

 **14 March 2025**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**for**

**Ipratropiumbromid+Fenoterolhydrobromid "Farmak", nebuliser solution**

**0. D.SP.NO.**

33689

**1. NAME OF THE MEDICINAL PRODUCT**

Ipratropiumbromid+Fenoterolhydrobromid "Farmak"

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each single-dose container of 4 ml contains ipratropium bromide equivalent to 0.5 mg anhydrous ipratropium bromide, corresponding to 0.125 mg/ml and 1.25 mg of fenoterol hydrobromide, corresponding to 0.3125 mg/ml.

For the full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**

Nebuliser solution.

Clear colourless liquid,

pH 3.0-4.0,

osmolality 260 – 330 mosmol/kg.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

Ipratropiumbromid+Fenoterolhydrobromid "Farmak" is indicated for the treatment of bronchospasm associated with acute exacerbation of asthma or chronic obstructive pulmonary disease in adults and children over 12 years of age.

**4.2 Posology and method of administration**

Posology

Treatment should be initiated and administered under the supervision of a doctor, e.g. in a hospital. Treatment at home can be done in exceptional cases (severe symptoms or experienced patients requiring higher doses) after consultation with an experienced doctor, when a low dose of a fast-acting beta-agonist bronchodilator is not sufficient to relieve symptoms.

Recommended doses:

**Acute episodes of bronchospasm**

*Adults (including the elderly):*

* In most cases, one nebula is enough to relieve a spasm.
* In very severe cases, a 2nd nebula may be needed to relieve symptoms. If an attack has not been relieved by 2 nebuli, further doses may be required. In these cases, patients should be advised to consult the doctor or the nearest hospital immediately.

*Special populations*

*Patients with renal or hepatic impairment*

No dose adjustment is required for patients with renal or hepatic impairment due to low systemic absorption of the active substances by inhalation.

*Children:*

* Adolescents over the age of 12: see “Adults”
* Children under 12 years of age: use is not recommended due to insufficient data on safety and efficacy.

Use should be discontinued when sufficient symptom relief is achieved.

Method of administration

*Precautions to be taken before using the drug*

Patients prone to glaucoma require eye protection (see section 4.4).

* Each nebula is ready to use and does not require dilution.
* The solution is intended for inhalation, not for injection or parenteral administration.
* Ipratropiumbromid+Fenoterolhydrobromid "Farmak" nebuliser solution is administered in single doses using a nebulizer or an intermittent positive pressure device.
* Lung exposure and systemic exposure depend on the type of inhaler used and may be higher than after administration of the recommended doses via an inhaler device that generates a spray.
* The solution can also be supplied under pressure with an oxygen stream (6-8 l/min).
1. Prepare the inhaler according to the manufacturer's or healthcare professional's instructions.
2. Open the single dose by twisting the top.
3. Pour the contents into the inhaler reservoir.
4. Use the inhaler according to the instructions.
5. After use, discard the remaining solution and wash the device.

As the single-dose vial does not contain preservatives, it should be used immediately after opening to avoid any microbial contamination and a new vial should be opened for each new aerosolization. Partially used vials should be disposed of.

**4.3 Contraindications**

* Hypersensitivity to the active substances, other sympathomimetic amines, atropine and its derivatives, or any of the excipients listed in section 6.1.
* Patients with hypertrophic obstructive cardiomyopathy or tachyarrhythmia.

**4.4 Special warnings and precautions for use**

Hypersensitivity

Sudden hypersensitivity reactions may occur after use of Ipratropiumbromid+Fenoterol­hydrobromid "Farmak", as evidenced by rare cases of urticaria, angioedema, rash, bronchospasm, oropharyngeal edema, and anaphylaxis (see section 4.8).

