## THE MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

## PATIENT INFORMATION LEAFLET

**FOR THE DRUG PRODUCT**

**POLYOXIDONIUM®**

**Registration number:** P N002935/02

**Trade name:** Polyoxidonium**®**

**International nonproprietary name:** Azoximer bromide(Аzoximeri bromidum)

**Chemical name:** copolymer of 1,4-ethylene piperazine N-oxide and (N-carboxymethyl)-

1,4-ethylene piperazinium bromide

**Pharmaceutical form:** lyophilizate for solution for injections and topical application

**Composition for 1 vial:**

Active substance: azoximer bromide, 3 mg or 6 mg;

Excipients:

Mannitol - 0.9 mg, povidone К 17 – 0.6 mg (for 3 mg dosage);

Mannitol - 1.8 mg, povidone К 17 – 1.2 mg (for 6 mg dosage);

Description: White porous mass with or without yellowish shade.

**Pharmacotherapeutic group: immunomodulatory agent.**

**ATC code:** [L0З]

**Pharmacological properties**

**Pharmacodynamics**

Azoximer bromide has a complex effect: immunomodulating, detoxifying, antioxidant and moderate anti-inflammatory.

The basis of the immunomodulating action of Azoximer bromide is a direct effect on phagocytic cells and natural killers, as well as stimulation of antibody formation and synthesis of interferon-alpha and interferon-gamma.

The detoxification and antioxidant properties of azoximer bromide are largely determined by the structure and high molecular nature of the drug. Azoximer bromide increases the body's resistance to local and generalized infections of bacterial, fungal and viral etiology. It also restores immunity in secondary immunodeficiency conditions, caused by various infections, injuries, complications after surgery, burns, autoimmune diseases, malignant neoplasms, the use of chemotherapeutic agents, cytostatics, steroid hormones.

A characteristic feature of Azoximer bromide in local (nasal, sublingual) use is the ability to activate factors of the body's early defense against infection: the drug stimulates the bactericidal properties of neutrophils, macrophages, enhances their ability to absorb bacteria, increases the bactericidal properties of saliva and the secretion of the mucous membranes of the upper respiratory tract.

Azoximer bromide blocks soluble toxic substances and microparticles, has the ability to remove toxins, salts of heavy metals from the body, inhibits lipid peroxidation, both through the capture of free radicals and through the elimination of catalytically active Fe 2+ ions. Azoximer bromide reduces the inflammatory response by normalizing the synthesis of pro- and anti-inflammatory cytokines.

Azoximer bromide is well tolerated, does not have mitogenic, polyclonal activity, antigenic properties, does not have allergenic, mutagenic, embryotoxic, teratogenic or carcinogenic effects. Azoximer bromide has no smell and taste, does not have a locally irritating effect when applied to the mucous membranes of the nose and oropharynx.

**Pharmacokinetics**

Azoximer bromide is characterized by rapid absorption and high speed of distribution in the body. Maximum concentration is achieved in blood during intramuscular administration 40 minutes after the injection. The half-life for different ages ranges from 36 to 65 hours. The bioavailability of the drug is high: more than 90% during parenteral administration.

Azoximer bromide is rapidly distributed throughout all organs and tissues of the body, penetrates the blood-brain and blood-aqueous barrier. No cumulative effect observed for this medicine. In the body, Azoximer bromide undergoes biodegradation to low molecular weight oligomers, excreted mainly by the kidneys, with feces – not more than 3%.

**Indications for use**

The drug is used in adults and children over 6 months old for the treatment and prevention of infectious and inflammatory diseases (of viral, bacterial or fungal etiology), in the stage of exacerbation and remission.

