SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Budesonid Zentiva 0.25 mg/mL nebuliser suspension
Budesonid Zentiva 0.5 mg/mL nebuliser suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Invented name> 0.25 mg/mL nebuliser suspension
Each ampoule of 2 mL contains 0.5 mg budesonide.

<Invented name> 0.5 mg/mL nebuliser suspension
Each ampoule of 2 mL contains 1 mg budesonide.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nebuliser suspension.
White homogeneous suspension (pH 4.5).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<Invented name> is indicated for patients with:

• bronchial asthma
• exacerbations of chronic obstructive pulmonary disease in people without signs of acute respiratory insufficiency
• very severe pseudocroup (subglottic laryngitis) requiring hospital treatment

This form of preparation is suitable for patients who are unable to take medicinal products via inhalation spray or turbohaler.

4.2 Posology and method of administration

Posology

Asthma
The dosage of <Invented name> should be adjusted to the need of the individual patient. The dose should be reduced to the minimum needed to maintain good asthma control. At daily doses up to 1 mg, the full dose can be administered once daily. At higher daily doses, the dose is divided into two dosing sessions per day. For children, the highest dose (2 mg per day) is given only in severe asthma and for a limited time. The maintenance dose should be as low as possible.

Initiation of therapy:
Children from 6 months: 0.25-0.5 mg per day. If necessary, the dose can be increased to 1 mg per day.

Adults: 1-2 mg per day.

Maintenance therapy:

Children from 6 months: 0.25-2 mg per day.

Adults: 0.5-4 mg per day. In very severe cases, the dose may be further increased.

In patients with asthma where an increased therapeutic effect is desired, due to the lower risk of systemic side effects, an increased dose of <Invented name> is generally recommended, rather than combined therapy with oral corticosteroids

<Invented name> may permit replacement or significant reduction in dosage of oral glucocorticosteroids while maintaining asthma control. ***When transferral from oral steroids to <Invented name> is started, the patient should be in a relatively stable phase. A high dose of <Invented name> is then given in combination with the previously used oral steroid dose for about 10 days. Thereafter, the oral steroid dose should be gradually reduced (by for example 2.5 mg prednisolone or the equivalent each month) to the lowest possible level. In many cases, it is possible to completely substitute the oral steroid with <Invented name>.*** For further information on the withdrawal of oral corticosteroids, see section 4.4.

Onset of effect in bronchial asthma
After an initial dose, effect may occur after a couple of hours. Full therapeutic effect is only achieved after a few weeks of treatment.

Exacerbations of COPD
Patients should be treated with a daily dose of 4 to 8 mg of <Invented name>, divided into two to four dosing sessions until clinical improvement is achieved, but not longer than 10 days.

The use of nebulized budesonide has not been evaluated in clinical studies in patients with exacerbations of COPD with respiratory failure requiring intubation or intensive care.

Onset of effect in exacerbations of COPD
The time to improvement of symptoms after inhaling <Invented name> for treatment of exacerbations of COPD is comparable to treatment with systemic corticosteroids.

Pseudocroup
In infants and children with pseudocroup, the usual dose is 2 mg of budesonide. This dose is given as a single administration, or as two 1 mg doses separated by 30 minutes. Dosing can be repeated every 12 hours for a maximum of 36 hours or until clinical improvement. For children who cannot breathe through the mouthpiece, a face mask is used.

Volume per dose

Dosage in mg	**Volume of <Invented name>**	
	0.25 mg/ml	**0.5 mg/ml**
0.25	1 ml*	-
0.5	2 ml	-
0.75	3 ml	-
1	-	2 ml
1.5	-	3 ml
2	-	4 ml
4	-	8 ml

* Should be mixed with 0.9% sodium chloride or nebulizer liquid to 2 mL, see 6.6.

Special populations

Renal and hepatic impairment
No data is available for treatment of patients with hepatic or renal impairment. Because budesonide is mainly eliminated by hepatic metabolism, an increased exposure can be expected in patients with severe liver cirrhosis.

