, NIDDM complicated by severe ketosis and acidosis, diabetic precoma and coma, patients undergoing surgery, after severe trauma or during infections, chronic obstructive pulmonary disease, coronary heart disease, cardiac failure, peripheral vascular disease, pregnancy, hypoglycemia and known hypersensitivity to Metformin.

WARNING :

Lactic acidosis is a rare, but serious metabolic complication that can occur due to Metformin hydrochloride accumulation. The reported incidence of lactic acidosis during Metformin hydrochloride treatment is lower than 0.1 case per 1000 patient-years, and the mortality risk is even lower.

Lactic acidosis is a medical emergency that must be treated in a hospital setting. In a patient with lactic acidosis, the drug should be discontinued immediately and general supportive measures promptly instituted.

PRECAUTIONS :

Adjust dose according to blood glucose levels during the first few months.

Lactation : Studies have not been conducted in nursing mothers, but caution should be excercised in such patients, and a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric use : Safety and effectiveness in children has not been established.

Geriatrics : As aging is associated with reduced renal function, care should be taken in dose selection and should be based on careful and regular monitoring of renal functions.

ADVERSE EFFECTS :

Gastrointestinal disturbances : Nausea, diarrhoea, gastric pain, constipation, vomiting, metallic taste in mouth.

Dermatological effects : rash, pruritus, urticaria, erythema and flushing.

Miscellaneous : headache and dizziness. Impaired gastrointestinal absorption of vitamin B_{12}, and folic acid has been associated with long-term Metformin hydrochloride therapy.

However if such symptoms occur, please consult with your physician or pharmacist.

DRUG INTERACTIONS :

Drug interactions of Metformin hydrochloride is seen with phenprocoumon, hyperglycemic agents (e.g. thiazides, corticosteroids), alcohol, furosemide, nifedipine and cationic drugs (amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, cimetidine and vancomycin). Acarbose and guar gum may reduce the absorption of Metformin hydrochloride.

OVERDOSAGE AND TREATMENT :

Hemodialysis may be useful for removal of accumulating drug from patients in whom Metformin hydrochloride over dosage is suspected.

STORAGE CONDITION :

Store at temperatures not exceeding 30°C. Protect from light and moisture

PRESENTATION :

Alu/Clear PVC/PVDC Blister x 20's (Box of 100's)

CAUTION :

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

NOTE :

Keep out of reach of children.
Read the instruction thoroughly before use.
For further information, consult your physician.

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Imported & Distributed by:
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I-P801-M25-00-03

For suspected adverse drug reaction, report to the FDA: **www.fda.gov.ph**

Metformin Hydrochloride (Panfor SR-500): DR-XY34377
Date of First Authorization: 13 March 2008

Metformin Hydrochloride (Panfor SR-1000): DR-XY34573
Date of First Authorization: 14 May 2008

Date of Revision of Package Insert: April 2018

AT2252L/03