SUMMARY OF PRODUCT CHARACTERISTICS

1. PRODUCT NAME
Polyoxidonium, 6 mg/mL, solution for injection and topical use.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active ingredient—azoximer bromide
One mL of solution contains 6 mg of azoximer bromide.
For the full list of excipients, see Section 6.1.

3. DOSAGE FORM
Solution for injection and topical use.
A colorless or slightly yellowish liquid.

4. CLINICAL DATA
4.1. Indications for use
The drug is used in adults and children aged 6 months and older for prevention and treatment of inflammatory infections (viral, bacterial, and fungal) in exacerbation or remission.

For treatment in adults (combination therapy):
- chronic recurrent infectious and inflammatory diseases of different localization with bacterial, viral, and fungal etiology during 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 chemotherapy and radiotherapy to reduce the immunosuppressive, nephrotoxic, and hepatotoxic effects of medicines;
- 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 immunosuppressive medicines;
- pulmonary tuberculosis.

For treatment of children aged 6 months and older (combination therapy):
- acute inflammatory diseases and exacerbations of chronic inflammatory diseases of any localization (including ENT organs—sinusitis, rhinitis, adenoiditis, pharyngeal tonsil hypertrophy, ARVI), caused by bacterial, viral, and fungal pathogens;
- acute allergic and toxic-allergic conditions complicated by bacterial, viral, or fungal infection;
- bronchial asthma complicated by chronic infections of the respiratory tract;
- atopic dermatitis complicated by purulent infection;
- intestinal dysbiosis (in combination with specific treatment).

For prevention (monotherapy) in adults and children aged 6 months and older:
- influenza and acute respiratory viral infections;
- postoperative infectious complications.

4.2. Posology and method of administration

Methods of administration, dosage regimen, and the need for and timing of subsequent courses of therapy are determined by the physician depending on the severity of the disease and the age of the patient.

Posology

Adults

Parenterally (intramuscularly, intravenously): the drug is prescribed to adults in doses of 6–12 mg once daily, every other day, or 1–2 times a week depending on the diagnosis and severity of the disease.

Table 1.

Indication(s)	**Dosage regimen**
For acute viral and bacterial infections of ENT organs, upper and lower respiratory tract, gynecological and urological diseases	6 mg daily for 3 days, then every other day, for a total of 10 injections
For generalized forms of surgical infections	
For activation of regenerative processes (fractures, burns, trophic ulcers)	
For chronic recurrent infectious and inflammatory diseases of various localizations, of bacterial, viral, and fungal etiology, during exacerbation	6 mg every other day, for a total of 5 injections then 2 times a week, for a total of 10 injections
For rheumatoid arthritis complicated by bacterial, viral, and fungal infection due to long-term use of immunosuppressive medicines	
For acute and chronic allergic diseases (including pollinosis, bronchial asthma, atopic dermatitis), complicated by bacterial, viral, and fungal infection	6–12 mg every other day, for a total of 5 injections
For prevention of postoperative infectious complications	6 mg every other day, for a total of 5 injections
For pulmonary tuberculosis	6 mg twice a week, for a total of 20 injections
In cancer patients before and during chemotherapy to reduce the immunosuppressive, hepatotoxic and nephrotoxic effects of chemotherapeutic agents	6 mg every other day, for a total of 10 injections; after that, frequency of treatment should be decided by physician based on tolerability and duration of chemotherapy and radiotherapy
In cancer patients for the prevention of the immunosuppressive effect of the tumor, for the correction of immunodeficiency after chemotherapy and radiation therapy, after surgical removal of the tumor	6 mg 1–2 times a week for a long-term therapy (from 2–3 months to 1 year) No cumulative effect, manifestations of toxicity, or addiction were observed in the long-term treatment cycles

Intranasally or sublingually (see section “Rules for use for sublingual and intranasal administration”):

Table 2.

Indication(s)	Dosage regimen
Treatment of acute infections and exacerbations of chronic ENT infections	Total volume of the drug per day is 1 mL (20 drops, 6 mg). Daily dose of the drug (6 mg) is administered intranasally or sublingually in 2–3 doses per day.
Treatment and prevention of influenza and ARVI	
Enhancement of regenerative processes of mucosa	
Prevention of complications and recurrence of chronic diseases	

Pediatric patients

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 total of 5–10 injections.

