MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

PATIENT INFORMATION LEAFLET FOR THE DRUG PRODUCT POLYOXIDONIUM®

Registration Number: P N002935/02

Trade name: Polyoxidonium®

International non-proprietary or generic name: Azoximer bromide

Dosage form: Lyophilized powder for solution for injection and topical application

Composition per 1 vial:

Active ingredient: Azoximer bromide 3 mg or 6 mg

Excipients:

Mannitol 0.9 mg, povidone 0.6 mg (for 3 mg dosage)

Mannitol 1.8 mg, povidone 1.2 mg (for 6 mg dosage)

Description: Porous mass, white to white-yellowish

Pharmacotherapeutic group: Immunomodulator

ATC code: [L03]

Pharmacological properties

Pharmacodynamics

Azoximer bromide exhibits a complex effect (immunomodulatory, detoxifying, antioxidant, and moderate anti-inflammatory effects).

The immunomodulatory effect of azoximer bromide is based on its direct effect on the phagocytes and natural killer cells, as well as stimulation of antibody production and synthesis of interferon-alpha and interferon-gamma.

The detoxification and antioxidant properties of azoximer bromide largely depend on its structure and high molecular weight. Azoximer bromide increases resistance to localized and generalized bacterial, fungal, and viral infections. It restores the immunity in patients with secondary immunodeficiency disorders caused by various infections, injuries, postoperative complications, burns, autoimmune diseases, malignant neoplasms, chemotherapy, and administration of cytostatic agents or steroid hormones.

A special feature of azoximer bromide administered topically (intranasally or sublingually) is that it can activate factors of the first line of defense against infection. Thus, it stimulates the bactericidal activity of neutrophils and macrophages, enhances their ability to enclose bacteria, and enhances the bactericidal properties of saliva and secretions of the upper respiratory tract mucosa.

Azoximer bromide blocks soluble toxic substances and microparticles can eliminate toxins and salts of heavy metals out of the body, and inhibits lipid peroxidation, both by intercepting free radicals and by eliminating 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, exhibits no mitogenic, polyclonal, or antigenic activity, and has no allergenic, mutagenic, embryotoxic, teratogenic, or carcinogenic effect. Azoximer bromide is odorless and tasteless and has no local irritating effect when applied to the nasal or oropharyngeal mucosa.

Pharmacokinetics

Azoximer bromide is characterized by rapid absorption and a high distribution rate. Maximum blood concentration of the drug is achieved within 40 min after i.m. administration. The half-life period for different ages ranges from 36 to 65 hours. The bioavailability of the drug is high: 90% after parenteral administration.

Azoximer bromide is rapidly distributed to all organs and tissues of the body, penetrates through the blood-brain and blood-ocular barriers. The product exhibits no cumulative effect. Azoximer bromide undergoes biodegradation to low-molecular oligomers in the human body, and is excreted mainly by kidneys; no more than 3% of the drug is excreted with feces.

Indications for use

The drug is used in adults and children aged 6 months or older for prevention and treatment of inflammatory infections (viral, bacterial, and fungus) in exacerbation or remission.

For treatment of adults (combination therapy):

- chronic recurrent infectious and inflammatory diseases of different localization with bacterial, viral, and fungal etiology at the stage of exacerbation;
- acute viral and bacterial infections of the ENT organs, upper and lower respiratory tract, gynecological and urological diseases;
- acute and chronic allergic diseases (including pollinosis, bronchial asthma, atopic dermatitis), complicated by bacterial, viral and fungal infections;
- malignant tumors during and after chemotherapy and radiotherapy to reduce the immunosuppressive, nephrotoxic and hepatotoxic effects of drug products;
- generalized forms of surgical infections for activation of regenerative processes (fractures, burns, trophic ulcers);
- rheumatoid arthritis complicated by bacterial, viral, or fungal infections due to long-term use of immunosuppressants;
- pulmonary tuberculosis.

For treatment of children aged 6 months or older (combination therapy):

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

(In monotherapy) in adults and children aged 6 months or older to prevent:

- influenza and acute respiratory viral infections;
- postoperative infectious complications.