For adults treatment of the following conditions (as a component of complex therapy):

* chronic recurrent infectious and inflammatory diseases of various localization, bacterial, viral and fungal etiology in the acute stage;
* acute viral, bacterial infections of ENT organs, upper and lower respiratory tract, gynecological and urological diseases;
* acute and chronic allergic diseases (including pollen fever, bronchial asthma, atopic dermatitis), complicated bacterial, viral and fungal infections;
* malignant tumors during and after chemotherapy and radiation therapy to reduce the immunosuppressive, nephro- and hepatotoxic effects of drugs;
* generalized forms of surgical infections; to activate regenerative processes (fractures, burns, trophic ulcers);
* Rheumatoid arthritis complicated by bacterial, viral and fungal infections associated with the prolonged use of immunosuppressants;
* lungs tuberculosis.

For the treatment of children over 6 months old (in complex therapy):

* acute and exacerbation of chronic inflammatory diseases of any localization (including ENT organs - sinusitis, rhinitis, adenoiditis, hypertrophy of the pharyngeal tonsil, acute respiratory infection) caused by pathogens of bacterial, viral, fungal infections;
* acute allergic and toxic-allergic conditions complicated by bacterial, viral and fungal infections;
* bronchial asthma, complicated by chronic respiratory tract infections;
* atopic dermatitis, complicated by purulent infection;
* intestinal disbacteriosis (in combination with specific therapy);

For prophylaxis (monotherapy) in children over 6 months old and in adults:

* flu and acute respiratory infections;
* post-surgery infectious complications;

**Contraindications**

* Known hypersensitivity;
* Pregnancy, lactation;
* Children aged below 6 months;
* Acute renal failure.

**With caution**

- chronic renal failure (the drug is used no more than 2 times a week).

**Use during pregnancy and lactation**

The use of the drug Polyoxidonium® is contraindicated for pregnant women and women during breastfeeding (there is no clinical experience of its use in these conditions).

During the experimental Polyoxidonium® study in animals, there was no effect on fertility function of males and females, embryotoxic and teratogenic effects, effects on the development of the fetus found, both with the introduction of the drug during pregnancy period and during lactation.

**Dosage and Administration**

Route of administration of Polyoxidonium ®: parenteral, intranasal, sublingual.

The methods of administration, the dosage regimen, the necessity and frequency of the subsequent courses of therapy are chosen by the doctor depending on the severity of the disease and the age of the patient.

Preparation of solutions for parenteral administration (intramuscularly and intravenously):

For intramuscular administration, Polyoxidonium® 3 mg is dissolved in 1 ml (dose 6 mg in 2 ml) of water for injection or 0.9% sodium chloride solution. After adding the solvent, the drug is left for 2-3 minutes to swell, then mixed with rotary movements without shaking.

For intravenous drop administration, Polyoxidonium® is dissolved in 2 ml of sterile 0.9% sodium chloride solution. After adding the solvent, the drug is left for 2-3 minutes to swell, then mixed with rotary movements. The dose adjusted for the patient is sterilely transferred into the vial
/bag with 0.9% sodium chloride solution.

The prepared solution for parenteral administration is not subjected to storage.

Preparation of the solution for intranasal and sublingual administration:

**for children**, 3 mg dose is dissolved in 1.0 ml (20 drops), 6 mg dose in 2.0 ml (40 drops) (one drop (0,05 ml) of the prepared solution contains 0.15 mg of the drug);

**for adults**, 6 mg dose is dissolved in 1.0 ml (20 drops) of distilled water,
0.9% sodium chloride solution or boiled water at room temperature.

**Posology and Administration in adults**

The medicinal product is administered parenterally (intramuscularly or intravenously): at doses 6-12 mg once daily, or every other day, or 1-2 times a week depending on diagnosis and disease severity.

During acute viral, bacterial infections of ENT organs, upper and lower respiratory tract, gynecological and urological diseases: 6 mg daily for 3 days, then every other day by total course 10 injections.

During chronic recurrent infectious and inflammatory diseases of various localization, bacterial, viral and fungal etiology in the acute stage: 6 mg every other day 5 injections, then 2 times a week by the course 10 injections.

