GLYSET

COMPOSITION:

Glyset 1mg Tablet:
Each tablet contains: Glimepiride (B.P).....
1mg
Glyset 2mg Tablet:
Each tablet contains: Glimepiride (B.P) 2mg
Glyset 3mg Tablet: Each tablet contains: Glimepiride (B.P) 3mg
Glyset 4mg Tablet: Each tablet contains: Glimepiride (B.P) 4mg
Glimepiride
Product conforms to the U.S.P Specifications.

DESCRIPTION:

Glyset is an oral Sulfonylurea that contains the active ingredient Glimepiride. Chemically, Glimepiride is identified as 1-[p-12-(3-ethyl-4-methyl-2-oxo-3-pyrroline 1carboxamido) ethyllphenyl]sulfonyl]-3-(trans-4-methylcyclohexyl)urea (C, HN,O,S) with a molecular weight of 490.62. Glimepiride is a white to yellowish-white,crystalline, odorless to practically adorless powder and is practically insoluble in water.

MECHANISM OF ACTION:

Glimepiride (Glyset) primarily lowers blood Glucose by stimulating the release of Insulin from pancreatic beta cells. Sulfonylureas bind to the Sulfonylurea receptor in the pancreatic beta cell plasma membrane, leading to closure of the ATP sensitive Potassium channel, thereby stimulatingthe release of Insulin.

PHARMACOKINETICS:

Absorption: Studies with single oral doses of Glimepiride (Glyset) in healthy subjects and with multiple oral doses in s in patients with type 2 diabetes showed peak drug concentrations (Cmax) 2 to 3 hours post dose. When Glimepiride (Glyset) was given with meals, the mean Cmax and AUC (area under the curve) were decreased by 8% and 9%, respectively, Glimepiride does not accumulate in serum following multiple dosing. The pharmacokinetics of Glimepiride (Glyset) does not differ between healthy subjects and patients with type 2 diabetes. Clearance of Glimepiride after oral administration does not change over the 1mg to 8mg dose range, indicating linear pharmacokinetics. In healthy subjects, the intra and inter individual variabilities of Glimepiride (Glyset) pharmacokinetic parameters were 15-23% and 24-29% , respectively. Distribution: Glimepiride has a very low distribution volume (approx. 8.8 liters), which is roughly equal to the Albumin distribution space, high protein binding (>99%).
Metabolism: Glimepiride is completely metabolized by oxidative biotransformation after oral dose. The major metabolites are the Cyclohexyl hydroxy methyl derivative (M1) and the Carboxyl derivative (M2). Cytochrome P450 2C9 is involved in the biotransformation of Glimepiride to M1. M1 is further metabolized to M2 by one or several cytosolic enzymes. M2 is inactive. In animals, M1 possesses about one third of the pharmacological activity of Glimepiride (Glyset), but it is unclear whether M1 results in clinically meaningful effects on blood glucose in humans.
Excretion: When "C Glimepiride was given orally to 3 healthy male subjects, approximately 60% of the total radioactivity was recovered in the urine in 7 days. M1 and M2 accounted for 80-90% of the radioactivity recovered in the urine. The ratio of M1 to M2 in the urine was approximately 3:2 in two

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subjects and 4:1 in one subject. Approximately 40% of the total radioactivity was recovered in feces, M1 and M2 accounted for approximately 70% (Ratio of M1 to M2 was 1:3) of the radioactivity recovered in feces. No parent drug was recovered from urine or feces.

INDICATIONS:

Glimepiride (Glyset) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Important Limitations of Use
Glimepiride (Glyset) should not be used for the treatment of type 1 diabetes mellitus or diabetic Ketoacidosis, as it would not be effective in these indications.

DOSAGE AND ADMINISTRATION:

Glimepiride (Glyset) should be administered with breakfast or the first main meal of the day. The recommended starting dose of Glimepiride (Glyset) is 1 mg or 2 mg once daily. Patients at increased risk of hypoglycemia (e.g. the elderly or patients with renal impairment) should be started on
1 mg once daily.
After reaching a daily dose of 2mg, further dose increases can be made in increments of 1mg or 2mg based upon the patient's glycemic response. Uptitration should not occur more frequently than every 1 to 2 weeks. A conservative titration scheme is recommended for patients at increased risk of hypoglycemia.
The maximum recommended dose is 8mg once daily.
Patients being transferred to Glimepiride (Glyset) from longer half life Sulfonylureas (e.g. Chlorpropamide) may have overlapping drug effect for 1 to 2 weeks and should be appropriately monitored for hypoglycemia.

CONTRAINDICATIONS:

TGlimepiride (Glyset) is contraindicated in patients with a history of a hypersensitivity reaction to Glimepiride or any of the product's ingredients.
Sulfonamide derivatives: Patients who have developed an allergic reaction to Sulfonamide derivatives may develop an allergic reaction to Glimepiride (Glyset). Do not use Glimepiride (Glyset) in patients who have a history of an allergic reaction to Sulfonamide derivatives.
Reported hypersensitivity reactions include eruptions with or without pruritus as well as more serious reactions (e.g. anaphylaxis, angioedema, Stevens-Johnson syndrome, dyspnea).