Method of administration
Inhalation use

Instruction for correct use of <Invented name>
An inhalation system including the nebulizer with compressor is required to inhale <Invented name> nebulizer suspension. <Invented name> should be administered via a jet nebulizer (e.g., PARI LC PLUS) and compressor (e.g., PARI Boy SX) equipped with a mouthpiece or suitable face mask (e.g., PARI Baby mask with PARI Baby bend). The nebulizer should be connected to an air compressor with an air flow of 5-8 L/min, and the fill volume should be 2-4 mL. The nebulisation time and the dose delivered are dependent on breathing pattern and fill volume.

Aerosol characteristic data for <Invented name> administered by PARI LC PLUS [1]

Performance parameter	**<Invented name> 0.25 mg/mL nebuliser suspension**		**<Invented name> 0.5 mg/mL nebuliser suspension**
	Infant	**Child**	**Adult**
Total drug delivered [µg]	56.8	84.5	307.2
Drug delivery rate [µg/min]	4.6	8.1	31.8
Fine particle mass < 5 µm [mg]	82.9		162.2
Droplet size distribution [µm]	Dv10: 1.9 Dv50: 4.5 Dv90: 9.8		Dv10: 1.9 Dv50: 4.5 Dv90: 9.5

[1] connected with the compressor PARI Boy SX

There is no information available in respect of pulmonary inhalation and deposition patterns across nebuliser systems that have not been studied in the development programme; the use of an alternative untested nebuliser system may alter the pulmonary deposition of the active substance, this in turn may alter the efficacy and safety of the product and dose adjustment may then become necessary.

The ampoule should be detached from the strip, shaken gently for 30 seconds and opened by twisting off the wing tab. The contents of the ampoule should be gently squeezed into the nebulizer cup. The empty ampoule should be thrown away and the top of the nebulizer cup replaced.

For instructions on dilution of the medicinal product before administration, see section 6.6.

The patient should be instructed in the correct use of the <Invented name>. Children should use <Invented name> only under adult supervision.

It is important to instruct the patient
- to carefully read the instructions for use of the nebulizer system which are packed together with each nebulizer.
- that Ultrasonic nebulizers are not suitable for the administration of <Invented name> and therefore must not be used.
- to minimize the risk of oropharyngeal Candida infection, the patient should rinse their mouth out with water after inhaling,.
- to wash the facial skin with water after using a face mask to prevent facial skin irritation.
- to adequately clean and maintain the nebulizer according to the manufacturer's instructions.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

General information
Budesonide is not intended for rapid relief of acute episodes of asthma where an inhaled short-acting bronchodilator is required.

The patient should be advised to contact a doctor if the effect of treatment is generally impaired as repeated inhalations in severe asthma attacks must not delay the initiation of other important therapy. In case of acute deterioration, treatment is supplemented with a short-term oral steroid treatment.

Steroid-dependent patients:
Caution must be taken when treating patients are transferred from oral steroids, as there is a risk of lingering adrenal insufficiency for a considerable period of time. Patients who previously required high doses of corticosteroids in acute situations or who have received treatment for a long time with the maximum recommended dose of inhaled corticosteroids may also be at risk. These patients may show signs and symptoms of adrenal insufficiency when exposed to various stress situations. The addition of systemic steroids should be considered in conjunction with periods of stress or elective surgery.

During transition from oral steroid therapy to <Invented name>, the patient may exhibit previous symptoms such as muscle and joint pain. In these cases, a temporary increase in the oral steroid dose may sometimes be necessary. If, in isolated cases, fatigue, headache, nausea, vomiting or similar symptoms should occur, a generally inadequate steroid effect should be suspected.

Systemic impact of corticosteroid inhalation therapy
Systemic effects may occur during corticosteroid inhalation therapy, especially at high doses for longer periods of treatment. This is less likely to occur with inhaled therapy compared to when corticosteroids are administered orally. Possible systemic side effects include Cushing's syndrome, a Cushing-like symptom picture, adrenal suppression, growth retardation in children and adolescents, decreased bone density, cataracts, glaucoma, and more rarely a range of psychological or behavioral disorders including psychomotor hyperactivity, sleep disturbances, anxiety, depression or aggression (especially in children). It is therefore urgent that the dose of corticosteroid in inhalation titrated to the lowest dose at which effective symptom control of asthma is achieved.

Systemic steroid therapy that is replaced with <Invented name> sometimes reveals allergic diseases, for example, rhinitis and eczema, previously controlled with the systemic treatment.