Table 3.

Indication(s)	Dosage regimen
For acute inflammatory diseases and exacerbations of chronic inflammatory diseases of any localization (including ENT organs—sinusitis, rhinitis, adenoiditis, pharyngeal tonsil hypertrophy, ARVI), caused by bacterial, viral, and fungal pathogens	0.1 mg/kg daily for 3 days, then every other day, for a total of 10 injections
For acute allergic and toxic-allergic conditions (including bronchial asthma, atopic dermatitis) complicated by bacterial, viral, and fungal infection, in combination with basic therapy	

For parenteral administration to children, the dose calculation is presented in Table 4.

Table 4. Calculation of maximum permissible doses for parenteral administration in children

Child's weight, kg	5	10	15	20	25	30	35	≥40
Dose, mg	0.75	1.5	2.25	5	3.75	4.5	5.25	6
Volume of solution administered from 6 mg/mL vial, mL V	0.1	0.5	0.4	0.5	0.7	0.8	0.9	1

Intranasally or sublingually (see section "Rules for use for sublingual and intranasal administration"):

Table 5.

Indication(s)	**Dosage regimen**
Acute and chronic rhinitis, rhinosinusitis, adenoiditis (treatment and prevention of exacerbations)	Daily dose of the drug is administered intranasally or sublingually in 2–3 doses per day, for a total of 5–10 days
Treatment (at any time after disease onset and during convalescence) and prevention of influenza and other acute respiratory viral infections (ARVI)	
Treatment of intestinal dysbiosis	Daily dose of the drug is administered sublingually in 2–3 doses per day, for a total of 10 days.

Calculation of doses for intranasal or sublingual use
Total volume of the drug is prescribed at the rate of 1 drop (0.3 mg) per 2 kg body weight.
Maximum dose for a child weighing **up to 20 kg** is no more than 10 drops (3 mg of active ingredient).
Maximum dose for a child weighing **over 20 kg** is no more than 20 drops (6 mg of active ingredient).

Table 6. Calculation of doses for intranasal and sublingual administration in adults and children from 6 months of age

Weight, kg	8	12	16	20	>20
Quantity of drops per day	4	6	8	10	1 drop per 2 kg of body weight, but no more than 20 drops

Safety and efficacy of Polyoxidonium in children aged 0 to 6 months have not yet been established. No data available.

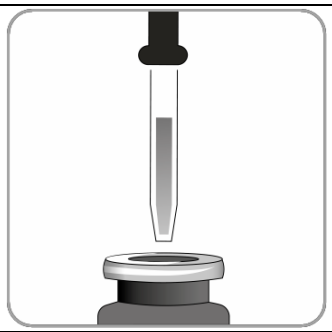
Method of administration
Methods of administration of Polyoxidonium: parenteral (intramuscular, intravenous), intranasal, sublingual.

Rules for intranasal and sublingual administration.
When using vials, the following rules must be observed:

Preparation for use:

Fig. 1. Wash your hands thoroughly.

For a vial containing 1 mL of the drug product:

	
Fig. 2. Remove the vial from the package, open the vial.	Fig. 3. Using a pipette, draw up the required amount of the drug (see Table 6).

For a vial containing 5 mL of medicinal product, complete with a dropper attachment:

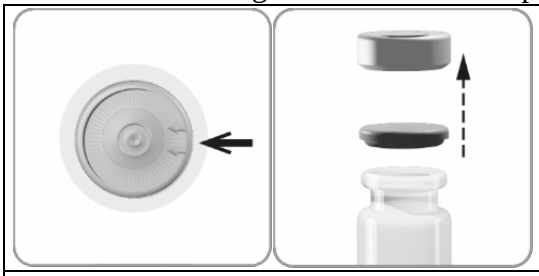
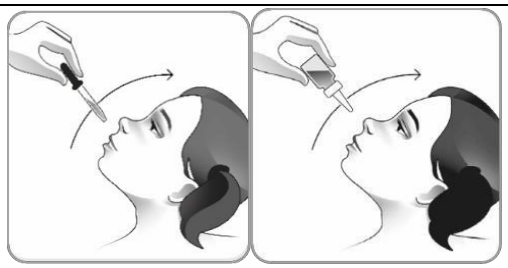


Fig. 4–5. Remove the vial from the package, open the vial.	Fig. 6. Remove the attachment, take it out of the package.	Fig. 7. Attach the attachment to the vial.

