XORMET XR

(Metformin HCl Extended Release) **Tablets**

COMPOSITION

XORMET XR 500mg Tablets: Each extended release tablet contains: Metformin HCl B.P. ..... 500mg.

XORMET XR 1000mg Tablets: Each extended release tablet contains: Metformin HCl B.P. ..... 1000mg.

DESCRIPTION

XORMET XR (Metformin HCl Extended Release) is an oral anti-diabetic medicine that belongs to the group of biguanides.

Metformin, the active ingredient in XORMET XR, reduces hepatic glucose production, increases insulin sensitivity in muscles and delays intestinal glucose absorption.

METFORMIN HYDROCHLORIDE

Metformin is a biguanide that improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

Pharmacokinetics

Following a single oral dose of 1000 mg (2x500 mg tablets) XORMET XR after a meal, the time to reach maximum plasma metformin concentration (Tmax) is achieved at approximately 7-8 hours. XORMET XR tablets must be administered immediately after a meal to maximize therapeutic benefit. Low-fat and high-fat meals increased the systemic exposure (as measured by AUC) from METFORMIN tablets by about 38% and 73%, respectively, relative to fasting. Both meals prolonged metformin Tmax by approximately 3 hours but Cmax was not affected. Metformin is negligibly bound to plasma proteins. Metformin is excreted unchanged in the urine and does not undergo hepatic metabolism (no metabolites have been identified in humans), nor biliary excretion. 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination half-life of approximately 6.2 hours.

INDICATIONS AND USAGE

XORMET XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use

XORMET XR should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

DOSAGE AND ADMINISTRATION

XORMET XR should be taken once daily with the evening meal. The dosage of XORMET XR must be individualized on the basis of both effectiveness and tolerability, while not exceeding the maximum recommended daily dose of 2000 mg. The starting dose of XORMET XR in patients who are not currently taking metformin is 500 mg once daily, with the evening meal. The dose can be up titrated in 500 mg increments no sooner than every 1-2 weeks if a higher dose of XORMET XR is needed and there are no gastrointestinal adverse reactions. If XORMET XR is considered appropriate for a patient already receiving immediate-release metformin, the patient can be switched to XORMET XR once daily at the same total daily dose, up to 2000 mg once daily. XORMET XR tablets must be swallowed whole and never split, crushed or chewed. If a dose of XORMET XR is missed, patients should be cautioned against taking two doses of 2000 mg the same day. Resume dosing as according to prescribing recommendations. Co-administration of XORMET XR with an insulin secretagogue (e.g., sulfonylurea) or insulin may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

CONTRAINDICATIONS

- METFORMIN is contraindicated in patients with: Renal impairment (e.g., serum creatinine levels ⩾ 1.5 mg/dl for men, ⩾ 1.4 mg/dl for women or abnormal creatinine clearance), which may also result from conditions such as cardiovascular collapse (shock), acute myocardial infarction, and septicemia.
- Known hypersensitivity to metformin hydrochloride.
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis.
- Diabetic ketoacidosis should be treated with insulin.

WARNING & PRECAUTIONS

- Lactic acidosis can occur due to metformin accumulation. The risk increases with conditions such as sepsis, dehydration, excess alcohol intake, hepatic insufficiency, renal impairment, and acute congestive heart failure. The symptoms include malaise, myalgia's, respiratory distress, increasing somnolence, and nonspecific abdominal distress. Laboratory abnormalities include low pH, increased anion gap and elevated blood lactate. If acidosis is suspected, discontinue XORMET XR and hospitalize the patient immediately.
- Conditions associated with hypoxia, such as acute heart failure, recent myocardial infarction. or shock, may increase the risk of lactic acidosis.
- Care should be taken in patients with renal impairment. Renal function should be monitored throughout the therapy. If renal dysfunction is anticipated particularly in elderly patients, renal function should be assessed more frequently and drug should be discontinued if evidence of renal impairment is present as it may increase the chance of lactic acidosis. Dehydration may contribute to renal impairment.
- Alcohol is known to potentiate the effect of metformin on lactate metabolism. Patients, therefore, should be warned against excessive alcohol intake while receiving XORMET XR.
- XORMET XR should generally be avoided in patients with clinical or laboratory evidence of hepatic disease.
- Driving: Diabetes Mellitus, its complications and the medications used to treat it, may affect a patient's' ability to drive safely.
- Owing to the possibility of decreased vitamin B12 absorption, annual monitoring of vitamin B12 concentrations is advisable during long term treatment.
- Safety and effectiveness of METFORMIN in pediatric patients under 18 years have not been established.
- May also need to be temporarily stopped for examinations using contrast media in some patients (intravascular administration of iodinated contrast materials in radiologic studies can lead to renal failure, metformin should be discontinued prior to, or at the time of the test and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal).
- Should be discontinued in patients undergoing surgery and only restarted once normal renal function has been established.