Use with other concomitant medicines
Concomitant use of ketoconazole, itraconazole, HIV protease inhibitors or other potent CYP3A4 inhibitors should be avoided. If this is not possible, the period between administrations should be be as long as possible (see also section 4.5).

Bronchospasm
As with other inhalation therapy, paradoxical bronchospasm can occur with an increased wheezing breathing immediately after dosing. If this occurs, treatment with inhaled budesonide should be immediately discontinued, the patient assessed and alternative treatment initiated if necessary;

Use in patients with hepatic impairment
Impaired liver function affects the elimination of corticosteroids, leading to lower elimination rate and increased systemic exposure. Pay attention to possible systemic side effects.

Influence on growth
It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroids is regularly monitored. If growth is slowed, therapy should be re-evaluated with the aim of reducing the dose of inhaled corticosteroid, if possible, to the lowest dose at which effective control of asthma is maintained. The benefits of the corticosteroid therapy and the possible risks of growth suppression must be carefully considered. In addition, consideration should be given to referring the patient to a paediatric respiratory specialist.

Oral candidiasis

Oral candidiasis may occur during the therapy with inhaled corticosteroids. This infection may require treatment with appropriate antifungal therapy and in some patients discontinuation of treatment may be necessary (see also section 4.2).

Infections of the respiratory tract
Special caution is necessary in patients with active or quiescent pulmonary tuberculosis, and in patients with fungal or viral infections of the respiratory tract;

Pneumonia in patients with COPD
An increase in the incidence of pneumonia, including pneumonia requiring hospitalization, has been observed in patients with COPD receiving inhaled corticosteroids. There is some evidence of an increased risk of pneumonia with increasing steroid dose, but this has not been demonstrated conclusively across all studies.

There is no conclusive clinical evidence for intra-class differences in the magnitude of the pneumonia risk among inhaled corticosteroid products.

Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations.

Risk factors for pneumonia in patients with COPD include current smoking, older age, low body mass index (BMI) and severe COPD.

Visual impairment
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 Interaction with other medicinal products and other forms of interaction

The metabolism of budesonide is primarily mediated by CYP3A4. Inhibitors of this enzyme, e.g. ketoconazole and itraconazole, troleandomycin, HIV protease inhibitors and cobicistat-containing products can therefore increase systemic exposure to budesonide, (see section 4.4 and 5.2). Since there is no data to support a dosage recommendation, the combination should be avoided. If this is not possible, the period between treatments should be as long as possible and a reduction of the budesonide dose could also be considered.

Limited data about this interaction for high-dose inhaled budesonide indicate that marked increases in plasma levels (on average four-fold) may occur if itraconazole, 200 mg once daily, is administered concomitantly with inhaled budesonide (single dose of 1 000 µg).

Raised plasma concentrations of and enhanced effects of corticosteroids have been observed in women concomitantly treated with estrogens and contraceptive steroids, but no effect has been observed with budesonide and concomitant intake of low dose combination oral contraceptives.

Because adrenal function may be suppressed, an ACTH stimulation test for diagnosing pituitary insufficiency might show false results (low values).

4.6 Fertility, pregnancy and lactation

Pregnancy
Most results from prospective epidemiological studies and data, received after marketing authorization approval worldwide, has not been able to demonstrate an increased risk of adverse reactions in the foetus and the newborn baby due to the use of inhaled budesonide during pregnancy.

It is important for both the foetus and mother to maintain adequate asthma treatment during pregnancy. The administration of budesonide during pregnancy requires that the benefits for the mother are weighed against the risks to the foetus.

Animal studies have shown that glucocorticosteroids can induce malformations (see section 5.3), This is not likely to be relevant for humans given recommended doses.

Animal studies have also identified that prenatal overexposure to glucocorticoids may be associated with an increased risk of intrauterine growth retardation, adult cardiovascular disease and permanent changes in glucocorticoid receptor density, neurotransmitter turnover and behavior at exposures below the teratogenic dose range.

During pregnancy, the lowest effective dose of budesonide should be sought while at the same time taking into account the risk of a worsening asthma condition. .

