Mectin®

Metformin hydrochloride 850 mg
Metformin hydrochloride 1000 mg

Extended-release tablets

Sale under prescription
Made in Argentine

Composition:
Mectin® / Metformin hydrochloride 850 mg
Each extended-release tablet contains: metformin hydrochloride 850.00 mg; hydrated lactose 119.00 mg; hydroxypropylmethylcellulose K 100 119.00 mg; polyvinylpyrrolidone 50.00 mg; magnesium stearate 12.00 mg.
Mectin® / Metformin hydrochloride 1000 mg
Each extended-release tablet contains: metformin hydrochloride 1000.00 mg; hydrated lactose 140.65 mg; hydroxypropylmethylcellulose K 100 140.65 mg; polyvinylpyrrolidone 59.50 mg; red ferric oxide dyeing 0.70 mg; magnesium stearate 13.50 mg.

Therapeutical action:
Oral antihyperglycemics member of the biguanide class.

Indications:
In Diabetes type II (adult non insulin dependent), as monotherapy, is indicated as an adjunct to diet and exercise to improve glycemic control.
Mectin®, is indicated in patients 17 years old and older.
Can be used concomitantly with a sulfonylurea or insulin to improve glycemic control in adults patients, older than 17 years old.
In Diabetes treated with insulin, as insulin therapy complement.
In Diabetes type II particularly in important overweight cases, associated to a secondary resistance to insulin action.
Was demostrated a reduction in complications in obese patients with diabetes type II treated with metformin as first class treatment after diet failure.

Pharmacological properties:
Is an oral antihyperglycemics member of the biguanide class.

Mechanism of Action.
Is an antihyperglycemic agent increasing insulin receptors in patient with type 2 diabtes, lowering both basal and postprandial glycemia.
Metformin reduces glycemia in patients with diabetes. This effect results of an increase of glucose use by the muscular tissue in presence of insulin; of hepatic neoglucogenesis and of a decrease in glucose digestive absoption.
Metformin does not increase insulin secretion, and does not produce hypoglycemia.
Reduces the overweight of the obese patient with diabetes because it decreases the high level of insulin and because it reduces lipogenesis and starving.
Metformin has a good oral absoption and an elimination plasmatic half-life of 3 to 6 hours. It is not metabolized, it eliminated without modifications by urine with a renal clearence of 440 ml/min.
Reduces lipids in blood, principally triglicerydes.
- *Lactic Acidosis:* this medicine, as all biguanides derivates, can produce, in some cases, lactic acidosis as secondary effect. The seriousness of this chart suggest follow strictly the use conditions.

Pharmacokinetics.
Following administration of an oral single dose of Metformin, the MaxC is obtained inside the 7 hours (range of 4 to 8 hours).
Peak plasmatic concentrations of the ER formula are approximately a 20 % lower than the ones compared with the same dose of metformin, however duration of absorption measured as area uncer the curve is similar to metformin.
The absorption duration of 2000 mg of Metformin ER administrated once daily is similar to conventional Metformin admistration 1000 mg administrated 2 time a day.
The hyper or hypocaloric alimentation has the same effect in the pharmacokinetics of Metformin ER.
Renal clearance is approximately 3.5 times greater than creatinine clearance, which indicates that tubular secretion is the major route of metformin elimination.
Following oral administration, approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination half-life of approximately 17.6 hours, suggesting that the erythrocyte mass may be a compartment of distribution.

Posology and Administration:
There is no fixed dosage regimen for the management of hyperglycemia in patients with type 2 diabetes with metformin or metformin ER or any other pharmacologic agent.
Dosage must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose.
The maximum recommended daily dose of metformin ER in adults is 2000 mg.
Mectin®, must be swallowed whole and not chewed or cut.
Although posology should be accoridng to medical criteria and clinical chart of the patient, the following is recommended:
- *Adults:* in general, significative clinical answers are not observed with doses inferior to 1500 mg/day. However, should be started at a low dose, with gradual dose escalation, both to reduce gastrointestinal side effects and to permit identification of the minimum dose required for adequate glycemic control of the patient.
  Glycosylated hemoglobin should be determined in intervals of approximately 3 months.
  The therapeutic goal should be to decrease both fasting plasma glucose and glycosylated hemoglobin levels to normal or near normal by using the lowest effective dose of *Mectin®*, either when used as monotherapy or in combination with sulfonylurea or insulin.
  The usual starting dose of *Mectin®* is 500 mg daily, with dinner.
  Dosage increases should be made in increments of 500 mg weekly, up to a maximum of 2000 mg once daily with the evening meal.
  If normoglycemia is not obtained with 2000 mg of metformin ER, it can be considered administration of *Mectin®* 1000 mg twice a day.

The patients that received metformin can continue it's treatment with metformin ER once a day in the same total daily dose, up to a maximum of 2000 mg of metformin ER once a day.
Was not established safety and effectiveness of metmorfin ER in pedriatric patients.

Contraindications:
Is contraindicated in the following cases:
- Renal and hepatic insufficiency.
- Heart failure requiring pharmacologic treatment (digoxin, furosemide).
- Hipersensitivity to the drug.
- Acute phatologies that have a risk of renal function alteration: dehydratation, high temperature, severe hypotoxic or/and infectious stages (septic shock, severe cardiac failure, neumopathyas, urinary infection, acute alcoholic intoxication).
- Acute or chronic illness able to cause tisular hypotoxia, as: respiratory or cardiac failure, recent myocardium infarct, shock.
- Alcoholism.
- Diabetic ketoacidosis and coma.
- Pregnancy and nursing
- Use of contrasting IV products (angiographies, as an example): in case of need discontinue metformin 48 hours before study and administrate again 48 hours after, to avoid possible lactic acidosis.
- 80 years old or older patients, without medical studies of its previous renal function.