Paradoxical bronchospasm

Like other inhaled medicinal products, Ipratropiumbromid+Fenoterolhydrobromid "Farmak" may cause paradoxical bronchospasm, which can be life-threatening (see section 4.8). If paradoxical bronchospasm occurs, Ipratropiumbromid+Fenoterolhydrobromid "Farmak" treatment should be discontinued immediately and replaced by alternative appropriate treatment.

Complications of vision

Ipratropiumbromid+Fenoterolhydrobromid "Farmak" should be used with caution in patients prone to angle-closure glaucoma.

In case of eye contact with aerosolized ipratropium bromide (alone or in combination with a beta-2-agonist), some cases of eye complications (such as mydriasis, increased eye pressure, angle-closure glaucoma, eye pain) have been reported.

Pain in the eyes, blurred vision, halos or colored images that appear along with redness of the eyes (due to conjunctival hyperemia and corneal swelling) can be symptoms of acute angle-closure glaucoma.

Should any combination of these symptoms develop, treatment with miotic eye drops should be initiated and specialist advice should be sought immediately.

Patients should be instructed on the proper use of Ipratropiumbromid+Fenoterol­hydrobromid "Farmak".

Care must be taken to avoid contact of the aerosol with eyes.

It is recommended to spray the solution through a mouthpiece. If a mask is used instead, it must be carefully fitted and adjusted. Patients at risk of glaucoma should be especially warned about careful eye protection.

Systemic adverse reactions

Ipratropiumbromid+Fenoterolhydrobromid "Farmak" should be used only after a careful risk/benefit assessment, especially if the dose used exceeds the recommended dose in patients with conditions such as hyperthyroidism, diabetes mellitus that is difficult to control (see below and section 4.8), pheochromocytoma, recent myocardial infarction, cardiac or vascular disease, or existing urinary tract obstruction (e.g., prostatic hyperplasia or bladder neck obstruction).

Diabetes

Caution should be exercised when using fenoterol in patients with diabetes. Beta-2-agonists can induce hyperglycemia, and patients with diabetes who are treated with fenoterol should initially be advised to have more frequent blood glucose measurements (see section 4.8).

Thyrotoxicosis

Caution should be exercised when using fenoterol in patients with thyrotoxicosis. The use of fenoterol in patients suffering from thyrotoxicosis may cause an increased effect on the heart (palpitations, arrhythmias) (see section 4.8).

Adverse reactions from the cardiovascular system

Cardiovascular adverse reactions may occur with sympathomimetic agents, including Ipratropiumbromid+Fenoterolhydrobromid "Farmak". Post-marketing data and literature indicate rare cases of myocardial ischemia and cardiac arrhythmias associated with beta-adrenergic agonists. Patients with serious underlying heart disease (e.g., coronary artery disease, arrhythmia, or severe heart failure) who are receiving Ipratropiumbromid+Feno­terol­hydrobromid "Farmak" should be advised to consult a doctor if they develop any chest pain or other symptoms of worsening heart disease. Caution should be exercised in evaluating symptoms such as shortness of breath and chest pain, as they may be of respiratory or cardiac origin.

Hypokalaemia

Potentially severe hypokalaemia can result from treatment with beta-2-mimetics (see sections 4.5, 4.8 and 4.9).

Disorders of gastrointestinal motility

Patients with cystic fibrosis may be more prone to gastrointestinal motility disturbances when treated with inhaled anticholinergics.

Shortness of breath

Patients should be warned that if acute dyspnoea worsens rapidly, they should seek medical attention immediately.

In patients with asthma, the use of increasing doses of beta-2-agonist medications to control symptoms of bronchial obstruction may indicate a loss of control of the disease. If the bronchial obstruction worsens, it is inappropriate and potentially dangerous to simply increase the dose of beta-2-agonists beyond the recommended dose and for a long time. In this case, the patient's treatment regimen should be reviewed, including the appropriateness of anti-inflammatory treatment with inhaled corticosteroids, to prevent any loss of control that could be life-threatening.