Breastfeeding
Budesonide is excreted in breast milk. However, at therapeutic doses of budesonide no effects on the suckling child are anticipated as the systemic exposure of the breastfed child is negligible. Budesonide can be used during breast feeding.

4.7 Effects on ability to drive and use machines

Budesonide has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following definitions apply to the incidence of undesirable effects: 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).

Table 3 Adverse Drug Reactions

System Organ Class	Frequency	Adverse Reactions
Infections and infestations	Common	Oropharyngeal candidiasis, pneumonia (in COPD patients)
Immune system disorders	Rare	Immediate and delayed hypersensitivity reactions* including rash, contact dermatitis, urticaria, angioedema and anaphylactic reactions
Endocrine disorders	Rare	Signs and symptoms of systemic corticosteroid effects, including adrenal suppression and growth retardation**
Eye disorders	Uncommon	Cataract***, vision blurred (see also section 4.4)
	Not known	Glaucoma
Psychiatric disorders	Uncommon	Anxiety, depression
	Rare	Restlessness, nervousness, behavioural changes (predominantly in children)
	Not known	Sleep disorders, psychomotor hyperactivity, aggression
Nervous system disorders	Uncommon	Tremor
Respiratory, thoracic and mediastinal disorders	Common	Cough, throat irritation
	Rare	Bronchospasm, dysphonia, hoarseness
Skin and subcutaneous tissue disorders	Rare	Bruising

Musculoskeletal and connective tissue disorders	Uncommon	Muscle spasm

* refer to Description of selected adverse reactions; facial skin irritation, below
** refer to Paediatric population, below
*** refer to eye disorder, below

Occasionally, signs or symptoms of systemic glucocorticosteroid-side effects may occur with inhaled glucocorticosteroids, probably depending on dose, exposure time, concomitant and previous corticosteroid exposure, and individual sensitivity (see section 4.4).

Immune system disorders
Facial skin irritation, as an example of a hypersensitivity reaction, has occurred in some cases when a nebuliser with a face mask has been used. To prevent irritation, the facial skin should be washed with water after use of a face mask.

Infections and infestations
Candidal infection in the oropharynx may result from local drug deposition. Advising the patient to rinse the mouth out with water after each dosing will minimise the risk.

Eye disorders
In placebo-controlled studies, cataract was also reported as an uncommon side effect in the placebo group.

Psychiatric disorders
Clinical trials with 13,119 patients on inhaled budesonide and 7,278 patients on placebo have been pooled. The frequency of anxiety was 0.52% on inhaled budesonide and 0.63% on placebo; that of depression was 0.67% on inhaled budesonide and 1.15% on placebo.

Paediatric population
Due to the risk of growth retardation in the paediatric population, growth should be monitored as described in section 4.4.

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 the national reporting system listed in Appendix V.

4.9 Overdose

Acute overdose with <Invented name> suspension for nebulizer, even high doses, is not expected to cause any clinical problems. When used chronically in high doses, systemic effects of glucocorticosteroids such as hypercortisolism and adrenal suppression may occur.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for obstructive airway diseases, Glucocorticoids.
ATC Code: R03BA02.

Mechanism of action
Budesonide is a glucocorticosteroid with potent local anti-inflammatory effect.

The exact mechanism of action of glucocorticosteroids in the treatment of asthma is not full elucidated. Anti-inflammatory effects such as inhibited release of inflammatory mediators and

inhibition of cytokine-mediated immune responses, is likely important. Budesonide activity measured as affinity to glucocorticosteroid receptors is about 15 times higher than that of prednisolone

Clinical efficacy
Budesonide has anti- inflammatory effects shown as reduced bronchial obstruction during both the early and late phase of an allergic reaction. Budesonide reduces histamine and methacholine reactivity of the respiratory tract in hyperreactive patients.

Studies have shown that the earlier treatment with budesonide is initiated after the onset of asthma, the better lung function can be expected.

Clinical safety

Effect on plasma cortisol concentration
Studies in healthy volunteers treated with budesonide Turbuhaler have shown dose-related effects on plasma and urinary cortisol. At recommended doses, budesonide Turbuhaler causes significantly less effect on adrenal function than prednisone 10 mg, as shown via ACTH stimulation testing.

