# Medical application instruction
**for**
**POLYOXIDONIUM®**

**Registration №**: P N002935/02
**Trade name**: Polyoxidonium®
**International Nonproprietary Name:** Azoximer bromide
**Chemical name**: copolymer of N-oxide 1,4-ethylene piperazine and (N- carboxymethyl)-1,4-ethylene piperazinium bromide
**Drug form**: lyophilizate for solution for injections and topical application
**Composition per ampoule or flask**:
Active substance: azoximer bromide – 3 mg or 6 mg
Excipients:
mannitol – 0.9 mg, povidone K17– 0.6 mg (for 3 mg dosage);
mannitol – 1.8 mg, povidone K17–1.2 mg (for 6 mg dosage).
**Description**: porous white with a yellowish tint mass
**Pharmaco-therapeutic group:** immune modulator
**ATC Code:** [L03]

## PHARMACOLOGICAL PROPERTIES

Polyoxidonium® tablets possesses an immune modulating action, increases the organism resistance to local and general infections. Polyoxidonium' main mechanism of action is the direct effect on the phagocytic cells and natural killers together with antibody production stimulation.

Polyoxidonium® recovers the immunity in different secondary deficiencies caused by different infections, traumas, burns, malignant neoplasm, post-surgical complications, chemotherapy, cytostatics, and steroid hormones.

Together with the immune modulating properties Polyoxidonium® possesses an expressed detoxicating and antioxidant properties; is able to eliminate toxins, heavy metals ions from the organism, and inhibits the lipid peroxidation. All propertied mentioned are determined by Polyoxidonium structure and high molecular nature. Polyoxidonium® inclusion into the chemotherapy of oncologic patients results in therapy-induced intoxication alleviation, and allows to perform complete standard chemo- or radiotherapy cycle without infection complications and side effects (myelosuppression, vomiting, diarrhea, cystitis, colitis etc.) that are often the reason for therapy preterm termination.

Polyoxidonium application for secondary immune deficiencies allows to increase therapy efficacy and to shorten its duration, significantly to reduce the antibiotics, broncholitics, clucocorticoids application, and to lengthen the remission period.

The preparation is well tolerated, has no mitogenic, polyclonal activity, free from antigen properties, and has no allergenic, mutagenic, embryo toxic, teratogenic and carcinogenic potential.

## PHARMACOKINETICS

After intramuscular injection Polyoxidonium has high bioavailability (about 86%). Polyoxidonium maximal blood plasma concentration is achieved 40 minutes after the application. Polyoxidonium is rapidly distributed into all organs and tissues; half-distribution period is 0.44 hours for quick phase, and 36.2 hours for slow (half-elimination) phase. In the organism drug is hydrolyzed to oligomers that are eliminated primarily by kidneys.

## INDICATIONS

Immunity correction and adults and children from 6 months.
**In adults in complex therapy of:**

- chronic recurrent infection-inflammatory diseases resistant to standard therapy both in exacerbation and remission period;

- acute and chronic viral and bacterial infections (including urogenital inflammatory diseases);
- Tuberculosis;
- acute and chronic allergic disturbances (including pollinosis, bronchial asthma, atopic dermatitis) complicated with chronic recurrent bacterial and viral infection;
- in oncology: during and after chemo- and radio- therapy for drugs' immunosupprerssive, nephro- and hepatotoxic action alleviation;
- for regeneration processes activation (fractures, burns, trophic ulcers);
- rheumatoid arthritis after prolonged therapy with immunosuppressors; for ARI-complicated rheumatoid arthritis therapy;
- post-surgical infection-induced complications prophylaxis;
- for ARI and influenza prophylaxis.

**In children in complex therapy of:**

- acute and chronic viral, bacterial, and fungal infections (including diseases of ENT such as sinusitis, rhinitis, adenoiditis, pharyngeal tonsil hypertrophy, ARIs);
- acute allergic and toxico-allergic states;
- bronchial asthma complicated with respiratory tract chronic infections;
- atopic dermatitis complicated with purulent infection;
- intestine dysbacteriosis (together aith specific therapy);
- for often falling ill rehabilitation;
- influenza and ARIs prophylaxis.