Concomitant use of other sympathomimetics

Other sympathomimetics in addition to Ipratropiumbromid+Fenoterolhydrobromid "Farmak" should be used only under medical supervision (see section 4.5).

This medicine contains less than 1 mmol sodium (23 mg) per polyethylene container (4 ml), that is to say essentially ‘sodium-free’.

**4.5 Interaction with other medicinal products and other forms of interaction**

Other anticholinergic drugs

Chronic simultaneous use of Ipratropiumbromid+Fenoterolhydrobromid "Farmak" with other anticholinergic drugs has not been studied. Therefore, long-term simultaneous administration of Ipratropiumbromid+Fenoterolhydrobromid "Farmak" with other anticholinergic drugs is not recommended.

Drugs associated with prolongation of the QT interval

Medications such as quinidine, disopyramide, procainamide, phenothiazines, antihistamines, and tricyclic antidepressants may be associated with prolongation of the QT interval and increased risk of ventricular arrhythmia.

Sympathomimetics or anticholinergics

The simultaneous use of other sympathomimetic or anticholinergic drugs may increase the adverse reactions of Ipratropiumbromid+Fenoterolhydrobromid "Farmak".

The simultaneous use of fenoterol and theophylline may lead to reciprocal potentiation and an increase in the frequency of cardiac arrhythmias. The combination of fenoterol with substances that enhance sympathomimetic effects, such as L-DOPA, L-thyroxine, oxytocin, or alcohol, may have cardiovascular effects.

Beta-blockers

Concomitant use of beta-blockers may result in a potentially serious decrease in bronchodilation and thus reduce or counteract the effect of Ipratropiumbromid+Feno­terolhydrobromid "Farmak". This can lead to a severe asthma attack in patients with asthma or chronic obstructive pulmonary disease. Beta-blockers can cause severe bronchostenosis in patients with asthma. Therefore, Ipratropiumbromid+Fenoterol­hydrobromid "Farmak" should be prescribed only in combination with beta-blockers (including eye drops) after assessing the risk-benefit ratio.

Xanthine derivatives, corticosteroids and diuretics

Hypokalaemia caused by beta-2-agonists may be aggravated by concomitant treatment with xanthine derivatives, steroids, and diuretics. This should be especially considered in patients with severe airway obstruction.

Hypokalaemia can lead to an increased tendency to arrhythmias in patients treated with digoxin.

In addition, hypoxia can worsen the effect of hypokalaemia on heart rate.

In such situations, it is recommended to monitor the level of potassium in the blood serum.

Monoamine oxidase (MAO) inhibitors and tricyclic antidepressants

Caution should be exercised when prescribing beta-2-agonists to patients treated with MAO inhibitors or tricyclic antidepressants, as the effect of beta-2-agonists may be enhanced. Caution should be exercised up to 14 days after use of MAO inhibitors.

Halogen-hydrocarbon anesthetics

Inhalation of halogenated hydrocarbon anesthetics, such as halothane, trichloroethylene, and enflurane, can increase the risk of cardiovascular adverse reactions from beta-2-mimetics. Ipratropiumbromid+Fenoterolhydrobromid "Farmak" should not be administered less than 12 hours before the start of anesthesia with halogenated hydrocarbon anesthetics.

Cisapride

The effect of cisapride on gastrointestinal motility may be reduced with simultaneous administration of Ipratropiumbromid+Fenoterolhydrobromid "Farmak".

**4.6 Fertility, pregnancy and lactation**

Pregnancy

There are only limited data on the use of fenoterol or ipratropium in pregnant women.

Animal studies do not indicate any direct or indirect adverse effects on pregnancy, embryo and fetal development, labor, or postnatal development (see section 5.3). The potential risk to humans is unknown.

The potential of beta-2-agonists to inhibit uterine contractions should be taken into account.

Use of beta-2-sympathomimetics in the end of pregnancy may cause negative effects in the newborn baby (tremor, tachycardia, blood glucose fluctuations, hypokalaemia).

