HOSPIMAX
Maximising Life

Glugrip 0.5mg 1mg 2mg

Repaglinide **Tablets**

Product description:

Each tablet of **Glugrip** contains:

Glugrip 0.5mg - Repaglinide 0.5mg

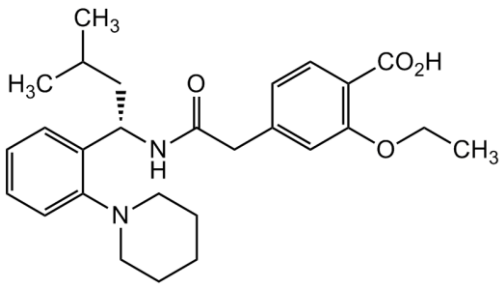
Glugrip 1mg – Repaglinide 1mg

Glugrip 2mg – Repaglinide 2mg

Description:

Glugrip (repaglinide) is an oral blood glucose-lowering drug of the meglitinide class used in the management of type 2 diabetes mellitus (also known as non-insulin dependent diabetes mellitus or NIDDM). Repaglinide, S(+)2-ethoxy-4(2((3-methyl-1-(2-(1-piperidinyl) phenyl)-butyl) amino)-2-oxoethyl) benzoic acid, is chemically unrelated to the oral sulfonylurea insulin secretagogues.

The structural formula is as shown below:



Clinical Pharmacology: Mechanism of Action:

Repaglinide lowers blood glucose levels by stimulating the release of insulin from the pancreas. This action is dependent upon functioning beta (ß) cells in the pancreatic islets. Insulin release is glucose-dependent and diminishes at low glucose concentrations. Repaglinide closes ATP-dependent potassium channels in the ß-cell membrane by binding at characterizable sites. This potassium channel blockade depolarizes the ß-cell, which leads to an opening of calcium channels. The resulting increased calcium influx induces insulin secretion. The ion channel mechanism is highly tissue selective with low affinity for heart and skeletal muscle.

Pharmacokinetics Absorption: After oral administration, repaglinide is rapidly and completely absorbed from the gastrointestinal tract. After single and multiple oral doses in healthy subjects or in patients, peak plasma drug levels (Cmax) occur within 1 hour (Tmax). Repaglinide is rapidly

eliminated from the blood stream with a half-life of approximately 1 hour. The mean absolute bioavailability is 56%. When repaglinide was given with food, the mean Tmax was not changed, but the mean Cmax and AUC (area under the time/plasma concentration curve) were decreased 20% and 12.4%, respectively.

Distribution: After intravenous (IV) dosing in healthy subjects, the volume of distribution at steady state (Vss) was 31 L, and the total body clearance (CL) was 38 L/h. Protein binding and binding to human serum albumin was greater than 98%.

Metabolism: Repaglinide is completely metabolized by oxidative biotransformation and direct conjugation with glucuronic acid after either an IV or oral dose. The major metabolites are an oxidized dicarboxylic acid (M2), the aromatic amine (M1), and the acyl glucuronide (M7). The cytochrome P-450 enzyme system, specifically 2C8 and 3A4, have been shown to be involved in the N-dealkylation of repaglinide to M2 and the further oxidation to M1. Metabolites do not contribute to the glucose-lowering effect of repaglinide. Repaglinide appears to be a substrate for active hepatic uptake transporter.

Excretion: Within 96 hours after dosing with 14C-repaglinide as a single, oral dose, approximately 90% of the radio label was recovered in the feces and approximately 8% in the urine. Only 0.1% of the dose is cleared in the urine as parent compound. The major metabolite (M2) accounted for 60% of the administered dose. Less than 2% of parent drug was recovered in feces.

Drug-Drug Interactions: Drug interaction studies performed in healthy volunteers show that Repaglinide had no clinically relevant effect on the pharmacokinetic properties of digoxin, theophylline, or warfarin. Coadministration of cimetidine with Glugrip did not significantly alter the absorption and disposition of repaglinide.

INDICATIONS AND USAGE: Glugrip is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

DOSAGE AND ADMINISTRATION

There is no fixed dosage regimen for the management of type 2 diabetes with Glugrip. The patient's blood glucose should be monitored periodically to determine the minimum effective dose for the patient; to detect primary failure, i.e., inadequate lowering of blood glucose at the maximum recommended dose of medication; and to detect secondary failure, i.e., loss of an adequate blood glucose-lowering response after an initial period of effectiveness. Glycosylated hemoglobin levels are of value in monitoring the patient's longer term response to therapy. Short-term administration of Glugrip may be sufficient during periods of transient loss of control in patients usually well controlled on diet.

Starting Dose:

For patients not previously treated or whose HbA1c is < 8%, the starting dose should be 0.5 mg with each meal. For patients previously treated with blood glucose-lowering drugs and whose HbA1c is > 8%, the initial dose is 1 or 2 mg with each meal preprandially.

Dose Adjustment:

Dosing adjustments should be determined by blood glucose response, usually fasting blood glucose. Postprandial glucose levels testing may be clinically helpful in patients whose pre-meal blood glucose levels are satisfactory but whose overall glycemic control (HbA1c) is inadequate. The preprandial dose should be doubled up to 4 mg with each meal until satisfactory blood glucose response is achieved. At least one week should elapse to assess response after each dose adjustment. The recommended dose range is 0.5 mg to 4 mg taken with meals. Glugrip may be dosed preprandially 2, 3, or 4 times a day in response to changes in the patient's meal pattern. The maximum recommended daily dose is 16 mg.

Combination Therapy:

If Glugrip monotherapy does not result in adequate glycemic control, metformin or a thiazolidinedione may be added. If metformin or thiazolidinedione monotherapy does not provide adequate control, Glugrip may be added. The starting dose and dose adjustments for Glugrip combination therapy is the same as for Glugrip monotherapy. The dose of each drug should be carefully adjusted to determine the minimal dose required to achieve the desired pharmacologic effect. Appropriate monitoring of FPG and HbA1c measurements should be used to ensure that the patient is not subjected to excessive drug exposure or increased probability of secondary drug failure.