Contraindications

- Individual hypersensitivity
- Pregnancy and breastfeeding
- Children under 6 months of age
- Acute renal failure.

Safety precautions

- Chronic renal failure (use no more than twice a week).

Use during pregnancy and breastfeeding

Polyoxidonium® is contraindicated in pregnant and breastfeeding women (due to the lack of clinical use experience).

The experimental study of Polyoxidonium® in animals did not reveal any effect on generative function (fertility) of male and female animals, embryotoxic and teratogenic effects, impact on fetal development both when administered throughout the entire period of pregnancy and during the lactation period.

Method of administration and dosage

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

The physician decides on administration routes, dosing regimen, need for subsequent treatment courses and their frequency depending on disease severity and patient's age.

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

For intramuscular administration, dissolve Polyoxidonium® 3 mg in 1 mL (6 mg dose in 2 mL) of water for injection or 0.9% sodium chloride solution. After adding the solvent, leave the preparation for 2–3 minutes for swelling, then stir by rotary movements without shaking.

For intravenous dropwise administration, dissolve Polyoxidonium® in 2 mL of sterile 0.9% sodium chloride solution. After adding the solvent, leave the preparation for 2–3 minutes for

swelling, then stir by rotary movements. Transfer the calculated patient dose into a vial/bag of 0.9% sodium chloride solution under sterile conditions.

The prepared solution for parenteral administration is not to be stored.

Preparation of solution for intranasal and sublingual administration:

For children, dissolve a dose of 3 mg in 1.0 mL (20 drops) of distilled water, 0.9% sodium chloride solution or boiled water at room temperature, dissolve a dose of 6 mg in 2.0 mL (40 drops). One drop (0.05 mL) of the prepared solution for children contains 0.15 mg of the drug.

For adults, dissolve a dose of 6 mg in 1.0 mL (20 drops) of distilled water, 0.9% sodium chloride solution or boiled water at room temperature. One drop (0.05 mL) of the prepared solution for adults contains 0.3 mg of the drug.

Methods of administration and dosage in adults

Parenteral (intramuscular or intravenous) administration: the drug product is prescribed for adults in doses of 6–12 mg once daily, every other day, or 1–2 times a week depending on the diagnosis and disease severity.

In patients with acute viral, bacterial, and fungal infections of the ENT organs, upper and lower respiratory tract, gynecological and urological diseases: 6 mg daily for 3 days, then every other day, for a course of 10 injections.

In case of chronic recurrent infectious and inflammatory diseases of different localization with bacterial, viral, and fungal etiology at the stage of exacerbation: 5 injections of 6 mg each every other day, then twice a week, for a course of 10 injections.

In case of acute and chronic allergic diseases (including pollinosis, bronchial asthma, atopic dermatitis), complicated by bacterial, viral, and fungal infections: 6–12 mg, for a course of 5 injections.

In case of rheumatoid arthritis complicated by bacterial, viral, and fungal infection associated with long-term use of immunosuppressants: 5 injections of 6 mg each every other day, then twice a week; for a course of 10 injections.

In case of generalized surgical infections: 6 mg daily for 3 days, then every other day, for a course of 10 injections.

For activation of regenerative processes (fractures, burns, trophic ulcers): 6 mg daily for 3 days, then every other day, for a course of 10 injections.

For prevention of postoperative infectious complications: 5 injections of 6 mg each every other day.

In the case of pulmonary tuberculosis: 6 mg twice a week, for a course of 20 injections.

In combination therapy of malignant tumors during and after chemo- and radiation therapy:

- During and after chemotherapy to reduce the immunosuppressive, hepatotoxic and nephrotoxic effects of chemotherapeutic agents administer 6 mg every other day for a course of 10 injections; further, the frequency of administration is determined by the doctor depending on the tolerance and duration of chemotherapy and radiation therapy.

- Long-term administration of Polyoxidonium® (from 2–3 months to 1 year), 6 mg once or twice a week, is indicated for reducing the immunosuppressive effect of the tumor, for immunodeficiency correction after chemotherapy and radiation therapy, and after surgical tumor resection. No cumulative effect, manifestations of toxicity, or addiction were observed in the long-term treatment courses.

