Metformin Hydrochloride (metformin hydrochloride) - Drug Summary

Amneal Pharmaceuticals

Related Drug Information

Glucophage XR
(metformin hydrochloride)

BOXED WARNING

Lactic acidosis reported (rare); increased risk w/ increased age, renal dysfunction, or CHF. Risk of lactic acidosis may be significantly decreased by regular monitoring of renal function and by use of the minimum effective dose of metformin. Avoid use in patients ≥80 yrs of age unless renal function is normal. Withhold therapy in the presence of any condition associated w/ hypoxemia, dehydration, or sepsis. Avoid w/ clinical or lab evidence of hepatic disease. Caution against excessive alcohol intake; may potentiate the effects of metformin on lactate metabolism. Temporarily d/c prior to any IV radiocontrast study and for any surgical procedure. Lactic acidosis should be suspected in any diabetic patient w/ metabolic acidosis lacking evidence of ketoacidosis (ketonuria and ketonemia). D/C use and institute appropriate therapy if lactic acidosis occurs.

COMMON BRAND NAMES

Glucophage, Glucophage XR

THERAPEUTIC CLASS

Biguanide

DEA CLASS

RX

ADULT DOSAGE & INDICATIONS

Type 2 Diabetes Mellitus

Tab:
Initial: 500mg bid or 850mg qd w/ meals
Titrate: Increase by 500mg/week or 850mg every 2 weeks, up to a total of 2000mg/day, given in divided doses; may also titrate from 500mg bid to 850mg bid after 2 weeks
Max: 2550mg/day; doses >2000mg/day may be better tolerated given tid

Tab, Extended-Release (ER):
Initial: 500mg qd w/ pm meal
Titrate: Increase by 500mg/week
Max: 2000mg/day; consider 1000mg bid if unable to achieve glycemic control on 2000mg qd

PEDIATRIC DOSAGE & INDICATIONS

Type 2 Diabetes Mellitus

10-16 Years:
Tab:
Initial: 500mg bid w/ meals
Titrate: Increase by 500mg/week
Max: 2000mg/day

DOSING CONSIDERATIONS

Concomitant Medications
Insulin Therapy in Adults:
Initial: 500mg qd while continuing current insulin dose
Titrate: Increase by 500mg/week; decrease insulin dose by 10-25% when FPG <120mg/dL

Max: 2500mg/day (tab) and 2000mg/day (tab, extended-release [ER])

Oral Sulfonylurea Therapy in Adults:
Consider gradual addition of an oral sulfonylurea if unresponsive to 4 weeks of max dose of Glucophage or Glucophage XR monotherapy; if patient has not satisfactorily responded to 1-3 months of concomitant therapy w/ the max dose of Glucophage or Glucophage XR and the max dose of an oral sulfonylurea, consider therapeutic alternatives (eg, switching to insulin w/ or w/o Glucophage or Glucophage XR)

Elderly
Dose conservatively; do not titrate to max dose

Other Important Considerations
Transferring Patients from Chlorpropamide: Exercise care during the first 2 weeks because of the prolonged retention of chlorpropamide in the body
Debilitated/Malnourished: Do not titrate to max dose

ADMINISTRATION

Oral route

Tab
Give in divided doses w/ meals.

Tab, ER
Give qd w/ the pm meal.
Must be swallowed whole; do not crush or chew.

HOW SUPPLIED

Tab: (Glucophage) 500mg, 850mg, 1000mg; **Tab, ER:** (Glucophage XR) 500mg, 750mg

CONTRAINDICATIONS

Renal disease/dysfunction (eg, SrCr ≥1.5mg/dL [males], ≥1.4mg/dL [females], or abnormal CrCl); acute or chronic metabolic acidosis, including diabetic ketoacidosis, w/ or w/o coma. Temporarily d/c (48 hrs) in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials.