PRECAUTIONS:

Hypoglycemia: All Sulfonylureas, including Glimepiride (Glyset), can cause severe hypoglycemia. The patient's ability to concentrate and react may be impaired as a result of hypoglycemia
Hypersensitivity Reactions: There have been post marketing reports of hypersensitivity reactions in patients treated with Glimepiride (Glyset) including serious reactions such as anaphylaxis angioedema and Stevens - Johnson syndrome. If a hypersensitivity reaction is suspected, promptly discontinue Glimepiride (Glyset), assess for other potential causes for the reaction and institute alternative treatment for diabetes.
Hemolytic Anemia: Sulfonylureas can cause hemolytic anemia in patients with Glucose-6-phosphate dehydrogenase (G6PD) deficiency. Because Glimepiride (Glyset) is a Sulfonylurea, use caution in. patients with G6PD deficiency and consider the use of a non Sulfonylurea alternative. There are also, post marketing reports of hemolytic anemia in patients receiving Glimepiride (Glyset) who did not

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have; known G6PD deficiency

DRUG-DRUG INTERACTIONS:

A number of medications affect Glucose metabolism and may require Glimepiride (Glyset) dose 'adjustment and particularly close monitoring for hypoglycemia or worsening glycemic control. The following are examples of medications that may increase the Glucose lowering effect of Sulfonylureas including Glimepiride (Glyset) increasing the susceptibility to and/or intensity of hypoglycemia: Oral anti-diabetic medications, Pramlintide acetate, Insulin, Angiotensin converting; enzyme(ACE) inhibitors, H2 receptor antagonists, Fibrates, Propoxy-phene, Pentoxifylline Somatostatin analogs, Anabolic Steroids and Androgens, Cyclophosphamide, Phenyramidol, 'Guanethidine, Fluconazole, Sulfinpyrazone, Tetracyclines, Clarithromycin, Disopyramide, Quinolones and those drugs that are highly protein bound, such as Fluoxetine, Nonsteroidal antiinflammatory drugs(NSAID), Salicylates, Sulfonamides, Chloramphenicol, Coumarins, Probenecid and Monoamine oxidase inhibitors(MAO1). When these medications are administered to a patient receiving Glimepiride (Glyset), monitor the patient closely for hypoglycemia. When these medications are withdrawn from a patient receiving Glimepiride (Glyset), monitor the patient closely for worsening glycemic control. The following are examples of medications that may reduce the Glucose lowering effect of Sulfonylureas including Glimepiride (Glyset), leading to worsening glycemic control: Danazol, Glucagon, Somatropin, Protease inhibitors, Atypical antipsychotic medications (e.g. Olanzapine and; Clozapine), Barbiturates, Diazoxide, Laxatives, Rifampin, Thiazides and other Diuretics Corticosteroids, Phenothiazines, Thyroid hormones, Estrogens, Oral contraceptives, Phenytoin, Nicotinic acid, Sympathomimetics (e.g. Epinephrine, Albuterol, Terbutaline) and Isoniazid. When these medications are administered to a patient receiving Glimepiride (Glyset), monitor the patient closely for worsening glycemic control. When these medications are withdrawn from a patient receiving Glimepiride (Glyset), monitor the patient closely for hypoglycemia.

* Beta blockers, Clonidine and Reserpine may lead to either potentiation or weakening of Glimepiride (Glyset) Glucose lowering effect.

* The signs of hypoglycemia may be reduced or absent in patients taking Sympatholytic drugs such as Beta blockers, Clonidine, Guanethidine and Reserpine.

ADVERSE DRUG REACTIONS:

AThe most common adverse reactions with Glimepiride (Glyset) are
Hypoglyceria, Hemolytic anemia, Dizziness, Asthenia, Headache and Nausea

OVER DOSAGE:

An overdosage of Glimepiride (Glyset), as with other Sulfonylureas, can produce severe hypoglycemia. Mild episodes of hypoglycemia can be treated with oral Glucose. Severe hypoglycemic reactions constitute medical emergencies requiring immediate treatment. Severe hypoglycemia with coma, seizure or neurological impairment can be treated with Glucagon or intravenous Glucose. Continuous observation and additional Carbohydrate intake may be necessary because hypoglycemia may recur after apparent clinical recovery.

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INSTRUCTIONS:

Store in a cool & dry place below 25°C
Protect from light, heat and moisture.
Keep out of reach of children,

PRESENTATION:

Glyset 1mg tablets are available in a blister pack of 20's
Glyset 2mg tablets are available in a blister pack of 20's
Glyset 3mg tablets are available in a blister pack of 20's
Glyset 4mg tablets are available in a blister pack of 20's