**CONTRAINDICATIONS**

Individual hypersensitivity to the drug and any excipient. Pregnancy, lactation (no clinical application experience available).

**PRECAUTIONS**

Acute kidney insufficiency, children under 6 months old (no clinical application experience available).

**POSOLOGY AND ADMINISTRATION WAY**

Routs of administration for Polyoxidonium®: parenteral, intranasal. Doctor chooses administration routes depending on disease severity and patient's age.

**Intramuscularly or intravenously (dropwise):** adults: 6 – 12 mg once daily or 1 – 2 times per week depending on the diagnosis and disease severity.

For intramuscular administration dissolve bottle content in 1.5 – 2 ml of 0.9 % sodium chloride solution or water for injection. For intravenous (dropwise) administration dissolve the product in 2 ml of 0.9 % of sodium chloride solution, Haemodez-n, rheopolyglucin or in 5 % dextrose solution, then transfer aseptically to flasks containing 200 – 400 ml of the specified solutions.

Prepared parenteral solution is non-storable.

**Intranasally:** dissolve 6 mg dose in 1 ml (20 drops) of distilled water, 0.9 % sodium chloride solution or boiled water with room temperature.

**Recommended therapy schedules for adults**

**Parenteral administration:**

For acute inflammatory diseases: 6 mg daily injections for three days, followed by every other day injections (No 10-15).

For chronic inflammatory diseases: 6 mg five injections every other day, followed by twice a week injections by the course of not less than 10 injections.

For tuberculosis therapy: 6-12 mg twice a week by the course of 10-20 injections.

In patients with acute and chronic urogenital diseases: 6 mg every other day by the course of 10 injections in combination with chemotherapy.
For chronic recurrent herpes: 6 mg every other day by the course of 10 injections in combination with antivirals, interferon-containing drugs and/or interferon synthesis inducers.
For complicated allergic diseases: 6 mg by the course of 5 injections; two first injections for two consecutive days followed by every other day injections. For acute allergic and toxic-allergic conditions slow intravenous drug 6-12 mg administration is recommended in combination with anti-allergic drugs.
For rheumatoid arthritis**:** 6 mg every other day by the course of five injections, followed by twice a week injections with not less that 10 administrations.
In oncologic patients:
- prior and together with chemotherapy for immunodeppressive, hepatic- and nephrotoxic action alleviation: 6-12 mg every other day by the course of not less than 10 injections. Further application frequency is determined by physician depending on chemo-drugs tolerability and chemo- and radiotherapy duration;
- for tumor immunodepressive action alleviation, for chemo- or radiotherapy-induced immune deficiency correction, after surgical tumor rejection Polyoxidonium® 6-12 mg 1-2 times a week prolonged therapy is recommended (from 2-3 months up to one years course).
In patients with acute liver insufficiency Polyoxidonium® not more than 2 times a week injections are recommended.

**Intranasal administration:**

For acute and chronic ENT-infections: 6 mg a day administration is recommended to enhance mucous regeneration, for complications and recurrency episodes prophylaxis; for influenza and ARIs prophylaxis.
3 drops into each nasal meatus three times a day once in 2-3 days for 5-10 days.

**Recommended therapy schedules for adults**

Polyoxidonium® administration ways: parenteral, intranasal.
Administration way is determined by physician depending on illness severity and patients' age.