As a precautionary measure, it is preferable to avoid the use of Ipratropiumbromid+Fenoterolhydrobromid "Farmak" during pregnancy.

Lactation

Preclinical studies have shown that fenoterol hydrobromide passes into breast milk.

There are insufficient data on the effects of fenoterol hydrobromide on newborns/infants.

It is not known whether ipratropium passes into breast milk, but it is unlikely that ipratropium passes to a significant extent into the infant, especially when used as an aerosol. However, a risk to newborns/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Ipratropiumbromid+Fenoterolhydrobromid "Farmak" therapy, taking into account the benefits of breastfeeding for the child and the benefits of therapy for the woman.

Fertility

Clinical data on fertility are not available for the combination of ipratropium bromide and fenoterol hydrobromide or for the two components of this mixture. In preclinical studies conducted with the individual substances, ipratropium bromide and fenoterol hydrobromide, no adverse effects on fertility were observed (see section 5.3).

**4.7 Effects on ability to drive and use machines**

No traffic warning.

No studies have been conducted on the ability to drive vehicles and use machines.

However, the patient should be warned that during treatment with Ipratropiumbromid+Fenoterolhydrobromid "Farmak", he or she may experience such unwanted effects as dizziness, tremor, accommodation disorders, mydriasis, and blurred vision.

Therefore, caution is recommended when driving or operating machinery. If a patient experiences the above adverse reactions, they should avoid potentially hazardous tasks such as driving or operating machinery.

**4.8 Undesirable effects**

Most adverse reactions can be explained by the anticholinergic and beta-adrenergic properties of Ipratropiumbromid+Fenoterolhydrobromid "Farmak". As with all inhalation therapy, Ipratropiumbromid+Fenoterolhydrobromid "Farmak" may cause local irritation. Adverse reactions were identified from data obtained in clinical trials and pharmacovigilance during post approval use of the medicinal product.

The most common adverse reactions reported in clinical trials were headache, cough, dry mouth, vomiting, nausea and dizziness, tremors, pharyngitis, dysphonia, tachycardia, palpitations, increased systolic blood pressure, and nervousness.

Adverse reactions are classified according to their frequency according to the following classification:

Very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1000 to <1/100); rare (≥ 1/10,000 to <1/1,000); very rare (<1/10,000), frequency unknown (cannot be estimated from the available clinical data).

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| --- | --- | --- |
| **Classes of organ systems** | **Frequency** | **Undesirable effect** |
| Immune system disorders | Rare | Skin or allergic reactions (hypersensitivity)\*, such as rashes, angioedema, urticaria, laryngospasm, and anaphylactic reactions\*. |
| Metabolic and nutritional disorders | Rare | Hypokalaemia\*. |
| Psychiatric disorders | Rare | Cases of mental changes, agitation |
| Uncommon | Nervousness |
| Nervous system disorders | Uncommon | Headache, slight trembling of skeletal muscles, dizziness |
| Frequency unknown | Hyperactivity |
| Eye disorders  | Rare | Accommodation disorders\*, angle-closure glaucoma\*, increased intraocular pressure\*, mydriasis\*, blurred vision\*, eye pain\*, corneal edema\*, conjunctival hyperemia\*, halo\*. See also section 4.4. |
| Cardiac disorders | Rare | Atrial fibrillation, arrhythmias, supraventricular tachycardia\*, myocardial ischemia\* |
| Uncommon | Tachycardia, increased heart rate, palpitations |
| Respiratory, thoracic and mediastinal disorders | Common | Cough |
| Uncommon | Pharyngitis, dysphonia |
| Rare | Bronchospasm, throat irritation, pharyngeal oedema, laryngeal spasm\*, paradoxical bronchospasm\*, dry throat\* |
| Gastrointestinal disorders | Uncommon | Dry mouth, nausea, vomiting |
| Rare | Stomatitis, glossitis, swelling of the mouth\*, gastrointestinal motility disorder, constipation\* and diarrhoea |
| Skin and subcutaneous tissue disorders | Rare | Hyperhidrosis\*, urticaria, pruritus, angioedema\* |
| Musculoskeletal and connective tissue disorders | Rare | Myalgia, muscle weakness and spasms |
| Renal and urinary disorders | Rare | Urinary retention |
| Investigations | Rare | Increased systolic blood pressure |
| Uncommon | Reduction of diastolic blood pressure |