ADVERSE EFFECTS

The reported adverse effects of metformin are Diarrhea, nausea, vomiting, flatulence, asthenia, indigestion, abdominal discomfort (abdominal pain & abdominal distention), headache, abnormal stools, hypoglycemia,

myalgia, lightheaded, dyspnea, nail disorder, rash, sweating increased, taste disorder, chest discomfort, chills, flu syndrome, flushing, palpitation, constipation, dyspepsia, heart burn, dizziness & upper respiratory tract infection. Patient may have taste disturbances, there may be a weight loss. Skin reactions have been reported rarely. Hypoglycemia is rare with biguanide given alone, although it may occur if other contributing factors or drugs are present.

DRUG INTERACTION

Carbonic Anhydrase Inhibitors

Carbonic anhydrase inhibitors; Topiramate or other carbonic anhydrase inhibitors (e.g., zonisamide, acetazolamide or dichlorphenamide) frequently decrease serum bicarbonate and induce non-anion gap, hyperchloremic metabolic acidosis. Concomitant use of these drugs may induce metabolic acidosis. Use these drugs with caution in patients treated with METFORMIN, as the risk of lactic acidosis may increase.

Cationic Drugs

Careful patient monitoring and dose adjustment of XORMET XR and/or the interfering drug is recommended in patients who are taking cationic medications (e.g., cimetidine, amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, or vancomycin) that are excreted via the proximal renal tubular secretory system.

Drugs Affecting Glycemic Control

Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazine's, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetic, calcium channel blockers, and isoniazid. When such drugs are administered to a patient receiving XORMET XR, the patient should be closely observed for loss of blood glucose control. When such drugs are withdrawn from a patient receiving XORMET XR, the patient should be observed closely for hypoglycemia.

USED IN SPECIAL POPULATION

Pregnancy Category B

There are no adequate and well controlled studies in pregnant women with METFORMIN or its individual Components. This drug should be used during pregnancy only if clearly needed,

Nursing Women

It is not known whether METFORMIN is excreted in human milk, because many drugs are excreted in human milk, caution should be exercised when METFORMIN is administered to a nursing woman.

Pediatric use

Safety and effectiveness of METFORMIN in pediatric patients under 18 years of age has not been established.

Geriatric Use

This drug (METFORMIN) is known to be substantially excreted by the kidney. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection in the elderly, and it may be useful to assess renal function in these patients prior to initiating dosing and periodically thereafter.

OVERDOSAGE

The symptoms of overdose are epigastric discomfort, nausea, and vomiting followed by diarrhea, drowsiness, weakness, dizziness, malaise and headache might be seen. Should those symptoms persist, lactic acidosis should be excluded.

Overdose of metformin hydrochloride has occurred, including ingestion of amounts greater than 50 grams. Hypoglycemia should be treated with urgency, initiate clinical monitoring (Including obtaining an electrocardiogram) & initiate supporting therapy as dictated by the patient clinical status. Prolonged hemodialysis may be considered if clinically appropriate.

PRESENTATION

XORMET XR 500mg tablets: Blister pack of 5 x 10's.
XORMET XR 1000mg tablets: Blister pack of 5 x 10's.

DOSAGE & INSTRUCTIONS

To be sold and used on the prescription of a registered medical practitioner only.
Keep out of the reach of children.
Store below 25°C in a dry place.
Protect from light.

زورمیٹ ایکس آر

(میٹ فارمن ہائیڈروکلورائیڈ ایکسٹینڈیڈ ریلیز)

گولیاں

خوراک وہدایات

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔
25°C سے کم درجہ حرارت میں خشک جگہ پر رکھیں۔
روشنی سے بچائیں۔

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