WARNINGS/PRECAUTIONS

D/C therapy if conditions associated w/ lactic acidosis and characterized by hypoxemia states (eg, acute CHF, cardiovascular [CV] collapse, acute MI), or prerenal azotemia develop. Temporary loss of glycemic control may occur when a patient stabilized on a diabetic regimen is exposed to stress (eg, fever, trauma, infection, surgery); may be necessary to withhold metformin and temporarily administer insulin; may reinstitute metformin after acute episode is resolved. May decrease serum vitamin B12 levels. Increased risk of hypoglycemia in elderly, debilitated/malnourished or w/ adrenal or pituitary insufficiency or alcohol intoxication. Consider therapeutic alternatives, including initiation of insulin, if secondary failure w/ combined metformin/sulfonylurea therapy occurs. Hypoglycemia may be difficult to recognize in the elderly; caution in elderly.

ADVERSE REACTIONS

Diarrhea, N/V, flatulence, asthenia, indigestion, abdominal discomfort, headache.

DRUG INTERACTIONS

See Boxed Warning and Contraindications. Furosemide, nifedipine, cimetidine, and cationic drugs that are eliminated by renal tubular secretion (eg, digoxin, amiloride, procainamide, quinidine, quinine, ranitidine, trimethoprim, vancomycin, triamterene, morphine) may increase levels. Observe for loss of glycemic control w/ thiazides, other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blockers, and isoniazid. May interact w/ highly protein-bound drugs (eg, salicylates, sulfonamides, chloramphenicol, probenecid). May decrease furosemide or glyburide levels. Caution w/ drugs that may affect renal function or result in significant hemodynamic change or may interfere w/ the disposition of metformin (eg, cationic drugs that are eliminated by renal tubular secretion). Hypoglycemia may occur w/ concomitant use of other glucose-lowering agents (eg, sulfonylureas, insulin) or ethanol. Hypoglycemia may be difficult to recognize w/ β-adrenergic blocking drugs.

PREGNANCY AND LACTATION

Pregnancy: There are no adequate and well-controlled studies in pregnant women w/ metformin; metformin should not be used during pregnancy unless clearly needed.
Lactation: Not for use in nursing.

MECHANISM OF ACTION

Biguanide; decreases hepatic glucose production and intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.

PHARMACOKINETICS

Absorption: (Tab) Absolute bioavailability (50-60%); (Tab, ER) T_{max}=7 hrs (median). Administration of different doses resulted in different parameters. **Distribution:** (Tab) V_d=654L. **Elimination:** Urine (90%); $T_{1/2}$=6.2 hrs (plasma), 17.6 hrs (blood).

ASSESSMENT

Assess for renal disease or renal dysfunction, hepatic impairment, acute/chronic metabolic acidosis, presence of a hypoxic state (eg, acute CHF, acute MI, CV collapse), dehydration, sepsis, alcoholism, nutritional status, adrenal/pituitary insufficiency, pregnancy/nursing status, or any other conditions where treatment is contraindicated or cautioned. Assess for possible drug interactions. Assess baseline renal function, FPG, HbA1c, and hematological parameters (eg, Hct, Hgb, RBC indices).

MONITORING

Monitor for lactic acidosis, hypoglycemia, hypoxemia (eg, CV collapse, acute CHF, acute MI), prerenal azotemia, decreases in vitamin B12 levels, and for any other adverse reactions. Monitor FPG, HbA1c, renal function, and hematological parameters (eg, Hgb, Hct, RBC indices).

PATIENT COUNSELING

Inform of the potential risks/benefits of therapy. Inform about the importance of adherence to dietary instructions, a regular exercise program, and of regular testing of blood glucose, HbA1c, renal function, and hematologic parameters. Inform of the risk of developing lactic acidosis during therapy; advise to d/c therapy immediately and contact physician if unexplained hyperventilation, myalgia, malaise, unusual somnolence, or other nonspecific symptoms occur. Instruct to avoid excessive alcohol intake. Counsel to take tab w/ meals and ER tab w/ pm meal. Instruct that ER tab must be swallowed whole and not crushed or chewed.

STORAGE

20-25°C (68-77°F); excursions permitted to 15-30°C (59-86°F).

Back to top