Paediatric population

Clinical effect – asthma
The efficacy of budesonide has been evaluated in a large number of studies, and it has been shown that budesonide is effective both in adults and children as once- or twice-daily medication for prophylactic treatment of persistent asthma. Some examples of representative studies are given below.

In children from the age of 3, systemic effects have not been demonstrated at doses up to 400 micrograms per day. In the range of 400-800 micrograms per day, biochemical signs of systemic effects may appear. At daily doses above 800 micrograms, such signs are common. These data refer to budesonide administered as inhalation spray and inhalation powder.

Asthma itself, as well as inhaled corticosteroids, can slow growth. Limited data from long-term studies indicate that most children and adolescents treated with inhaled budesonide eventually reach their adult height goal. However, a small initial, but transient, reduction in growth (about 1 cm) has been observed. The growth reduction usually occurs during the first year of treatment.

Exercise-induced asthma
Inhaled therapy with budesonide is effective in preventing exercise-induced asthma.

Clinical effect - exacerbations of COPD
Several studies with nebulized budesonide 4-8 mg/day have shown efficacy in the treatment of COPD exacerbations.

The efficacy of nebulized budesonide was evaluated in an open-label, randomized, controlled trial in 78 hospitalized patients with acute exacerbations of COPD in two parallel groups receiving nebulized budesonide (n=37) 4 mg/day (2 mg twice daily) or intravenous infusion of prednisolone 120-180 mg/day (n=41) for 7-14 days. Patients treated with nebulized budesonide or prednisolone showed similar improvements in FEV1, Sp02 (oxygen saturation as measured by pulse oximetry) and symptoms (COPD Assessment Test (CAT).

In a multicenter, randomized, controlled, single-blind study in 471 patients with acute exacerbations of COPD, patients were treated with nebulized budesonide 6 mg/day (2 mg three times daily) or intravenously injected methylprednisolone (40 mg/day) for 10 days. Clinical efficacy of nebulized budesonide versus systemic methylprednisolone as measured by FEV1, PaCO2 and symptoms (CAT) was comparable, while Pa02 improved more in the methylprednisolone group.

In a double-blind, randomized, placebo-controlled trial of 199 patients with acute exacerbations of COPD, patients were treated with nebulized budesonide 8 mg/day (2 mg four times daily (n=71) or

prednisolone 30 mg orally every 12 hours (n=62) or placebo (n=66) for three days. Improvement in FEV1 after bronchodilators compared to placebo was 0.10 litres for budesonide and 0.16 litres for prednisolone; the difference between the active treatments was not statistically significant. The proportion of patients who showed clinical improvement in FEV1 of at least 0.15 litres after bronchodilators was greater in the nebulized budesonide (34%) and prednisolone (48%) groups than in the placebo group (18%). The differences were statistically significant for both active treatments compared to placebo ($p < 0.05$), but not between the active treatments.

Clinical effect - croup
A number of studies in children with croup have compared budesonide with placebo. Examples of representative studies evaluating the use of budesonide for the treatment of children with croup are given below.

Efficacy in children with mild to moderate croup
A randomized, double-blind placebo-controlled trial in 87 children (aged 7 months to 9 years), admitted to hospital with a clinical diagnosis of croup, was conducted to determine whether budesonide improves croup symptom scores or shortens the duration of stay in hospital. An initial dose of budesonide (2 mg) or placebo was given followed by either budesonide 1 mg or placebo every 12 hours. Budesonide statistically significantly improved croup score at 12 and 24 hours and at 2 hours in patients with an initial croup symptom score above 3. There was also a 33% reduction in the length of stay.

Efficacy in children with moderate to severe croup
A randomized, double-blind, placebo-controlled study compared the efficacy of budesonide and placebo in the treatment of croup in 83 infants and children (aged 6 months to 8 years) admitted to hospital for croup. Patients received either budesonide 2 mg or placebo every 12 h for a maximum of 36 h or until discharge from hospital. The total croup symptom score was assessed at 0, 2, 6, 12, 24, 36 and 48 hours after the initial dose. At 2 hours, both the budesonide and placebo groups showed a similar improvement in croup symptom score, with no statistically significant difference between the groups. By 6 hours, the croup symptom score in the budesonide group was statistically significantly improved compared with the placebo group, and this improvement versus placebo was similarly evident at 12 and 24 hours.