\* This adverse reaction was reported spontaneously in post-marketing surveillance data. This adverse reaction has not been observed in any of the selected clinical trials of Ipratropiumbromid+Fenoterolhydrobromid "Farmak". The estimate is based on the upper limit of the 95% confidence interval calculated for all patients treated in the clinical trials and studies.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Lægemiddelstyrelsen

Axel Heides Gade 1

DK-2300 København S

Website: www.meldenbivirkning.dk

**4.9 Overdose**

Symptoms

The effects of overdose are expected to be primarily related to the component fenoterol: the expected symptoms are those resulting from excessive beta-2-mimetic stimulation, the most common of which are tachycardia, palpitations, tremors, hypertension, hypotension, dissociation of systolic and diastolic blood pressure, anginal pain, arrhythmias, and flushing. Metabolic acidosis and hypokalaemia have also been observed with fenoterol at doses higher than those recommended for the registered indications of Ipratropium­bromid+Fenoterolhydrobromid "Farmak". Potassium level should be monitored.

The expected symptoms of an overdose of ipratropium (such as dry mouth, visual accommodation disorders, and increased heart rate) are mild and transient in nature, as the systemic bioavailability of ipratropium by inhalation is very low.

Management

Treatment with Ipratropiumbromid+Fenoterolhydrobromid "Farmak" should be discontinued. Consideration should be given to monitoring the acid-base balance, electrolyte, blood glucose, ECG and blood pressure.

Administration of sedatives, tranquilizers; and intensive care, if necessary in severe cases. Beta-blockers, preferably beta-1-selective, may be used as specific antidotes; however, the possible increase in bronchial obstruction should be taken into account and the dose should be carefully adjusted in patients with asthma or chronic obstructive pulmonary disease due to the risk of precipitating severe bronchospasm, which can be fatal.

**4.10 Legal status**

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**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Adrenergics in combination with anticholinergics incl. triple combinations with corticosteroids, ATC code: R03AL01

Ipratropiumbromid+Fenoterolhydrobromid "Farmak" contains 2 bronchodilators: ipratropium, an anticholinergic substance, and fenoterol, a beta-2-adrenergic sympathomimetic.

Ipratropiumbromid+Fenoterolhydrobromid "Farmak" combines fenoterol and ipratropium, which, due to their different mechanisms of action, have a synergistic bronchodilator effect without potentiating the adverse reactions of either substance. In case of bronchial pathology, the combination of two substances with complementary bronchodilator effect is effective in a larger number of patients whose response to one or the other component (beta-2-mimetic or anticholinergic) was incomplete.

Due to the fast action of Ipratropiumbromid+Fenoterolhydrobromid "Farmak", it can be used in acute episodes of bronchospasm.

Ipratropium bromide

Ipratropium is a four-component ammonium derivative with anticholinergic (parasympathicolytic) properties. Bronchodilation after inhalation of ipratropium is predominantly a specific local rather than systemic effect. Anticholinergic substances prevent an increase in the intracellular concentration of Ca++ as a result of the interaction of acetylcholine with muscarinic receptors in the smooth muscle of the airways. Ca++ release occurs through a system of secondary mediators consisting of IP3 (inositol triphosphate) and DAG (diacylglycerol).

