1. NAME OF THE MEDICINAL PRODUCT

Salbutamol Sandoz 100 microgram/dosis CFK-vrij, aërosol, suspensie

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose (ex-valve) contains 100 micrograms of salbutamol (as salbutamol sulfate).
Target delivered dose is 80 micrograms of salbutamol (as sulfate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Pressurised inhalation, suspension
White to off white colour suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

(Invented name) 100 micrograms/actuation pressurized inhalation suspension is indicated in adults, adolescents and children 4 to 11 years of age (for children under 4 years see sections 4.2 and 5.1):

- for the treatment of reversible airways diseases with narrowing of the airways due to spasm of the bronchial muscles (obstructive airways diseases), such as bronchial asthma (as rescue medication in mild, moderate or severe asthma), chronic obstructive pulmonary disease (COPD) and (hyper)inflated lung (emphysema).

• as prophylaxis of bronchospasm induced by physical exercise or before exposure to a known and unavoidable allergenic stimulus.

4.2 Posology and method of administration

Posology

Adults and adolescents aged 12 years and older
Relief of attacks: 1-2 inhalations (100 – 200 micrograms), as required.
Maximum dose: 8 inhalations (800 micrograms) per day.

To prevent allergen- or exercise-induced symptoms, two inhalations (200 micrograms) taken 10-15 minutes before challenge.

Children below 12 years of age
Relief of attacks: 1 inhalation (100 micrograms) as required. The dose may be increased to two inhalations (200 micrograms), if required.

Children <4 years can benefit from the use of this medicinal product by using an inhalation chamber for paediatric patients fitted with a mask (such as Babyhaler) (see section 5.1).

Maximum dose: On-demand use of this medicine should not exceed 2 inhalations (200 micrograms) four times daily. Reliance on such frequent supplementary use, or a sudden increase in dose, indicates poorly controlled or deteriorating asthma (see section 4.4).

To prevent allergen- or exercise-induced symptoms, one inhalation, or two if necessary, should be taken 10-15 minutes before challenge. The maximum dose is up to two inhalations 4 times daily.

Method of administration

(Invented name) is for administration by inhalation via the mouth only.

Salbutamol has a duration of action of 4 to 6 hours in most patients.

Inhaled salbutamol should be used on demand for the relief of acute bronchospasm and as rescue medication in mild, moderate or severe asthma as long as it does not delay the adoption and regular use of inhaled corticosteroid therapy.

Notice: Longer-term treatment should be symptom-oriented and only in conjunction with continuous anti-inflammatory therapy (see section 4.4.).

Precautions to be taken before handling or administering the medicinal product

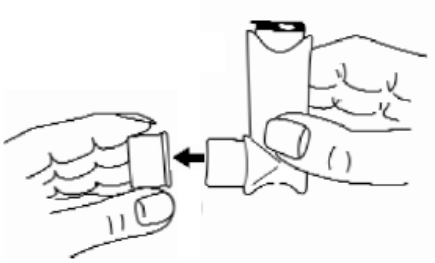
Handling
A faulty inhalation technique with pressurised inhalers is very common. It is therefore important that the patient be instructed in the correct inhalation technique. The patient's inhalation technique should be checked at visits.

Patients who have difficulty coordinating the MDI can use a *Volumatic* or *Babyhaler* (children up to 5 years of age) with this medicine. For instructions on the use of the spacer device, please refer to the information leaflets of the spacer devices.

Inhaler check
Before using the inhaler for the first time, or if it has not been used for 5 days or more, it is important to check that the spray is functioning. The protective cap should be removed, the inhaler be shaken and sprayed twice into the air.

Instructions for use
The inhalation should be performed sitting or standing, wherever possible.

1. The protective cap should be removed.
2. The inside and outside the inhaler should be checked for foreign particles to make sure that the mouthpiece is clean.

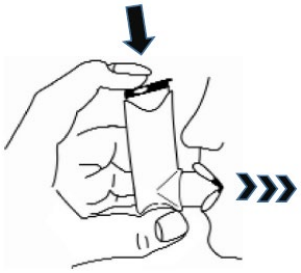


3. The inhaler should be shaken well for a couple of seconds before use to make sure that the contents of the inhaler are mixed properly.

4. The inhaler should be held upright with the bottom of the container upwards. The thumb should be put on the base, below the mouthpiece. The patient should breathe out as much air as reasonably possible, but not to breathe into the mouthpiece.

5. The mouthpiece should be placed in the mouth between the teeth and the lips around it without biting it.

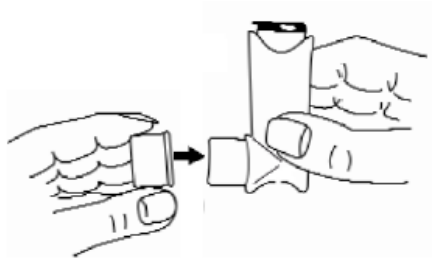
6. Just after starting to breathe in through the mouth, the patient should press down on the top of the inhaler to release a puff while still breathing in steadily and deeply.