Acute and chronic allergic diseases (including pollen fever, bronchial asthma, atopic dermatitis), complicated bacterial, viral and fungal infections: 6-12 mg course of 5 injections.

Rheumatoid arthritis complicated by bacterial, viral and fungal infections associated with the prolonged use of immunosuppressants: 6 mg every other day 5 injections, then 2 times a week by the course 10 injections.

Generalized surgical infections: 6 mg daily for 3 days, then every other day by total course 10 injections.

For activation of regeneration processes (fractures, burns, trophic ulcers); 6 mg for 3 days, then every other day by total course of 10 injections.

Prevention of post-surgery infectious complications: 6 mg every other day, course of 5 injections.

Lungs tuberculosis: 6 mg 2 times a week by the course of 20 injections.

In oncological patients:

- ahead and against the background of chemotherapy to decrease immunosuppressive, hepato- and nephrotoxic action of chemotherapeutic agents 6 mg every other day by course of
10 injections; further the frequency of injection is defined by a doctor depending on tolerance and duration of chemo- and X-ray therapy treatment;

- for the prevention of immunosuppressive effect of tumor, for correction of immunodeficiency after chemo- and radiation therapy, after surgical tumor removal long-term using of Polyoxidonium (from 2-3 months to 1 year) 6 mg 1-2 times a week is indicated. When prescribing a long-term course, there is no accumulation effect, manifestations of toxicity and addiction.

For intranasal administration administer 6 mg per day (3 drops in each nasal lumen 3 times a day - for 10 days):

- for the treatment of acute and exacerbations of chronic ENT-organs infections;

- to enhance the regenerative processes of the mucous membranes;

- to prevent chronic diseases complications and relapses;

- for prophylaxis of influenza and ARVI

**Posology and Administration in children**

Route of administration of Polyoxidonium ®: parenteral, intranasal, sublingual. The methods of administration are chosen by a physician depending on disease severity and age of the patient.

Parenteral (intramuscular or intravenous): administered to children from 6 months at a dose of 0.1-0.15 mg/kg daily, every other day or 2 times a week with a course of 5-10 injections.

Intranasal and sublingual:daily at a daily dose of 0.15 mg/kg for the period up to 10 days.

The drug is administered in 1-3 drops in one nasal passage or under the tongue with an interval of at least 1-2 hours, in 2-3 doses per day.

One drop (0.05 ml) of the prepared solution contains 0.15 mg of the drug.

Calculation of the daily dose for nasal and sublingual administration is provided in Table 1.

Table 1. Calculation of Polyoxidonium ® daily dose for nasal and sublingual administration in children.

|  |  |
| --- | --- |
| Weight of a child | Numberof drops a day |
| 5 kg | 5 drops |
| 10 kg | 10 drops |
| 15 kg | 15 drops |
| 20 kg | 20 drops |

If a child's body weight is more than 20 kg, the daily dose is calculated at the rate of 1 drop per 1 kg of body weight, but not more than 40 drops (6 mg of the active substance).

*The prepared solution for nasal and sublingual administration can be stored at room temperature in the manufacturer's packaging up to 48 hours.*

The recommended therapeutic regimen for children:

Parenterally:

During acute and exacerbation of chronic inflammatory diseases of any localization (including ENT organs - sinusitis, rhinitis, adenoiditis, hypertrophy of the pharyngeal tonsil, acute respiratory infection) caused by pathogens of bacterial, viral, fungal infections: 0.1 mg/kg for 3 consecutive days, further 10 injections every other day.

During acute allergic and toxico-allergic diseases (including bronchial asthma, atopic dermatitis), complicated with bacterial, viral and fungal infections: intravenous drop infusion at a dose of 0.1 mg/kg, 3 consecutive days, then every other day, a course of 10 injections in combination with basic therapy.