Warnings and precautions:
Some hyperglycemia producer drugs (as for example: corticoids, diuretics thiazides, oral contraceptives) can make modifications in diabetes evolution and therefore is necessary to adjust the metformin dose or associate to sulfamides.
If it is indicated to insulindependent patients, glycemia should be monitored before modifying insulin dose.
Mectin® should be retired, temporally or definetely, is a clinical symptomatology appears that predispose to tisular hypoxia, as severe infections (mainly urinary), severa haemorrhage, advance anemia, etc.
Serum creatinine should be measured before establishing a treatment with *Mectin®* and checked frequently (in general, 1 or 2 a year).
In case of radiologic exploration, with intravenous constrant administration (IVU, angiography, the treatment with *Mectin®* should be discontunued and withheld for 48 hours subsequent to the radiologic exam. In case of surgical procedure or other possible causes of diabetes descompensation, treatment with insulin should be considerated.
The treatment with metformin hydrochloride should be discontinnued 48 hours before programmed surgery with general anaesthesia, and normally it should not be withheld after 48 hours.
All patients should continue it's diet with a regular distribution of carbohydrates ingest during the day. Patients with overweight should continue it's hypocaloric diet. Usual laboratory test should be done to control diabetes.
Mectin®, alone does not usually cause hypoglycemia, although it may occur when *Mectin®* is used in conjunction with hypoglycemia sulfoamides and insulin, due to action potentiation. Patients should avoid alcohol intake, while treatment.
- *Lactic acidosis treatment:* if in spite of all the precautions a lactic acidosis chart appears, should be treated energetically for being a condition of quick evolution and severe prognostication.
  The patient should be entered with maximum urgency in a assistance center to receive suitable treatment, with base is acidosis correction through an intravenous infusion of sodium bicarbonate, in massive doses if it is necessary.
  The first symptoms of lactic acidosis are: nauseas, vomits, abdominal pain, loss of appetite or lethargy.
  The patient should ask to the doctor if one or some of this symptoms appears, and specially, if they do not have relation with medicine initiation, dose increase, or a nutritional cause or medicines ease to identify (antibiotics, analgesics, etc.), or an occasional disease not related with diabetes.

USE DURING PREGNANCY AND NURSING: BIGUANIDES SHOULD NOT BE USED IN PREGNANT WOMEN BECUASE THEY ARE TERATOGENIC IN ANIMALS. IT IS NOT KNOWN IF THE DRUG IS EXCRETED IN HUMAN MILK, SO AVOID ADMINISTRATION DURING NURSING.

- *Pediatric use:* is not recommended in children.

Interactions:
- *Danazol:* diabetogenic effect of Danazol. If association can not be avoided, warn the patient and strengthen blood and urinary glucose mantainance. Adapt eventually the antidiabetic posology accodring to Danazol treatment and before finishing adjust the dose.
- *Alcohol:* major risk of lactic acidosis after acute alcohol intoxication, particularly in cases of short age or malnutrition, hepatocelular deficiency. Avoid taking alcoholic drinks and medicines containing alcohol.

Associations that need use precautions:
- *Chlorpromazine in high doses (100 mg/ day):* glycemia increase (insulin release decrease). Warn the patient and strengthen urinary and blood glucose mantainance. Adapt eventually the antidiabetic posology according to treatment with neuroleptic and before finishing adjust the dose.
- *Glucocorticoids* (general and local routes: intraarticular, cutaneous and rectal wash): glycemia increase with occasional ketosis (glucose tolerance decrease for corticoids). Warn the patient and strengthen blood glucose mantainance specially at treatment beggining. Adapt eventually the antidiabetic posology according to treatment with corticoids and adjust the dose when finished.
- *Diuretics:* lactic acidosis due to metformin burst by an eventual insufficiency of the renal function due to diuretics and specially to asa diuretics. Do not use metformin after creatinine exceeds the miromoles/l in men and 110 micromoles / l in women.
- *Inhibitors of the angiotensin converter enzim* (- ACE): can reduce glucose levels in blood. If it is necessary, adjust antidiabetic posology during therapy with the other medicine and after it's suspension.
- *Iodine contrasting products:* lactic acidosis burst by renal function insufficiency due to radiological exploration of a diabetic patient, should be suspended the metformin 48 hours before exploration for re-establish it after two day of the radiological exam.
- *Sympathicomimetics beta-2:* salbutamol and terbutaline (injectable route): glycemia increase due to stimulation of beta-2. Stregthen urinary and blood glucose mantainance, Pass eventually to insulin.

Adverse reactions:
In general the medicine is well tolerated, and at therapeutical doses does not present secundary effects. Although can be presented, in less frequent way, gastrointestinal problems as nauseas, vomits, diarrhea that stops spontaneously in majority of the cases. To avoid then is suggested to administrate medicine in one or two takes, according to cases after food. Metallic flavor can appear.
As another rare effects are enumerated alergic reactions and lactic acidosis. The last one is a serious complication of biguanides wich frequency with metformin is reduced to the minimum expression, being it's risk can not be experience if contraindication of the product is respected.

Overdosage:
In case of overdosage go to the nearest hospital or communicate with toxicology centers.

KEEP THIS AND ALL DRUGS IN ITS ORIGINAL PACKAGE AND OUT OF CHILDREN.

Conservation and storage conditions:
Keep between 15 and 30 °C.

Presentations:
Packages containing 30 extended-release tablets.

Medicinal Speciality authorized
by Ministry of Health and Enviroment.
Mectin® 850 mg: certificate N° 194120.
Mectin® 1000 mg: certificate N° 194121.
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