		
Fig. 8. Clear the nasal cavity of any accumulated mucus.	Fig. 9. Take a comfortable position (sit or lie on your back), tilt your head back slightly. Instill half of the calculated number of drops into the nasal passage (see Table 6).	Fig. 10. Press the nostril to the nasal septum with your finger to prevent the medication from leaking out. Maintain this position for 20–25 seconds. Instill the second half of the calculated dose of the medication into the other nasal passage.

Rules for sublingual administration:

		
Fig. 11. Do not eat or drink for 20 minutes before and after administration.	Fig. 12. Instill under the tongue (see Table 6).	Fig. 13. Drug has a neutral taste and does not require washing down.

After use, close the vial.

4.3. Contraindications

- Hypersensitivity to azoximer bromide or any of the excipients listed in Section 6.1:
- Pregnancy, breastfeeding (see Section 4.6). Women of childbearing potential should use effective contraception during treatment;
- Acute renal failure.

4.4. Special warnings and precautions

In case of allergic reaction or hypersensitivity to the components of the drug, discontinue Polyoxidonium.

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

If you miss the next dose of the drug, please administer the next dose as usual as indicated in these instructions for use.

This drug should be prescribed with caution in chronic renal failure (use no more than 2 times a week).

4.5. Interactions with other drug products and other forms of interaction

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

4.6. Fertility, pregnancy, and lactation

Pregnancy

Polyoxidonium is contraindicated in pregnant women (no clinical experience available).

Lactation

Polyoxidonium is contraindicated in breastfeeding women (no clinical experience available).

4.7. Effects on the ability to drive and use machines

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

4.8. Adverse reactions Tabular summary of adverse reactions

According to the World Health Organization (WHO), the frequency of adverse effects is as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

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

Uncommon: at the administration site with parenteral administration—tenderness, redness, and skin induration.

Very rare: fever up to 37.3°C, mild anxiety, chills within the first hour after injection.

Reporting of suspected adverse reactions

Reporting suspected reactions after the drug product authorization is important. It allows continued monitoring of the benefit/risk ratio of the drug product. Healthcare professionals should report any suspected adverse reactions via the national reporting systems of the member-states of the Eurasian Economic Union.

Russian Federation

Federal Service for Surveillance in Healthcare
Address: 4 Slavyanskaya Square, building 1, 109012 Moscow
Phone: +7 800 550-99-03
Email: pharm@roszdravnadzor.gov.ru
Website:
https://www.roszdravnadzor.gov.ru/

Republic of Belarus

Center for Examinations and Tests in Health Service Unitary Enterprise
Address: 2a Tovarishchesky per., 220037 Minsk
Phone: +375-17-242-00-29
Fax: +375-17-242-00-29
Email: rcpl@rceth.by
Website:
http://www.rceth.by

Republic of Armenia

CJSC "Scientific Center of Drug and Medical Technology Expertise named after Academician E. Gabrielyan"
49/5 Komitas av., 0051 Yerevan
Phone: +374 10 20-05-05; +374 96 22-05-05
Email: vigilance@pharm.am
Website:
http://www.pharm.am

Republic of Kazakhstan

RSE on the REM "National Center for Expertise of Medicines and Medical Devices" of the Medical and Pharmaceutical Activity Control Committee of the Ministry of Health of the Republic of Kazakhstan
Address: 13 A. Imanov St., 010000 Nur-Sultan
Phone: +7 7172 78-99-11
Email: farm@dari.kz
Website:
http://www.ndda.kz

The Kyrgyz Republic
Department of Medicines and Medical Devices of the Ministry of Health of the Kyrgyz Republic
Address: 25 3rd Line St., 720044 Bishkek
Phone: +996 312 21-92-86
Fax: +996 312 21 05 08
Email: dlsmi@pharm.kg
Website:
http://pharm.kg

4.9. Overdose

No overdose cases have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Immunostimulants; other immunostimulants.
ATC code: [L03AX].

