**PRESTAZYNE**

**Instructions**
**on medical use of the drug**

**Tradename:** Prestazyne.
**International nonproprietary name:** Hydroxyzine.
**Dosage form:** Film- coated tablets , for oral administration.
**Compound:** Each *film- coated tablet contains:*
Hydroxyzine hydrochloride USP 25 mg;
Excipients qs.
Dye: Titanium Dioxide USP.
**Pharmacotherapeutic group:** Tranquilizer (anxiolytic).
**ATX code:** N05BB01.
**Pharmacological action:**
*Pharmacodynamics:*
Derivative diphenylmethane, has moderate anxiolytic activity; also has a sedative, antiemetic, antihistamine and m- anticholinergic action. Blocks central m- cholinergic receptors and histamine H receptors and inhibits the activity of certain subcortical zones. Does not cause mental dependence or addiction. The clinical effect occurs 15-30 minutes after taking the drug orally.
Has a positive effect on cognitive abilities, improves memory and attention. Relaxes skeletal and smooth muscles, has bronchodilator and analgesic effects, and a moderate inhibitory effect on gastric secretion. Hydroxyzine significantly reduces itching in patients with urticaria, eczema and dermatitis. With long-term use, no withdrawal symptoms or deterioration of cognitive functions were observed. Polysomnography in patients with insomnia and anxiety clearly demonstrates an increase in sleep duration and a decrease in the frequency of night awakenings after a single or repeated dose of hydroxyzine at a dose of 50 mg. A decrease in muscle tension in patients with anxiety was noted when taking the drug at a dose of 50 mg 3 times a day.
*Pharmacokinetics:*
Absorption - hydroxyzine is highly absorbed from the gastrointestinal tract. Cmax is observed 2 hours after taking the drug.
After a single dose of the drug in a single dose of 25 mg or 50 mg in adults, the plasma concentration is 30 ng /ml and 70 ng /ml, respectively.
Bioavailability when taken orally is 80%.
Distribution - Hydroxyzine is more concentrated in tissues (particularly skin) than in plasma. The distribution coefficient is 7-16 l/kg.
Hydroxyzine penetrates the BBB and placental barrier, concentrating to a greater extent in the fetal tissues than in the mother's body.
Metabolites are found in breast milk.
Metabolism and excretion - hydroxyzine metabolized in the liver. The main metabolite (45%) is cetirizine , which is a histamine H-receptor blocker.
*Pharmacokinetics in special clinical situations:*
In children, the general clearance is 4 times less than in adults, T1/2 in children aged 14 years is 11 hours, in children aged 1 year - 4 hours.
In elderly patients, T1/2 is 29 hours, the distribution coefficient is 22.5 l/kg.
In patients with impaired liver function, T1/2 increases to 37 hours, the concentration of metabolites in the blood serum is higher than in young patients with normal liver function . The antihistamine effect can last for 96 hours.
**Indications for use:**
- for the relief of anxiety, psychomotor agitation, feelings of internal tension, increased irritability in neurological, mental (including generalized anxiety, adaptation disorders) and somatic diseases, chronic alcoholism; withdrawal syndrome in chronic alcoholism, accompanied by psychomotor agitation;
- as a sedative during premedication ;
- for skin itching (as symptomatic therapy);
- for depression;
- for insomnia;
- with neurosis;
- during menopause;
- for epilepsy.

**Contraindications:**
- porphyria;
- pregnancy;
- period of labor;
- lactation period (breastfeeding);
- hypersensitivity to the components of the drug;
- children under 3 years old;
- hypersensitivity to cetirizine and other piperazine derivatives, aminophylline or ethylenediamine.

*with caution* for myasthenia gravis, prostatic hyperplasia with clinical manifestations, difficulty urinating, constipation, increased intraocular pressure, dementia, and a tendency to seizures; with a predisposition to the development of arrhythmia; with simultaneous use of drugs that are arrhythmogenic action; simultaneously with other CNS depressants or anticholinergics (dose reduction required). A reduction in the dose of the drug is required in patients with severe and moderate renal failure , with liver failure, and in elderly patients with decreased glomerular filtration.
**Directions for use and dosage:**
The drug is taken orally. It is recommended to begin treatment with low doses of the drug and gradually increase to the optimal dose, adjusting it in accordance with the patient's response to therapy.

