METFORMIN

Description

Metformin is an oral antidiabetic agent (Biguanids).

Clinical pharmacology

Metformin is used for management of type 2 diabetes mellitus (noninsulin dependent, NIDDM) when hyperglycemiacannot be managed with diet and exercise alone. Metformin potentiates the effect of insulin by mechanisms not fully understood. It does not stimulate pancreatic beta cells to increase secretion of insulin; insulin secretion must be present for metformin to work properly. It is postulated that metformin decrease hepatic glucose production and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Specifically, it is thought that metformin may increase the number and/or affinity of insulin receptors on cell surface membranes, especially at peripheral receptor sites, and help to correct down regulation of the insulin receptor. This effect increase the sensitivity to insulin at receptor and post receptor binding sites and increase glucose uptake peripherally. Insulin concentrations remain unchanged or are slightly reduced as glucose metabolism improves. At therapeutic doses, metformin does not cause hypoglycemia in diabetic or nondiabeticindiviuals.

Pharmacokinetics

- Oral absorption: Absorbed over 6 hours; bioavailability is 50 to 60% under fasting condition. Food delays absorption (lower peak concentration by 40%) and decreases the extent of absorption (lower area under the concentration-time curve [AUC] by 25%).
- Distribution: Apparent volume of distribution is 654 ± 358 L.
- Protein binding: Negligible
- Biotransformation: metformin is not metabolized
- Half-life: plasms elimination- 6.2 hours, mean, based on an initial elimination of 1.7 to 3 hours and terminal elimination of 9 to 17 hours.
- Elimination: renal: up to 90% of dose. Fecal: up to 30% of a dose

Indication

Type 2 diabetes (treatment)- metformin is indicated in patients with type 2 diabetes to control hyperglycemia that can not be controlled by diet management, exercise, or weight reduction, or when insulin therapy is not required or feasible. It is used as monotherapy or as an adjunct to sulfonylurease or insulin when either alone does not achieve adequate glycemia control. It can be tried if primary or secondary failure of sulfonylurease occurs. However, caution and clinical judgment should be used when combining metformin with maximum doses of sulfonylurease for treating nonobese patients with type 2 diabetes who clearly are not responding to the sulfonylurease; insulin may be the preferred treatment in such cases.

Contraindication

Hypersensitivity to metformin or any component of the formulation, renal disease or renal dysfunction or abnormal creatinine clearance from any cause, including shock, acute myocardial infraction, or septicemia, acute or chronic metabolic acidosis with or without coma (including diabetic ketoacidosis)

Precaution

Pregnancy: pregnancy category B.

Breast- feeding: problems in humans have not been documented. Metformin is distributed into breast milk.

Dosage

Initial: 500 mg two times a day; taken with morning and evening meals; the daily dose may be increased by 500 mg at weekly intervals as needed, an alternative dose is 850 mg a day, taken with the morning meal. The daily dose may be increased by 850 mg at fourteen – day intervals.

Maintenance: 500 or 850 mg two to three times a day, taken with meal.

Note: swallow whole. Do not crush or chew.

Patient consultation

Use of any oral antidiabetic medication is discouraged during pregnancy; diet or diet/insulin is recommended to prevent maternal and fetal problems.

Age- related renal function impairment or peripheral vascular disease may require discontinuation of metformin treatment or special precaution in the elderly.

Missed dose: taking as soon as possible; not taking if almost time for next dose, not doubling doses.

Regular visits to physician to check progress

Warning

Lactic acidosis is a rare, but potentially severe consequence of therapy with metformin that requires urgent care and hospitalization. The risk is increased in patients with acute congestive heart failure, dehydration, excessive alcohol intake, hepatic or renal impairment, or sepsis. Symptoms may be nonspecific (eg, abdominal distress, malaise, myalgia, respiratory distress somnolence); low pH, increased anion gap and elevated blood lactate may be observed. Discontinue immediately if acidosis is suspected.

Interaction

- Metformin may increase the levels/effects of Dalfampridine; Dofetilide.
- The levels/ effects of metformin may be increased by Carbonic Anhydrase inhibitors, Cephalexin; Cimetidine; Dalfampridine; Dolutegravir; Glycopyrrolate; Iodinated Contrast agents; Lamotrigine; pegvisomant; Ranolazine; Topiramate; Trimethoprim.
- Metformin may decrease the levels/effects of Trospium.
- The levels/effects of metformin may be decreased by: Corticosteroids (Orally inhaled); Corticosteroids (Systemic); Luteinizing Hormone-Releasing Hormone Analogs; Somatropin; Thiazide Diuretics
- Ethanol: Avoid or limit ethanol (incidence of lactic acidosis may be increase; may cause hypoglycemia).
- Food: Food decreases the extent and slightly delays the absorption. May decrease absorption of vitamin B12 and /or folic acid.
- Herb/ Nutraceutical: caution with chromium, garlic, gymnema (may cause hypoglycemia).

Adverse reaction

Cardiovascular: Chest discomfort, flushing, palpitation

Central nervous system: Chills, dizziness, headache, lightheadedness

Dermatologic: Rash

Endocrine and metabolic: hypoglycemia

Gastrointestinal: Abdominal discomfort, abdominal distention, abdominal stools, constipation, diarrhea, dyspepsia, flatulence, heartburn, indigestion, nausea, taste disorder, vomiting

Neuromuscular and skeletal: Myalgia, weakness

Respiratory: Dyspnea, upper respiratory tract infection

Miscellaneous: Decreased vitamin B12 levels, flu-like syndrome, increased diaphoresis, nail disorder

Rare but important or life-threatening: lactic acidosis, leukocytoclasticvasculitis, megaloblastic anemia, pneumonitis

Overdose

See emergency medical attention if you think you have used too much of this medicine.

Storage and stability condition

- Take with food or after it.
- Do not use with any other product containing alcohol.
- Store below 30°C. protect from light and moisture.
- Keep out of- the reach of- children.
- Read the laeflet for more information.

Packaging

100 film coated tablets containing 500 mg metformin hydrochloride in a box.

References:

- Lexicomp Drug information handbook, 2015, 23rd edition, Pages: 1324-1326
- USP Drug Information (USPDI) for the Health Care Professional (27th edition), Pages: 1937-1942
- Drug facts and comparisons, 2010, Pages: 437-442

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