SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Salbutamol Neutec 2.5 mg nebuliser solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2.5 mL single-dose container contains 2.5 mg of salbutamol (as salbutamol sulphate), which is equivalent to 1 mg of salbutamol per 1 mL.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Nebuliser solution.
A clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Salbutamol Neutec is indicated in adults, adolescents and children, aged 4 to 11 years.

Salbutamol Neutec is indicated for symptomatic treatment of acute reversible airway obstruction in patients with asthma or in patients with severe chronic obstructive pulmonary disease (COPD) when the use of a metered dose inhaler or dry powder inhaler is ineffective or impossible.

4.2 Posology and method of administration

Posology

Adults and adolescents aged 12 years and over
The starting dose of salbutamol by wet inhalation is 2.5 mg. This may be increased to 5 mg. Treatment may be repeated up to four times daily. In adult dosing, up to 40 mg per day, can be given under strict medical supervision in hospital for the treatment of severe airways obstruction.

Paediatric population
For children aged 4 to 11 years: The starting dose of salbutamol by wet inhalation is 2.5 mg. This may be increased to 5 mg. Treatment may be repeated up to four times daily.

Other pharmaceutical forms may be more appropriate for administration in children under 4 years old.

As transient hypoxaemia may occur, supplemental oxygen therapy should be considered.

Method of administration

Salbutamol inhaled formulations are administered by the inhaled route only, to be breathed in through the mouth with a nebuliser. The solution must not be injected or swallowed.

Salbutamol has a duration of action of 4 to 6 hours in most patients.
Salbutamol Neutec is intended to be used undiluted.

Salbutamol Neutec may be administered from a suitable nebuliser, e.g. jet nebuliser or mesh nebuliser, after the single dose ampoule has been opened and its contents transferred to the nebuliser chamber. The use of the solution for nebulization is not only limited to the given examples but can also be based

on the experience of the clinical professional. For full instructions on the use of the nebuliser the patient should be instructed to read the leaflet of the respective device carefully before starting the inhalation.

Active substance delivery characteristics were studied *in vitro* using a jet nebuliser and a mesh nebuliser device:

Nebuliser	**Active substance**	**Breathing pattern**	**Mass median aerodynamic diameter** (micrometer)	**Active substance delivery rate** (mg/min)	**Total active substance delivered** (mg/2.5 mL)
Jet nebuliser*	Salbutamol	Adult	4.5	0.13	0.39
		Child		0.07	0.21
Mesh nebuliser**	Salbutamol	Adult	5.2	0.18	0.95
		Child		0.16	0.82

* PARI LC Plus Nebuliser and PARI BOY® SX Compressor was used in *in vitro* studies
** Deepro HCM-86C Nebuliser was used in *in vitro* studies

No information is available in respect of pulmonary inhalation and deposition patterns across nebuliser systems that have not been studied.
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.

As many nebulisers operate on a continuous flow basis, it is likely that nebulised medicinal product will be released in the local environment. Salbutamol Neutec should therefore be administered in a well-ventilated room, particularly in hospitals when several patients may be using nebulisers in the same space at the same time.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

General considerations

Patients who are prescribed regular anti-inflammatory therapy (e.g., inhaled corticosteroids) should be advised to continue taking their anti-inflammatory medication even when symptoms decrease, and they do not require Salbutamol Neutec.

Increasing use of short-acting inhaled beta-2 agonists to control symptoms indicates deterioration of asthma control, and patients should be warned to seek medical advice as soon as possible. If either the usual relief is diminished or the usual duration of action reduced, the patient’s therapy plan should be reassessed.

Overuse of short-acting beta-agonists may mask the progression of the underlying disease and contribute to deteriorating asthma control, leading to an increased risk of severe asthma exacerbations and mortality.

Patients who take more than twice a week “as needed” salbutamol, not counting prophylactic use prior to exercise, should be re-evaluated (i.e., daytime symptoms, night- time awakening, and activity limitation due to asthma) for proper treatment adjustment as these patients are at risk for overuse of salbutamol.

Bronchodilators should not be the only or main treatment in patients with persistent asthma. In patients with persistent asthma, maintenance treatment such as inhaled glucocorticoids is warranted to achieve

and maintain control. Failing to respond to treatment with salbutamol may signal a need for urgent medical advice or treatment.

Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to starting or increasing corticosteroid therapy.

A responsible adult must supervise the treatment with salbutamol in children.

Salbutamol should be administered cautiously to patients with thyrotoxicosis.

Salbutamol inhalation formulations must not be used to prevent or inhibit premature labour or threatened abortion.

Acute angle closure glaucoma

A small number of cases of acute angle closure glaucoma have been reported in patients treated with a combination of nebulised salbutamol and ipratropium bromide. A combination of nebulised salbutamol with nebulised anticholinergics should therefore be used cautiously. Patients must receive adequate instruction in correct administration and be warned not to let the solution or mist enter the eye.

Serious hypokalaemia

Potentially serious hypokalaemia may result from beta-2 agonist therapy mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

Metabolic changes

In common with other beta-adrenoceptor agonists, Salbutamol can induce reversible metabolic changes, for example increased blood sugar levels. The diabetic patient may be unable to compensate for this and the development of ketoacidosis has been reported. Concurrent administration of corticosteroids can exaggerate this effect.

Lactic acidosis has been reported very rarely in association with high therapeutic doses of intravenous and nebulised short-acting beta-agonist therapy, mainly in patients being treated for an acute asthma exacerbation (see section 4.8). Increase in lactate levels may lead to dyspnoea and compensatory hyperventilation, which could be misinterpreted as a sign of asthma treatment failure and lead to inappropriate intensification of short-acting beta-agonist treatment. It is therefore recommended that patients are monitored for the development of elevated serum lactate and consequent metabolic acidosis in this setting.

Cardiovascular effects

Cardiovascular effects may be seen with sympathomimetic medicinal products, including salbutamol. There is some evidence from post-marketing data and published literature of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol must be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

Paradoxical bronchospasm

As with other inhalation therapy, paradoxical bronchospasm may occur, resulting in an immediate increase in wheezing after dosing. This should be treated immediately with an alternative presentation

or a different fast-acting inhaled bronchodilator, if immediately available. The specific salbutamol presentation should be discontinued, and if necessary, a different fast-acting bronchodilator instituted for ongoing use.

4.5 Interaction with other medicinal products and other forms of interaction

Salbutamol and non-selective beta-blocking medicinal products such as propranolol, should not usually be prescribed together.

A small number of cases have been reported where combined treatment of nebulised salbutamol and ipratropium bromide have triggered narrow angle glaucoma. The combination should be avoided in predisposed patients.

Hypokalaemia can be potentiated in the event of concomitant treatment with xanthine derivatives, steroids or diuretics (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Salbutamol crosses the placental barrier. Experience with the use of short-acting beta-agonists during early pregnancy suggests that there is no harmful effect at the doses normally used in inhalation therapy. High systemic doses at the end of pregnancy can cause inhibition of uterine contractions and may give rise to the occurrence of beta-2-specific foetal/neonatal reactions such as tachycardia and hypoglycaemia. With inhalation therapy at recommended doses, the occurrence of these adverse side effects at the end of pregnancy is not expected. Animal studies have shown reproductive toxicity (see section 5.3).

Salbutamol may be used during pregnancy when considered necessary. High doses should only be used when strictly necessary.

Breast-feeding

Information on whether salbutamol passes into breast milk is insufficient to assess the risk to the child.

Fertility

There is no information on the effect of salbutamol on human fertility. No negative effects on fertility were observed in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

Salbutamol Neutec has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: 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) including isolated reports. Very common and common reactions were generally determined from clinical trial data. Rare and very rare reactions were generally determined from spontaneous data.

System organ class	Adverse reaction	Frequency
Immune system disorders	Angioedema	Very Rare
	Urticaria	Very Rare
	Bronchospasm	Very Rare
	Hypotension	Very Rare

System organ class	Adverse reaction	Frequency
	Collapse	Very Rare
Metabolism and nutrition disorders	Hypokalaemia	Rare
	Lactic acidosis	Very Rare
Nervous system disorders	Tremor	Common
	Headache	Common
	Psychomotor hyperactivity	Very Rare
Cardiac disorders	Tachycardia	Common
	Palpitations	Uncommon
	Arrhythmia	Very Rare
	Atrial fibrillation	Very Rare
	Supraventricular tachycardia	Very Rare
	Extrasystoles	Very Rare
	Myocardial ischaemia	Not known
Vascular disorders	Vasodilatation	Rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm paradoxical	Very Rare
Gastrointestinal disorders	Stomatitis	Uncommon
	Throat irritation	Uncommon
Musculoskeletal and connective tissue disorders	Muscle cramps	Uncommon

