Metformin

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Name in Cyrillic: Метформин, Метформин Лонг, Метформин Канон, Сиофор®, Глюкофаж®

Active substance: Metformin hydrochloride

Pharmachologic effect:
Metformin reduces hyperglycemia without leading to the development of hypoglycemia. Unlike sulfonylurea derivatives, Metformin does not stimulate insulin secretion and does not have a hypoglycemic effect in healthy individuals. Metformin increases the sensitivity of peripheral receptors to insulin and glucose utilization by cells. Metformin reduces the production of glucose by the liver by inhibiting gluconeogenesis and glycogenolysis and delays the absorption of glucose in the intestine. Metformin stimulates glycogen synthesis by acting on glycogen synthase, increases the transport capacity of all types of membrane glucose transporters. In addition, Metformin has a beneficial effect on lipid metabolism: it reduces the content of total cholesterol, low density lipoproteins and triglycerides.
While taking Metformin, the patient's body weight either remains stable or moderately decreases. Clinical studies have also shown the effectiveness of Metformin for the prevention of diabetes in patients with prediabetes with additional risk factors for the development of overt type 2 diabetes, in whom lifestyle changes did not allow achieving adequate glycemic control.

Pharmacokinetics:
After oral administration, Metformin is slowly absorbed from the gastrointestinal tract. Cmax in plasma is reached after about 2.5 hours. The absolute bioavailability is 50-60%. With the simultaneous intake of food, the absorption of Metformin is reduced and delayed.
Metformin is rapidly distributed into body tissues. It practically does not bind to plasma proteins, accumulates in the salivary glands, liver and kidneys.
Metformin is excreted by the kidneys unchanged. T1/2 from plasma is 2-6 hours.
In case of impaired renal function, accumulation of Metformin is possible.

Indications:
Diabetes mellitus type 2, especially in obese patients, with ineffective diet and exercise:
- In adults, as monotherapy or in combination with other oral hypoglycemic agents, or with insulin;
- In children from 10 years of age, as monotherapy or in combination with insulin.
Prevention of type 2 diabetes in patients with prediabetes with additional risk factors for type 2 diabetes, in whom lifestyle changes did not allow achieving adequate glycemic control.

Contraindications:
Acute or chronic metabolic acidosis, diabetic ketoacidosis, diabetic precoma, and coma;
renal failure, impaired renal function (Creatinine clearance <60 ml/min);
dehydration, severe infection, hypoglycemic shock, which can lead to impaired renal function;
clinically pronounced symptoms of acute and chronic diseases that can lead to the development of tissue hypoxia (including heart failure, acute myocardial infarction, respiratory failure);
the use of contrasting iodine-containing substances for intravascular administration (including during intravascular urography, intravenous cholangiography, angiography, CT);
acute alcohol intoxication, chronic alcoholism;
severe impairment of liver or kidney function
hypersensitivity to metformin.

Use with caution:
Care should be taken to use Metformin in elderly patients and those performing heavy physical work, which is

associated with an increased risk of lactic acidosis. In elderly patients, asymptomatic renal dysfunction is often observed. Particular care is required if renal impairment is triggered by taking antihypertensive drugs or diuretics, as well as NSAIDs.

Pregnancy and breast-feeding:
Decompensated diabetes mellitus during pregnancy is associated with an increased risk of birth defects and perinatal mortality. Limited evidence suggests that taking Metformin in pregnant women does not increase the risk of developing birth defects in children.
When planning a pregnancy, as well as in case of pregnancy while taking Metformin for prediabetes and type 2 diabetes mellitus, the drug should be canceled, and insulin therapy should be prescribed in case of type 2 diabetes. Plasma glucose should be kept close to normal to reduce the risk of fetal malformations.
Metformin passes into breast milk. Side effects were not observed in newborns with breastfeeding while taking Metformin. However, due to the limited amount of data, the use of the drug during breastfeeding is not recommended. The decision to stop breastfeeding should be made taking into account the benefits of breastfeeding and the potential risk of side effects in the baby.

Side effects:
Possible:
(usually at the beginning of treatment) nausea, vomiting, diarrhea, flatulence, abdominal discomfort.

in isolated cases:
impaired liver function indicators, hepatitis (disappear after stopping treatment).

Very rarely:
lactic acidosis (discontinuation of treatment is required);
impaired absorption of vitamin B12.

Interaction:
Contraindicated combinations:
Iodine-containing X-ray contrast agents: against the background of functional renal failure in patients with diabetes, radiological examination using iodine-containing X-ray contrast agents can cause the development of lactic acidosis. Treatment with Metformin should be canceled, depending on renal function, 48 hours before or at the time of X-ray examination using iodine-containing X-ray contrast agents and not resumed earlier than 48 hours after, provided that during the examination, renal function was recognized as normal.

Combinations not recommended:
Alcohol: with acute alcohol intoxication, the risk of developing lactic acidosis increases, especially in the case of:
- insufficient nutrition, adherence to a low-calorie diet;
- liver failure..
While taking Metformin, you should avoid taking alcohol and medicines containing ethanol.

Combinations requiring caution:
Danazol: It is not recommended to take danazol at the same time in order to avoid the hyperglycemic effect of the latter. If it is necessary to treat with danazol and after stopping the intake of the latter, a dose adjustment of Metformin is required under the control of the concentration of glucose in the blood.

Chlorpromazine: When taken in high doses (100 mg / day), it increases the concentration of glucose in the blood, decreasing the release of insulin. When treating with antipsychotics and after stopping the reception of the latter, a dose adjustment of the drug is required under the control of the concentration of glucose in the blood.