**Parenteral administration:**

For children from 6 months old in the dose of 3 mg (intramuscularly or intravenously dropwise 0.1-0.5 mg/kg) daily administration, every other day administration or twice a week, by the course of 5-10 administrations. (doses are shown in the table hereafter).
For intramuscular injections: dissolve the drug in 1 mL of water for injections or 0.9% sodium chloride solution.
For intravenous dropwise administration: dissolve the drug in 1.5-2 mL of sterile 0.9% sodium chloride solution, Reopolyglukin, Hemodez H or 5% dextrose solution. than transfer aseptically into the flask containing 150-200 mL of one of the solutions mentioned.
**For intranasal or sublingual administration:** daily 0.15 mg/kg dose for 5-10 days. Introduce 1-3 drops into each nasal meatus or sublingually every 2-3 hours.
To prepare the solution for intranasal or sublingual administration 3 mg of drug dissolve in 1 mL (20 drops), for dose of 6 mg – in 2 mL of distillated water, 0.9% sodium chloride solution or boiled water having room temperature. Each prepared solution drop (50 μL) contains 0.15 mg of Polyoxidonium® that will be indicated for each body weight kilogram.
Prepared solution for sublingual and intranasal application store in refrigerator for not more than 7 days. Prior the application pipette containing the solution must be heated to room temperature (20-25°C).

**Recommended schedules for children**

- for acute inflammatory diseases: 0,1 mg/kg every other day by the course of 5-7 injections.
- For chronic inflammatory diseases: 0.15 mg/kg twice a week by the course of 10 injections.
- For acute allergic and toxic-allergic conditions: intravenously dropwise in the dose of 0.15 mg/kg together with anti-allergic drugs.

- For complicated allergic diseases: together with basic therapy: intramuscularly 0.1 mg/kg by the course of 5 injections with 1-2 days intervals.

**Intranasal administration:** 1-3 drops in each nasal meatus every 2-3 hours (2-4 timed a day). Daily dose calculation for intranasal and sublingual administration in children is presented hereafter:

| Child' body weight | Daily drops number | Injected solution volume (mL) |
|---|---|---|
| 5 kg | 5 drops | 0.25 mL |
| 10 kg | 10 drops | 0.5 mL |
| 15 kg | 15 drops | 0.75 mL |
| 20 kg | 20 drops | 1.00 mL |

**Sublingual administration:** for all indications: daily dose 0.15 mg/kg for 10 days; for intestinal dysbacteriosis – for 10-20 days. Introduce 1-3 drops sublingually every 2-3 hours.

**SIDE EFFECTS**
Soreness at the injection site may occur when drug injected intramuscularly.

**OVERDOSE**
Not described.

**INTERACTION WITH OTHER DRUG PREPARATIONS**
Polyoxidonium® is compatible with many drugs, including antibiotics, antivirals, antifungal and antihistamine preparations, broncholytics, glucocorticoids, and cytostatics.

**SPECIAL WARNINGS**
In the case of soreness at the injection site dissolve drug in 1 mL of 0.25% procaine solution (if no sensitiveness for procaine was detected prior). For intravenous dropwise injection it is not recommended to dissolve drug in protein-containing infusional solutions.
Polyoxidonium® does not influence on the ability to drive and operate with machines.

**PHARMACEUTICAL FORM**
Lyophilizate for solution for injection and topical application, 3 mg and 6 mg.
4.5 mg of medicinal product (for 3 mg dose) or 9 of medicinal product (for 6 mg dose) per hydrolytic class 1 amber glass bottle, air-tightly sealed with rubber stoppers and crimped with aluminum caps.
5 bottles with the product per polyvinylchloride film blister. One blister together with Instruction on Use per carton pack or 5 bottles together with Instruction on Use per carton pack with carton insert element.
50 bottles (for hospitals) with medicinal product together with 50 Instructions on Use per box with carton dividers.

**SHELF LIFE**
Two years. Do not apply the preparation after the indicated shelf life completion. Shelf life is printed on the package.

**STORAGE CONDITIONS**
Keep in a dry place protected from light at temperature of 2 - 8 °C. Keep out of reach of children

**LEGAL CLASSIFICATION**
On prescription.

**Manufacturer/Address for reclamations:**
**Manufacturer:**
**LLC "NPO Petrovax Pharm"**
Russian Federation, 142143, Moscow region, Podolsk district, Pokrov village, Sosnovaya str., 1, tel/fax: (495) 329-17-18, (495) 926-21-07, Hotline: (495) 410-66-34, e-mail: info@petrovax.ru

Reclamations concerning quality, physical properties, and package mismatch sent to LLC "NPO Petrovax Pharm" address; drug batch number and manufacture date indication is obligatory.