Intranasally: daily 1-2 drops in each nasal lumen 3 times a day up to 10 days
(See the calculation of the daily dose for nasal and sublingual administration in Table 1):

During acute and chronic rhinitis, rhinosinusitis, adenoiditis (treatment and prevention of exacerbations);

For pre-operative preparation of patients during ENT pathology surgical interventions, as well as in the post-operative period in order to prevent infectious complications or relapses of the disease;

Treatment and prevention of influenza and other acute respiratory viral infections (within 1 month before the alleged epidemic), at any time after the onset of the disease and during the period of recovery);

Sublingually, for children of early, preschool and primary school age: daily at a daily dose of 0.15 mg/kg in 2 doses for 10 days:

During adenoiditis, tonsil hypertrophy: (as a component of conservative treatment);

For pre-surgery preparation and post-surgery rehabilitation ;

For seasonal prevention of exacerbations of chronic infections of the oropharynx, upper respiratory tract, inner and middle ear;

For the treatment of intestinal dysbiosis (in combination with basic therapy) for 10 days.

**Adverse effects**

While using Polyoxidonium ®, the following general and local reactions were observed:

During parenteral administration: Rare (≥1/1 000 to <1/100): at the site of administration - tenderness, redness and thickening of the skin.

During parenteral administration and topical application. Very rare (≥1/10000): increased body temperature, slight anxiety, chills, hypersensitivity to the components of the drug (allergic reactions).

**Overdosage**

No case of overdoses registered. In case of unintentional intake of a dosage exceeding the recommended, you should consult a doctor.

**Interactions**

Azoximer bromide does not inhibit the isoenzymes CYP1A2, CYP2C9, CYP2C19, CYP2D6 of cytochrome P-450 and is compatible with many drugs, including antibiotics, antiviral, antifungal agents and antihistamines, glucocorticosteroids and cytostatics.

**Special precautions**

Please, discontinue drug intake in case of hypersensitivity reaction and apply to your doctor.

If you need to stop taking Polyoxidonium®, the discontinuation can be done immediately, without a gradual dose reduction.

If you miss successive dose of the drug, its subsequent use should be carried out as usual, as indicated in this leaflet or recommended by a doctor. The patient should not administer a double dose in order to compensate the missed doses.

Do not use the drug in the presence of visual signs of its unsuitability (packaging defect, discoloration of the powder).

In tenderness at site of injection dissolve the product in 1 ml of 0.5% of procain (novocaine) solution in the absence of hypersensitivity for procain (novocaine) in patient. During intravenous (drop) infusion do not dissolve in protein-bearing infusion solutions.

**Effect on ability to drive and use machines**

The use of Polyoxidonium® does not affect the ability to perform potentially hazardous activities, that require an increased concentration of attention and speed of psychomotor reactions (including driving vehicles, working with moving mechanisms).

**Presentation**

Lyophilizate for solution for injections and topical application, 3 mg, 6 mg.

4.5 mg of the drug (for 3 mg dosage) or 9 mg of the drug (for 6 mg dosage) in glass vials of 1 hydrolytic class, hermetically sealed with rubber stoppers and crimped with aluminum caps.

5 vials with the drug in PVC blister strip packaging. One blister pack together with patient information leaflet into a carton pack or 5 vials together with patient information leaflet into a carton pack with a cardboard insert.

50 vials (for hospitals) together with 50 patient information leaflets are placed in a box with cardboard partitions.

**Shelf life**

3 years. Do not use after the expiry date.

**Storage conditions**

Store at <8°С. Do not freeze. Keep out of the reach of children.

**Purchasing terms**

Available on prescription

**Manufacturer/Legal entity in whose name the marketing authorization is given**

Marketing authorization holder and manufacturer:

NPO Petrovax Pharm LLC

Legal address/Manufacturing site address/Address for consumers' claims: Russia, 142143, Moscow Region, Podolsk,

Pokrov village, Sosnovaya street, 1, tel./fax: +7(495) 926-21-07, e-mail: info@petrovax.ru;

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