Active substance: Telmisartan+Hydrochlorothiazide

Pharmachologic effect: Antihypertensive

Pharmacodynamics:
Micardis®Plus is a combination of Telmisartan (angiotensin II receptor antagonist) and Hydrochlorothiazide (thiazide diuretic). The simultaneous use of these components leads to a greater antihypertensive effect than the use of each of them separately. Taking MicardisPlus® 1 time per day leads to a significant gradual decrease in blood pressure.

Pharmacokinetics:
The simultaneous use of hydrochlorothiazide and telmisartan does not affect the pharmacokinetics of each of the components of the drug.

Telmisartan :

When taken orally, telmisartan is rapidly absorbed from the gastrointestinal tract. Bioavailability - 50%.
When taken simultaneously with food, the decrease in AUC values ranges from 6% (when used at a dose of 40 mg) to 19% (when used at a dose of 160 mg). After 3 hours after ingestion, the concentration in the blood plasma levels off, regardless of the time of the meal.
Plasma protein binding - more than 99.5%, mainly with albumin and α_1-glycoprotein. The average value of the apparent V_d in the equilibrium state is 500 liters.
Telmisartan is metabolized by conjugation with glucuronic acid. Metabolites are pharmacologically inactive.
$T_{1/2}$ - more than 20 hours. Excreted through the intestines unchanged, excretion by the kidneys - less than 2% of the dose taken. The total plasma clearance is high (900 ml/min) compared to hepatic blood flow (about 1500 ml/min).
There is a difference in concentration between men and women. In women, C_{max} and AUC were approximately 3 and 2 times higher, respectively, than in men (without a significant effect on efficacy).
The pharmacokinetics of telmisartan in elderly patients does not differ from the pharmacokinetics in young patients. Dose adjustment is not required.
Dose modification is not required in patients with renal insufficiency, including patients on hemodialysis. Telmisartan is not removed by hemodialysis.
In patients with mild to moderate hepatic impairment (Child-Pugh class A and B), the daily dose of the drug should not exceed 40 mg.

Hydrochlorothiazide :

After oral administration MikardisPlyus® C_{max} of hydrochlorothiazide is achieved within 1-3 hours. Absolute bioavailability is estimated by cumulative renal excretion of hydrochlorothiazide and is about 60%.
Hydrochlorothiazide is not metabolized in the human body and is excreted in the urine almost unchanged. About 60% of the dose taken orally is eliminated within 48 hours. Renal clearance is about 250-300 ml / min. $T_{1/2}$ - 10-15 hours.
There is a difference in plasma concentrations between men and women. Women tend to have a clinically significant increase in plasma concentrations of hydrochlorothiazide.
In patients with impaired renal function, the rate of excretion of hydrochlorothiazide is reduced.

Indications:
arterial hypertension (in case of ineffectiveness of telmisartan or hydrochlorothiazide in the form of monotherapy).

Contraindications:
- obstructive diseases of the biliary tract;
- severe liver dysfunction (Child-Pugh class C);
- refractory hypokalemia, hypercalcemia;
- simultaneous use with aliskiren in patients with diabetes mellitus or renal insufficiency (GFR <60 ml / min / 1.73 m2);
- fructose intolerance, glucose/galactose malabsorption syndrome or sucrase/isomaltase deficiency;

- age up to 18 years (efficacy and safety have not been established);
- pregnancy and the period of breastfeeding;
- hypersensitivity to the active substance or auxiliary components of the drug.

Use with caution:
bilateral stenosis of the renal arteries or stenosis of the artery of a single kidney;
abnormal liver and / or kidney function;
decrease in BCC due to previous diuretic therapy, restriction of salt intake, diarrhea or vomiting;
hyponatremia;
hyperkalemia;
conditions after kidney transplantation (no experience of use);
chronic heart failure;
stenosis of the aortic and mitral valve;
idiopathic hypertrophic subaortic stenosis;
primary aldosteronism (efficacy and safety not established).

Pregnancy and breast-feeding:
The use of Micardis®Plus is contraindicated during pregnancy and during the period of breastfeeding.
Patients planning pregnancy should be given alternative therapy. If treatment with Telmisartan was carried out in the second trimester of pregnancy, ultrasound of the kidneys and skull bones in the fetus is recommended. Newborns whose mothers took Micardis®Plus should be carefully monitored for hypotension.