5.2 Pharmacokinetic properties

Absorption
In adults the systemic availability of budesonide following administration of budesonide nebuliser suspension via a jet nebuliser is approximately 15% of the nominal dose and 40% to 70% of the dose delivered to the patients. A minor fraction of the systemically available drug comes from swallowed drug. The maximal plasma concentration, occurring about 10 to 30 min after start of nebulisation is approximately 4 nmol/L after a single dose of 2 mg.

Distribution
Budesonide has a volume of distribution of approximately 3 L/kg. Plasma protein binding averages 85 - 90%.

Biotransformation
Budesonide undergoes extensive (≈ 90%) first pass metabolism in the liver to metabolites of low glucocorticosteroid activity. The glucocorticosteroid activity of the major metabolites, 6β-hydroxybudesonide and 16α-hydroxyprednisolone, is less than 1% of that of budesonide. The metabolism of budesonide is primarily mediated by CYP3A4, a subfamily of cytochrome P450.

Elimination
The metabolites of budesonide are excreted unchanged or in conjugated form mainly via the kidneys. No unchanged budesonide has been detected in the urine. Budesonide has high systemic clearance (approximately 1.2 L/min) in adults, and the terminal half-life of budesonide after intravenous dosing averages 2-3 hours.

Linearity/ non-linearity

The kinetics of budesonide is dose-proportional at clinically relevant doses.

Pediatric population
Budesonide has a systemic clearance of approximately 0.5 L/min in 4 - 6 years old asthmatic children. Per kg body weight children have a clearance which is approximately 50% greater than in adults. The terminal half-life of budesonide after inhalation is approximately 2.3 hours in asthmatic children. This is about the same as in healthy adults. In 4 - 6 years old asthmatic children, the systemic availability of budesonide following administration of budesonide nebuliser suspension via a jet nebuliser (Pari LC Jet Plus® with Pari Master® compressor) is approximately 6% of the nominal dose and 26% of the dose delivered to the patients. The systemic availability in children is about half of that in healthy adults.

The maximal plasma concentration, occurring approximately 20 min after start of nebulisation is approximately 2.4 nmol/L in 4 - 6 year old asthmatic children after a 1 mg dose. The exposure (C_{max} and AUC) of budesonide following administration of a single 1 mg dose by nebulisation to 4 - 6 year old children is comparable to that in healthy adults given the same delivered dose by the same nebuliser system.

Renal impairment
The pharmacokinetics of budesonide in patients with renal impairment are unknown.

Hepatic impairment
The exposure of budesonide may be increased in patients with liver disease

5.3 Preclinical safety data

In toxicity studies, budesonide has only produced the expected glucocorticoid effects.
Budesonide has not shown any genotoxic effects.

In animal reproduction studies, corticosteroids such as budesonide have been shown to induce malformations of various kinds (cleft palate, skeletal malformations). However, these animal experimental results do not seem to be relevant in humans at the recommended doses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate E385
Sodium chloride
Polysorbate 80 E433
Citric acid E330
Sodium citrate E331
Hydrochloric acid for pH adjustment
Sodium hydroxide for pH adjustment
Water for injection

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

For 0.25 mg/mL and 0.5 mg/mL – 2 years

Shelf life after opening the aluminium pouch: 3 months.

Shelf life after opening of the vial 12 hours.

6.4 Special precautions for storage

Do not freeze.
Store in the original package and pouch in order to protect from light.
This medicinal product does not require any special temperature storage conditions.

6.5 Nature and contents of container

2 mL nebuliser suspension in a single-dose LDPE ampoule. Sheets of 5 ampoules are packed in a sealed aluminium foil pouch (PET/Alu/PE).

On each single-dose ampoule there is a line indicating 1 mL when holding the ampoule upside down.

Pack sizes: 10, 20, 40, 60, 80 and 120 ampoules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

<Invented name> can be mixed with saline 9 mg/ml (0.9%), the mixture should be used within 30 minutes.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7. MARKETING AUTHORISATION HOLDER

<To be completed nationally>

8. MARKETING AUTHORISATION NUMBER

<To be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<To be completed nationally>

10. DATE OF REVISION OF THE TEXT

2025-04-17