Mechanism of action

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.

Azoximer bromide contributes to a significant increase in the expression of HLA-DR (Human Leukocyte Antigens) on monocytes. HLA-DR belongs to the molecules of the major histocompatibility complex class II (MHC class II), which present antigens to T-lymphocytes, thereby promoting the process of antigen elimination (including infectious and tumor antigens).

Azoximer bromide has the ability to enhance the expression of the MDA-5 gene in lymphocytes and monocytes of peripheral blood. MDA-5 (Melanoma Differentiation-Associated protein 5) is a receptor of the RIG-I-like receptor group. MDA-5 is an intracellular pattern recognition receptor involved in the innate immune response to viral infection. MDA-5 recognizes mRNA without a 2'-O-methylated 5'-end and long double-stranded RNAs (over 2,000 nucleotides). Activation of MDA-5 triggers the transcription of innate immune response genes, including interferons IFN-alpha and IFN-beta. Activation of MDA-5 is most significant in viral infections and oncological processes. MDA-5 activation also plays a role in the antitumor response by activating apoptotic processes.

Azoximer bromide increases the expression of ICOSL on the surface of dendritic cells. ICOSL (CD 275) is a ligand for ICOS (Inducible T-cell COStimulator Molecule). The ICOS/ICOSL reaction cascade acts as a costimulator in the process of immune cell activation and, in particular, is necessary for successful T-lymphocyte activation, as well as for the interaction of antigen-presenting cells with T-lymphocytes.

Azoximer bromide reduces the formation of neutrophil extracellular traps by activated neutrophils, which consist of DNA and proteins, including antimicrobial proteins, equally toxic to both bacteria and the body's own cells. 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 and steroid hormones.

Polyoxidonium administration in the context of secondary immunodeficiency states allows for increased effectiveness and reduced duration of treatment, significantly reduce the use of antibiotics, bronchodilators, glucocorticoids, and prolong the period of remission. Inclusion of Polyoxidonium in the complex therapy of cancer patients reduces intoxication during chemotherapy and radiotherapy, in most cases allows for standard therapy to be administered without changing the regimen due to the development of infectious complications and adverse effects (myelosuppression, vomiting, diarrhea, cystitis, colitis, etc.)

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 phagocytose bacteria, and enhances the bactericidal properties of saliva and secretions of the mucosa of the upper respiratory tract.

Azoximer bromide blocks soluble toxic substances and microparticles, and can eliminate toxins and heavy metal salts from the body, and inhibits lipid peroxidation by intercepting free radicals and eliminating catalytically active Fe2+ ions. Azoximer bromide reduces the inflammatory response by normalizing the synthesis of pro- and anti-inflammatory cytokines.

Azoximer bromide is well-tolerated, does not exhibit mitogenic, polyclonal activity, or antigenic properties, and does not have allergenic, mutagenic, embryotoxic, teratogenic, or carcinogenic effects.

Azoximer bromide is odorless and tasteless and has no local irritating effect when applied to the nasal or oropharyngeal mucosa.

5.2. Pharmacokinetic properties

Absorption

Azoximer bromide is characterized by rapid absorption and a high distribution rate. Maximum plasma concentration of the drug is achieved within 40 minutes after intramuscular administration. The drug has high bioavailability of 90% after parenteral administration.

Distribution

Azoximer bromide is rapidly distributed to all organs and tissues of the body and penetrates through the blood-brain and blood-ocular barriers.

Biotransformation

Azoximer bromide undergoes biodegradation to low-molecular oligomers in the human body.

Elimination

The half-life for different age groups ranges from 36 to 65 hours. The drug exhibits no cumulative effect. Azoximer bromide is excreted mainly by the kidneys, via the intestines—no more than 3%.