Side effects:
headache, dizziness, fatigue, insomnia, anxiety, depression, convulsions.
abdominal pain, dyspepsia, nausea, diarrhea, increased activity of hepatic transaminases.
cough, pharyngitis, upper respiratory infections.
decrease in hemoglobin level.
rash; in a single case - angioedema.
peripheral edema, urinary tract infections, increased uric acid levels, hypercreatininemia.
pronounced decrease in blood pressure, palpitations, chest pain.
back pain, myalgia, arthralgia.
hyperkalemia, anemia, hyperuricemia.
flu-like syndrome

Interaction:

Telmisartan :

Simultaneous use with antihypertensive drugs may increase the antihypertensive effect.
Simultaneous use with potassium-sparing diuretics, heparin, dietary supplements, salt substitutes containing potassium, may cause development of hyperkalemia.
Simultaneous use with lithium preparations, may cause an increase in the concentration of lithium in the blood plasma.
Simultaneous use with digoxin may cause an increase in the concentration of digoxin in the blood plasma.

Hydrochlorothiazide :

When used simultaneously with:

- ethanol, barbiturates or opioid analgesics, there is a risk of developing orthostatic hypotension;
- oral hypoglycemic agents and insulin may require dose adjustment of oral hypoglycemic agents and insulin;
- metformin, there is a risk of developing lactic acidosis;
- cholestyramine and colestipol - in the presence of anionic exchange resins, the absorption of hydrochlorothiazide is impaired;
- cardiac glycosides increase the risk of developing hypokalemia or hypomagnesemia caused by thiazide diuretics, the development of arrhythmias caused by cardiac glycosides;

- pressor amines (for example, norepinephrine) may weaken the effect of pressor amines;
- non-depolarizing muscle relaxants (for example, tubocurarine chloride) hydrochlorothiazide may enhance the effect of non-depolarizing muscle relaxants;
- Anti-gout drugs may increase the concentration of uric acid in the blood serum and therefore may require changes in the dose of uricosuric agents. The use of thiazide diuretics increases the incidence of hypersensitivity reactions to allopurinol;
- calcium preparations - thiazide diuretics can increase the content of calcium in the blood serum due to a decrease in its excretion by the kidneys. If you need to use calcium supplements, you should regularly monitor the calcium content in the blood and, if necessary, change the dose of calcium supplements;
- beta-blockers and diazoxide - thiazide diuretics can increase hyperglycemia caused by beta-blockers and diazoxide;
- m-anticholinergics (for example, atropine, biperidine) - a decrease in gastrointestinal motility, an increase in the bioavailability of thiazide diuretics;
- amantadine - thiazide diuretics may increase the risk of adverse effects caused by amantadine;
- cytotoxic agents (for example, cyclophosphamide, methotrexate) - a decrease in renal excretion of cytotoxic agents and an increase in their myelosuppressive effect;
- NSAIDs - combined use with thiazide diuretics can lead to a decrease in the diuretic and antihypertensive effect;
- medicines that lead to the excretion of potassium and hypokalemia (for example, diuretics that remove potassium, laxatives; gluco- and mineralocorticosteroids; corticotropin; amphotericin B; carbenoxolone; benzylpenicillin, acetylsalicylic acid derivatives) - increased hypokalemic effect. Hypokalemia caused by hydrochlorothiazide is offset by the potassium-sparing effect of telmisartan;
- potassium-sparing diuretics, potassium preparations, other meds that can increase the content of potassium in the blood serum (for example, heparin) or replacing sodium in table salt with potassium salts may develop hyperkalemia. It is recommended to periodically monitor the content of potassium in the blood plasma in cases where the drug MicardisPlus® is used simultaneously with drugs that can cause hypokalemia, as well as with drugs that can increase the content of potassium in the blood serum.

Dosing and Administration:
MicardisPlus® should be taken orally 1 time per day, regardless of food intake.
MicardisPlus® 40/12.5 mg may be prescribed to patients in whom the use of Micardis® 40 mg or hydrochlorothiazide does not lead to adequate control of blood pressure.
MicardisPlus® 80/12.5 mg may be administered to patients in whom the use of Micardis® 80 mg or MicardisPlus® 40/12.5 mg does not lead to adequate blood pressure control.
In patients with severe arterial hypertension, the maximum daily dose of telmisartan is 160 mg/day. This dose was effective and well tolerated.

Overdose:
Symptoms: pronounced decrease in blood pressure, tachycardia, bradycardia, disturbances in the water and electrolyte balance of the blood (hypokalemia, hypochloremia), a decrease in BCC, which can lead to muscle spasms and / or increase disorders of the cardiovascular system (arrhythmias caused by the simultaneous use of cardiac glycosides or some antiarrhythmic drugs).
Treatment: symptomatic therapy. Hemodialysis is ineffective.

Manufacturer:
Boehringer Ingelheim (Germany)

Storage:
The temperature is not above 25 °C (77 °F)