Clinical and preclinical studies show that ipratropium has no harmful effects on the respiratory system, in particular on mucosal secretions, mucociliary clearance and gas exchange.

Fenoterol hydrobromide

In therapeutic doses, fenoterol is a beta-2-adrenergic sympathomimetic.

In doses above therapeutic levels, it stimulates beta-1 receptors. The use in bronchospasm is based on the bronchodilator effect, which is achieved by stimulating beta-2 receptors of the smooth muscle of the airways.

Occupation of beta-2 receptors activates adenylate cyclase through the stimulatory protein G.

An increase in cAMP activates protein kinase A, which phosphorylates target smooth muscle proteins.

Fenoterol hydrobromide relaxes bronchial and vascular smooth muscle and protects against bronchoconstriction caused by irritants such as histamine, methacholine, cold air and allergens. The release of bronchoconstrictive and inflammatory mediators from mastocytes is inhibited by the administration of fenoterol.

After administration of fenoterol (0.6 mg) in animals, there was an increase in mucociliary clearance.

High plasma concentrations achieved after oral or intravenous administration inhibit uterine motility.

The following metabolic effects are observed in high doses: lipolysis, glycogenolysis, hyperglycemia, and hypokalaemia.

Beta-adrenergic effects on the heart such as increased heart rate and contractility occur as a result of the effect of fenoterol on blood vessels, stimulation of cardiac beta-2 receptors and, in doses exceeding therapeutic doses, by stimulating beta-1 receptors.

As with other beta-adrenergic agents, prolongation of the QTc interval has been reported. For fenoterol pressurised inhalation, such reports have been isolated and were observed at doses higher than recommended. However, the systemic exposure after nebulization may be higher than after doses recommended for inhalation solutions in pressurized vials. The clinical significance has not been established.

Tremors are a common effect of beta-agonists. In contrast to the effects on smooth muscles, a tolerance phenomenon may occur with respect to the systemic effects of beta-agonists on skeletal muscle.

Clinical efficacy and safety

Two studies (one in patients with asthma and the other in patients with chronic obstructive pulmonary disease) showed that Ipratropiumbromid+Fenoterolhydrobromid "Farmak" is as effective as double-dose fenoterol and without ipratropium, but provides better tolerability of cumulative doses.

It is more effective than each of its components separately.

**5.2 Pharmacokinetic properties**

The therapeutic effect of the combination of ipratropium bromide and fenoterol hydrobromide is due to its local effect on the airways. Thus, the bronchodilation caused in this way does not depend on the pharmacokinetics of fenoterol and ipratropium in the body. After inhalation, typically 10-39% of the dose is deposited in the lungs, depending on the formulation, inhalation technique and device, while the remainder of the administered dose is deposited in the mouthpiece, mouth and upper airway (oropharynx). Part of the dose deposited in the lungs reaches the bloodstream very quickly (within minutes).

The amount deposited in the oropharynx is slowly swallowed and enters the gastrointestinal tract. Thus, systemic exposure depends on both oral and pulmonary bioavailability.

There is no reason to believe that the pharmacokinetics of each of the components is different when used in combination compared to their use separately.

Fenoterol hydrobromide:

The ingested fraction is mainly metabolized to sulfo-conjugated derivatives. Absolute bioavailability after oral administration is low (about 1.5%). The cumulative renal excretion (0-24 h) is estimated to be 15% of the intravenously administered dose for free fenoterol and 27% for conjugated fenoterol.

After inhalation, cumulative renal elimination (0-24 hours) is estimated at 1% of the inhaled dose. Based on these data, the total bioavailability of inhaled doses of fenoterol hydrobromide is estimated at 7%.

Pharmacokinetic parameters were determined by plasma levels after intravenous administration. After intravenous administration, the plasma level profile over time can be described as a three-component pattern with a half-life of 3 hours. The apparent equilibrium volume of distribution of fenoterol (Vdss) is approximately 189 liters (≈ 2.7 l/kg) according to the three-component model. Plasma protein binding is approximately 40%. Preclinical studies in rats have demonstrated that fenoterol and its metabolites do not penetrate the blood-brain barrier. Fenoterol has a clearance of 1.3 l/min, and a renal clearance of 0.27 l/min.