Glucocorticosteroids (GCS) of systemic and local action reduce glucose tolerance, increase the concentration of glucose in the blood, sometimes causing ketosis. In the treatment of corticosteroids and after discontinuation of the latter, a

dose adjustment of Metformin is required under the control of blood glucose concentration.

Diuretics: Concomitant use of loop diuretics can lead to the development of lactic acidosis due to possible functional renal failure. You should not prescribe Metformin if creatinine clearance is below 60 ml/min.

Prescribed in the form of injections β2 - adrenergic agonists: increase the concentration of glucose in the blood due to stimulation of β2 -adrenergic receptors. In this case, it is necessary to control the concentration of glucose in the blood. Insulin administration is recommended if necessary. With the simultaneous use of the above drugs, more frequent monitoring of blood glucose may be required, especially at the beginning of treatment. If necessary, the dose of Metformin can be adjusted during and after treatment.

Antihypertensive drugs, with the exception of angiotensin-converting enzyme inhibitors, can lower blood glucose levels. The dose of Metformin should be adjusted if necessary.

Simultaneous use of Metformin with sulfonylurea derivatives, insulin, acarbose and salicylates, may cause hypoglycemia.

Nifedipine increases the absorption and Cmax of Metformin.

Cationic drugs (amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim and vancomycin) secreted in the renal tubules compete with Metformin for tubular transport systems and can lead to an increase in its Cmax.

Dosing and Administration:
In Adults:
Monotherapy and combination therapy in combination with other oral hypoglycemic agents for type 2 diabetes:
- The usual starting dose is 500 mg or 850 mg 2-3 times daily after or during a meal.
- It is recommended to adjust the dose every 10-15 days based on the results of measuring the concentration of glucose in blood plasma. A slow increase in dose helps to reduce side effects from the gastrointestinal tract.
- The maintenance dose of the drug is usually 1500–2000 mg / day. To reduce side effects from the gastrointestinal tract, the daily dose should be divided into 2-3 doses. The maximum dose is 3000 mg / day, divided into three doses.

If you are planning to switch from taking another hypoglycemic agent: you must stop taking the other agent and start taking Metformin at the dose indicated above.

Combination with insulin:
To achieve better blood glucose control, Metformin and insulin can be used in combination therapy in patients with type 2 diabetes.
The usual starting dose of Metformin is 500 mg or 850 mg 2-3 times a day, while the dose of insulin is adjusted based on the blood glucose concentration.

Children and adolescents: in children from 10 years of age, Metformin can be used both in monotherapy and in combination with insulin. The usual starting dose is 500 mg or 850 mg once daily after or during a meal. After 10-15 days, the dose must be adjusted based on the blood glucose concentration. The maximum daily dose is 2000 mg, divided into 2-3 doses.

Monotherapy for prediabetes:
The usual dose is 1000-1700 mg daily after or during a meal, divided into 2 doses.
It is recommended to regularly carry out glycemic control to assess the need for further use of the drug.

Patients with renal impairment:
Metformin can be used in patients with moderate renal failure (creatinine clearance 45–59 ml/min) only in the absence

of conditions that may increase the risk of lactic acidosis.
- Patients with creatinine clearance of 45-59 ml / min: the initial dose is 500 mg or 850 mg once a day. The maximum dose is 1000 mg per day, divided into 2 doses.
- Kidney function should be monitored closely (every 3–6 months).
If creatinine clearance is below 15 ml / min, the drug should be discontinued immediately.

Elderly patients:
Due to a possible decrease in renal function, the dose of Metformin must be selected under regular monitoring of renal function indicators (determine the concentration of creatinine in the blood serum at least 2-4 times a year).

Duration of treatment:
Metformin should be taken daily, without interruption. In case of termination of treatment, the patient must inform the doctor about it.

Overdose:
When Metformin was used at a dose of 85 g (42.5 times the maximum daily dose), hypoglycemia was not observed. However, in this case, the development of lactic acidosis was observed. Significant overdose or associated risk factors can lead to the development of lactic acidosis.

Treatment: if signs of lactic acidosis appear, treatment with the drug should be stopped immediately, the patient should be urgently hospitalized and, having determined the concentration of lactate, the diagnosis should be clarified. The most effective measure for removing lactate and Metformin from the body is hemodialysis. Symptomatic treatment is also indicated.

Special instructions:
The use of Metformin is not recommended for acute infections, exacerbation of chronic infectious and inflammatory diseases, trauma, acute surgical diseases, the risk of dehydration.
Do not use before surgery and within 2 days after surgery.
If, during treatment, the patient has muscle cramps, indigestion (abdominal pain) and severe asthenia, then it should be borne in mind that these symptoms may indicate the onset of lactic acidosis.
During the period of treatment, it is necessary to monitor kidney function; determination of the lactate content in plasma should be carried out at least 2 times a year, as well as when myalgia appears.
When Metformin is used as monotherapy in accordance with the dosage regimen, hypoglycemia usually does not occur. However, when combined with insulin or sulfonylurea derivatives, there is a risk of hypoglycemia. In such cases, it is necessary to especially carefully monitor the concentration of glucose in the blood.
During the period of treatment, patients should avoid drinking alcohol because of the risk of developing lactic acidosis.

Manufacturer:
Metformin : Ozon pharma (Russia), Canon pharma (Russia), Vertex pharma (Russia), Gedeon Richter
Siofor®: Berlin-Chemie
Glucophage® : Merck

Reliable supplier with fast Worldwide shipping:
RussianMeds Online Store
https://russianmeds.com

Storage:
The temperature is not above 25 °C (77 °F)
Keep out of the reach of children.