Regarding undesirable effects linked to metabolism and nutrition disorders, potentially serious hypokalaemia may result from beta-2 agonist therapy. Furthermore, Lactic acidosis has been reported very rarely in patients receiving intravenous and nebulised salbutamol therapy for the treatment of acute asthma exacerbation.

Regarding undesirable effects linked to respiratory and thoracic disorders, as with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This has to be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator. Inhaled salbutamol should be discontinued immediately, the patient assessed, and, if necessary, alternative therapy instituted.

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

Doses above the recommended maximum daily dose (40 mg) have been reported to cause mild to moderate toxicity in all patient groups in the post-marketing reports concerning other products containing the same active ingredient.

Symptoms

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events: tachycardia, palpitations, arrhythmia, restlessness, sleep disturbances, chest pain and marked tremor, especially in the hands, but also of the whole body. Nausea, dizziness, increased systolic blood pressure and decreased diastolic blood pressure may be observed.

Occasionally, psychotic reactions have been observed after an excessive salbutamol dosage.

Hypokalaemia, hyperglycaemia, hyperlipidaemia and hyperketonaemia may occur following overdose

with salbutamol.

Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of short-acting beta-agonist therapy, therefore monitoring for elevated serum lactate and consequent metabolic acidosis (particularly if there is persistence or worsening of tachypnea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

Management

Treatment of an overdose with a beta-2 sympathomimetic active substance is mainly symptomatic. Depending on individual circumstances, the following measures may be considered:

- Gastric lavage, if warranted.
- Activated charcoal.
- Give diazepam in the event of agitation.
- For cardiac symptoms of salbutamol overdose, a cardioselective beta blocker may be considered, but beta-2-blockers should be used with caution and avoided where possible in patients with a history of bronchospasm. In these patients, ECG monitoring is indicated.
- In the event of a decrease in blood pressure, volume substitution is recommended (e.g. plasma expanders).
- If hypokalaemia develops, serum potassium levels should be monitored and, if appropriate, it may be necessary to administer electrolytes.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Adrenergics, inhalants. Selective beta-2-adrenoreceptor agonists

ATC code: R03AC02

Mechanism of action and pharmacodynamic effects

Salbutamol is a selective beta-2-adrenoceptor agonist. At therapeutic doses it acts on the beta-2-adrenoceptors of bronchial muscle providing short acting (4 to 6 hours) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

5.2 Pharmacokinetic properties

Salbutamol is primarily metabolised in the liver. 90 % of an oral dose is excreted via urine and 10 % via faeces within 24 hours. The quantity excreted via urine amounts to approximately 40 % of unchanged salbutamol.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. The effects observed in toxicity studies are related to the beta-adrenergic activity of salbutamol. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50 mg/kg/day orally throughout pregnancy resulted in no significant negative effects on fertility, embryofoetal development, litter size, birth weight or growth rate, with the exception of a reduced number of surviving offspring at day 21 postpartum at a dose of 50 mg/kg/day. In mice, cleft palate was seen in foetuses at doses four times the maximum human oral dose. No teratogenic effect was demonstrated at relevant doses in rats and rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sulfuric acid (for pH adjustment)
Water for injections

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30 °C.

Keep single-dose containers in the foil overwrap pouch and/or carton in order to protect from light and moisture.

6.5 Nature and contents of container

Single-dose containers in packs of 20.

Salbutamol Neutec is contained in disposable translucid low-density polyethylene single-dose containers in strips of 5, overwrapped in an aluminium foil pouch.

6.6 Special precautions for disposal and other handling

Since the single-dose containers contain no preservatives, it is important that the contents are used immediately after opening and that a fresh single-dose container is used for each administration to avoid microbial contamination. Partly used, open or damaged single-dose containers should be discarded.

Do not use the product if discoloured.

Any unused solution in the chamber for the nebuliser must be discarded.

No special requirements for disposal. 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(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2024-03-14