Intranasally administered at 6 mg per day (3 drops in each nasal passage 3 times a day for 10 days):

- treatment of acute infection and exacerbations of chronic ENT infections;
- intensification of the regeneration processes of mucosa;
- prevention of complications and recurrence of chronic diseases;
- prevention of influenza and acute respiratory viral infections.

Methods of administration and dosage in children

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

Parenteral (intramuscular or intravenous) administration: for children aged 6 months and older, at doses of 0.1–0.15 mg/kg daily every other day or twice per week, for a course of 5–10 injections.

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

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

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

Calculation of the daily dose for intranasal and sublingual administration is presented in Table 1.

Table 1. Calculation of the daily dose of Polyoxidonium® for intranasal or sublingual administration in children.

Child's weight	Quantity drops per day
5 kg	5 drops
10 kg	10 drops
15 kg	15 drops
20 kg	20 drops

If the 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 ingredient).

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

Recommended treatment regimen in children:

Parenterally:

In patients with acute chronic inflammatory diseases of any localization (including inflammatory diseases of the ENT organs: sinusitis, rhinitis, adenoiditis, pharyngeal tonsil hypertrophy, ARVI) caused by bacterial, viral, or fungal pathogens: 0.1 mg/kg daily for 3 consecutive days, then every other day, for a course of 10 injections.

In acute allergic and toxic-allergic conditions (including bronchial asthma, atopic dermatitis) complicated by bacterial, viral, and fungal infection: intravenously dropwise at a dose of 0.1 mg/kg, for 3 days daily, then every other day, for a course of 10 injections in combination with basic therapy.

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

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

For preoperative preparation of patients in ENT surgeries as well as during the postoperative period to prevent infectious complications or disease recurrence.

For treatment and prevention of influenza and other ARVIs (within a month before the anticipated epidemy, at any time after disease onset, and during the convalescence period).

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

In case of adenoiditis, tonsil hypertrophy: (as a component of conservative treatment)

For preoperative preparation and postoperative rehabilitation

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

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

Adverse reactions

The following local and systemic reactions were reported during treatment with Polyoxidonium®:

Parenteral administration. Uncommon (≥1/1000 to <1/100): at the administration site — tenderness, redness and swelling of the skin.

Parenteral and topical administration. Very rare (≥1/10,000): fever, mild anxiety, chills, hypersensitivity to the components of the drug (allergic reactions).

Overdose

No cases of overdose have been reported. In the case of accidental overdose (administering a dose higher than the recommended one), contact your physician.

Drug-drug interaction

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

Special indications

In case of allergic reaction in the event of hypersensitivity to the components of the drug, discontinue Polyoxidonium® and seek medical help.

If treatment with Polyoxidonium® needs to be discontinued, it can be done immediately, without titration.

If you miss the next dose of the drug, please administer the next dose as usual as indicated in the instructions or by your physician. Please do not administer a double dose to compensate for the missed doses.

Do not use the drug product if there are visual signs of its unsuitability (packaging defect or powder discoloration).

In case of tenderness at the injection site, dissolve the drug in 1 mL of 0.5% procaine (novocaine) solution in the absence of increased individual sensitivity to procaine (novocaine) in the patient. Do not dissolve the drug in protein-containing infusion solutions for intravenous (dropwise) infusions.

Effects on ability to drive and use machines

Polyoxidonium® does not affect one's ability to perform potentially dangerous activities that require increased concentration or rate of psychomotor activity (including driving vehicles or working with machinery).

Formulation:

Lyophilized powder for solution for injections and topical application, 3 mg, 6 mg.

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

5 vials per blister of polyvinyl chloride film. One blister together with the Instructions for Use per carton pack or 5 vials together with the Instructions for Use per carton pack with a carton insert.

50 vials (for hospitals) with the drug together with 50 Instructions for Use are placed in a box with cardboard dividers.

Shelf life

3 years. Do not use after the expiration date.

Storage conditions

Store at a temperature not exceeding 8°C. Do not freeze. Keep out of reach of children.

Prescription status

Available on prescription.

Manufacturer / Legal entity that obtained the marketing authorization

NPO Petrovax Pharm, LLC

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