5.3. Preclinical safety data

In non-clinical studies of Polyoxidonium in animals, no effect on the reproductive function (fertility) of males and females, embryotoxic and teratogenic effects, or effects on fetal development were found, when the drug was administered throughout pregnancy and during lactation.

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

Mannitol
Povidone
Water for injections

6.2. Incompatibilities

For intravenous (drip) administration, do not dissolve in protein-containing infusion solutions. This medicinal product must not be mixed with other medicinal products except those mentioned in Section 6.6.

6.3. Shelf life (storage period)

2 years.

After first opening:

After opening a vial for parenteral administration, do not reuse the remaining solution from the opened vial for parenteral administration. Do not store an opened vial with solution for parenteral administration.

For intranasal or sublingual administration:

After opening the vial, store in a refrigerator at 2 to 8°C or at room temperature not exceeding 25°C for no more than 14 days.

6.4. Special precautions for storage

Store at 2°C to 8°C.

For storage conditions after first opening of the drug product, see Section 6.3.

6.5. Nature and contents of the container

1.0 mL in colorless glass vial, 5 vials in a blister, 1 blister in a carton together with a package leaflet; or 5.0 mL in colorless glass vial, 1 vial in a carton together with a dropper attachment and a package leaflet.

6.6. Special precautions for disposal of the used drug product or waste materials derived from the use of the drug, and other handling of the drug

For intravenous infusion, aseptically transfer the dose calculated for the patient from the syringe into a vial/bag with 0.9% sodium chloride solution.

In case of tenderness at the site of administration, when transferring Polyoxidonium from the vial to the syringe, add 1 mL of 0.5% procaine (novocaine) solution, provided that the patient does not have hypersensitivity to procaine (novocaine).

Appearance after reconstitution: colorless to slightly yellowish liquid.

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

Any unused medicinal product or waste material should be disposed of in accordance with established procedures and national legislation requirements.

7. MARKETING AUTHORIZATION HOLDER

Russian Federation
NPO Petrovax Pharm LLC
1 Sosnovaya str., Pokrov village, 142143 Podolsk, Moscow Region, Russia
Phone: +7 495 926-21-07
Fax: +7 (495) 926-21-07
Email: info@petrovax.ru

7.1. Representative of the Marketing Authorization Holder in the Union

Customer claims should be sent to the following address:

Russian Federation
NPO Petrovax Pharm LLC
1 Sosnovaya str., Pokrov village, 142143 Podolsk, Moscow region, Russia
Phone: 8 (800) 234-44-80
Email: adr@petrovax.ru; pv@petrovax.ru

Republic of Kazakhstan
LLP “LEKARSTVENNAYA BEZOPASNOST”
Sayaly Microdistrict, building 16, apartment 8, Alatau District, 050047 Almaty, Kazakhstan
Phone: +7 777 064-27-02; +7 499 504-15-19
Email: adversereaction@drugsafety.ru
Republic of Belarus
Autonomous Non-profit Organization “National Scientific Center for Pharmacovigilance”
6 Baumanskaya St., building 2, floor 9, office 923, 105005 Moscow, Russia
Phone: +7 499 504-15-19; +7 903 799-21-86
Email: adversereaction@drugsafety.ru
Republic of Armenia
Autonomous Non-profit Organization “National Scientific Center for Pharmacovigilance”
6 Baumanskaya St., building 2, floor 9, office 923, 105005 Moscow, Russia
Phone: +7 499 504-15-19; +7 903 799-21-86
Email: adversereaction@drugsafety.ru
The Kyrgyz Republic
Autonomous Non-profit Organization “National Scientific Center for Pharmacovigilance”
6 Baumanskaya St., building 2, floor 9, office 923, 105005 Moscow, Russia
Phone: +996 99 901-50-45, +7 499 504-15-19
Email: adversereaction@drugsafety.ru

8. MARKETING AUTHORIZATION NUMBER

9. DATE OF FIRST AUTHORIZATION (RENEWAL OF THE AUTHORIZATION, RE-AUTHORIZATION)

Date of first authorization:

10. DATE OF REVISION OF THE TEXT

Summary of Product Characteristics for Polyoxidonium is available on the website of the Eurasian Economic Union (http://eec.eaeunion.org/).