In the excretion balance study, the cumulative renal excretion (2 days) of the radioactivity bound to the substance (including the parent substance and other metabolites) was 65% of the dose after intravenous administration, and the total radioactivity excreted in the feces was 14.8% of the dose.

After oral administration, the total radioactivity excreted in the urine after 48 hours was approximately 39% of the dose, and in the feces - approximately 40.2% of the dose.

Ipratropium bromide:

The cumulative renal excretion (0-24 hours) of the parent substance is 46% of the dose administered intravenously, less than 1% of the dose administered orally, and approximately 3-13% of the dose administered by inhalation.

Based on these data, the total bioavailability of ipratropium bromide for oral and inhalation administration is 2% and 7-28%, respectively. Taking this into account, ingested doses of ipratropium bromide do not contribute significantly to systemic exposure.

Pharmacokinetic properties were determined by plasma levels after intravenous administration. A rapid biphasic decrease in plasma levels was observed. The apparent equilibrium volume of distribution (Vdss) is approximately 176 liters (≈ 2.4 l/kg). Binding to plasma proteins is low (less than 20%). Preclinical studies in rats and dogs have shown that quaternary amine ipratropium does not penetrate the blood-brain barrier. The half-life of the active substance in the terminal phase is approximately 1.6 hours.

The total clearance of ipratropium is 2.3 l/min, and the renal clearance is 0.9 l/min. After intravenous administration, approximately 60% of the dose is metabolized, most likely in the liver by oxidation.

In a balance of excretion study, the cumulative renal excretion (6 days) associated with the radioactivity (including the parent substance and other metabolites) was 72.1% after intravenous administration, 9.3% after oral administration and 3.2% after inhalation. The total radioactivity excreted in the feces was 6.3% after intravenous administration, 88.5% after oral administration and 69.4% after inhalation. Thus, most of the radioactivity associated with the substance is excreted through the kidneys. The half-life of the radioactivity bound to the substance (parent substance and metabolites) is 3.6 hours. Binding between the main urinary metabolites and muscarinic receptors is weak. Therefore, urinary metabolites are considered ineffective.

**5.3 Preclinical safety data**

Preclinical data from routine studies of safety pharmacology, repeated dose toxicology, genotoxicity, carcinogenicity, reproduction and development have not revealed any particular hazard to humans.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Sodium chloride

Hydrochloric acid, dilute (for pH-adjustment)

Water for injections

**6.2 Incompatibilities**

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

**6.3 Shelf life**

2 years.

**6.4 Special precautions for storage**

This medicinal product does not require any special temperature storage conditions.

After the first opening of a foil film pouch, keep unused polyethylene containers (nebulas) in the same pouch.

Use the product immediately after first opening of the single-dose container.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of the user.

After use, the remaining solution should be discarded immediately.

**6.5 Nature and contents of container**

4 ml single-dose containers made of low density polyethylene. Strips of five containers are packed in a laminated aluminium foil pouch. 2 or 4 pouches are packed into a carton.

Pack sizes: 10 or 20 single-dose containers.

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

Ipratropiumbromid+Fenoterolhydrobromid "Farmak" nebuliser solution can be mixed with 0.9% sodium chloride.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. No special requirements for disposal.

**7. MARKETING AUTHORISATION HOLDER**

Farmak International Sp. z o.o.

ul. Aleja Jana Pawla II 22

00-133 Warszawa

Polen

**8. MARKETING AUTHORISATION NUMBER(S)**

70590

**9. DATE OF FIRST AUTHORISATION**

14 March 2025

**10. DATE OF REVISION OF THE TEXT**

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