*Adults:*
*For the symptomatic treatment of anxiety:* 50 to 100 mg per day (2 to 4 tablets) in the evening before bedtime, if anxiety is manifested primarily by insomnia;
*For the symptomatic treatment of itching of allergic origin:* from 25 to 100 mg (1 to 4 tablets) per day;
*For premedication in surgical practice:* once from 25 to 100 mg (1 to 4 tablets) at night, before surgery;
The maximum daily dose of the drug for adults and children weighing more than 40 kg is 100 mg.
*Children:*
*For the symptomatic treatment of itching of allergic origin:*
- Over the age of 12 years (with a body weight of more than 40 kg): from 25 to 100 mg (1 to 4 tablets) per day;
- At the age of 9 to 12 years (with body weight from 28 to 40 kg): from 25 to 75 mg (from 1 to 3 tablets) per day;
- At the age of 7 to 9 years (with body weight from 23 to 28 kg): from 25 to 50 mg (1 to 2 tablets) per day;
- At the age of 4 to 7 years (with body weight from 17 to 23 kg): from 25 to 37.5 mg (from 1 to 1.5 tablets) per day;
- At the age of 3 to 4 years (with body weight from 12.5 to 17 kg): from 12.5 to 25 mg (from ½ to 1 tablet) per day.

For children, the dose is determined taking into account body weight at the rate of 1 mg/kg/ day to a maximum of 2 mg/kg/ day, in divided doses.

**Side effects:**
From the central nervous system and peripheral nervous system: drowsiness, fatigue, tremor, convulsions, headache, dizziness, ataxia, weakness.
From the organ of vision: acute glaucoma, disturbance of accommodation. From the urinary system: acute urinary retention.
From the cardiovascular system: tachycardia, decreased blood pressure.
From the digestive system: dry mouth, constipation, increased transaminase activity.
Other: bronchospasm, allergic reactions, increased sweating.

**Overdose:**
*Symptoms:* increased anticholinergic effects, depression or paradoxical stimulation of the central nervous system, nausea, vomiting, involuntary motor activity, hallucinations, impaired consciousness, arrhythmia, arterial hypotension; rarely - tremors, convulsions, disorientation, which occur with significant overdose.
*Treatment:* if spontaneous vomiting is absent, it is necessary to induce it artificially or perform gastric lavage. General measures are taken aimed at maintaining the vital functions of the body, and monitoring of the patient until the symptoms of intoxication disappear in the next 24 hours.
If it is necessary to obtain a vasopressor effect, norepinephrine or metaramenol is prescribed . Epinephrine should not be used . There is no specific antidote. The use of hemodialysis is ineffective.

**Interaction with other drugs:**
Prestazyne potentiates the effect of drugs that depress the central nervous system, such as opioid analgesics, barbiturates, tranquilizers, hypnotics, ethanol (combinations require individual selection of drug doses).
Prestazyne, when used simultaneously, prevents pressor action epinephrine (adrenaline) and anticonvulsant activity of phenytoin, and also interferes with the action betahistine and cholinesterase blockers.
The use of the drug Prestazyne does not affect the activity of atropine, belladonna alkaloids, cardiac glycosides, antihypertensive drugs, histamine H -p receptor blockers.
Co-administration of Prestazyne with MAO inhibitors and anticholinergics should be avoided .
Hydroxyzine is an inhibitor of the CYP2D6 isoenzyme and, when used in high doses , may cause interactions with CYP2D6 substrates.
Because hydroxyzine metabolized in the liver, an increase in its concentration in the blood can be expected when administered together with liver enzyme inhibitors.

**Special instructions:**
allergy tests are necessary, hydroxyzine should be stopped 5 days before the test.

**Impact on the ability to drive vehicles and operate machinery:**
During therapy, it is necessary to refrain from engaging in potentially hazardous activities that require increased attention and rapid psychomotor reactions.

**Release form:**
film-coated tablets in each PVC blister. 2 blisters along with instructions for use in cardboard packaging.

**Storage conditions:**
Store in a dry place, protected from light, at a temperature not exceeding 25 °C and out of the reach of children.

**Best before date:**
Indicated on the packaging.
Do not use after expiration date.

**Conditions of release:**
By doctor's prescription.

**Made for:**
**MAXX PHARM LTD.**
**London, Great Britain**