7. The breath should be held, the inhaler taken from the mouth and the finger from the top of the inhaler. The breath should be held as much as reasonably possible.

8. If another puff is required, the inhaler should be held upright and the patient should wait about half a minute before repeating steps 3 to 7.

9. After use, the mouthpiece should always be covered to keep dust and foreign particles out of the mouthpiece. The mouthpiece cover should be replaced firmly and snapped into position.



Cleaning
For instructions on cleaning the inhaler see section 6.6.

Inhaler content:
The spray should be shaken to check the remaining amount of medicine in it. (Invented name) should not be used if no liquid can be detected in the inhaler while shaking.

Cold temperature use:
If the inhaler has been stored beneath 0 °C, it has to be warmed in the hands of the patient for 2 minutes, be shaken and sprayed twice into the air before use.

4.3 Contraindications

Hypersensitivity to the active substance or to the excipient listed in section 6.1.

4.4 Special warnings and precautions for use

Treatment of asthma normally follows a gradually adjusted programme, and the patient's response to therapy must be monitored clinically and with lung function tests. An increased use of beta-2 agonist indicates deterioration of the asthma, patients should be warned to seek medical advice as soon as possible, and the need for reassessment of the treatment.

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 (Invented name).

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 (e.g., 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.

Sudden and progressive deterioration of asthma control is potentially life-threatening. If the effect of salbutamol becomes less effective, the patient should be warned to seek medical advice, as repeated inhalations must not delay the initiation of other important therapy. Treatment with or increasing the dose of (inhaled) corticosteroids should be considered.

Bronchodilators should not be the only or main treatment in patients with persistent asthma.

In the following cases salbutamol should only be used with caution and if strictly indicated:
- serious cardiac disorders, in particular recent myocardial infarction
- coronary heart disease, hypertrophic obstructive cardiomyopathy and tachyarrhythmia
- severe and untreated hypertension
- aneurysm
- diabetes which is difficult to control
- pheochromocytoma
- uncontrolled hyperthyroidism
- untreated hypokalaemia
- concomitant use of cardiac glycosides (see section 4.5).

Cardiovascular effects may be seen with sympathomimetic medicinal products, including salbutamol.

There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with beta agonists. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol should 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.

Potentially serious hypokalaemia due to the use of ß2 sympathomimetics may occur, especially with nebulization or parenteral administration. Caution is advised in acute severe asthma, as this hypokalaemia may be enhanced by concomitant treatment with xanthine derivatives, steroids, and diuretics and by hypoxia. It is recommended to monitor serum potassium levels in such situations."

When initiating treatment with salbutamol in diabetics, extra checks of blood glucose levels are recommended, as beta2-agonists increase the risk of hyperglycaemia.

As with other inhalation therapy, paradoxical bronchospasm may occur, with increased wheezing immediately after administration. Should this occur, the preparation should be immediately discontinued and replaced by alternative treatment.

Parents or caregivers of babies and young children for whom 200 micrograms of Salbutamol does not produce the desired results should consult a doctor."
Reports of dental caries have been reported with the use of salbutamol. It is recommended with especially in children, pay attention to good oral hygiene and regular dental check-ups."

4.5 Interaction with other medicinal products and other forms of interaction

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

Salbutamol and non-selective β-receptor blocking medicinal products should not usually be prescribed together. In patients with asthma administration of β-receptor blocking medicinal products is associated with a risk of severe bronchoconstriction.

When administering halogenated anaesthetics, e.g. halothane, methoxyflurane or enflurane, to patients treated with salbutamol an increased risk of severe dysrhythmia and hypotension must be expected. If anaesthesia with halogenated anaesthetics is planned, care should be taken to ensure that salbutamol is not used for at least 6 hours before initiation of the anaesthesia.

Monoamine oxidase inhibitors and tricyclic antidepressants may increase the risk of cardiovascular side-effects.

Salbutamol induced hypokalemia may increase susceptibility to digoxin induced arrhythmias.

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
As salbutamol is probably secreted in breast milk, its use in breast-feeding mothers requires careful consideration. A risk to the suckling child cannot be excluded. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with this medicine should be made taking into account the benefit of breast-feeding to the child and the benefit of salbutamol therapy to the woman.

Fertility
There is no information on the effects of salbutamol on human fertility. There were no adverse effects on fertility in animals (see section 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Tabulated summary of adverse reactions
Frequency is defined using the following convention:
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).

System Organ system	Adverse reactions	Frequency
Immune System Disorders	Hypersensitivity reactions including angioedema, collapse, bronchospasm, hypotension, urticaria	Very rare
Metabolism and nutrition disorders	Hypokalaemia	Rare
	Lactic acidosis (see section 4.9)	Not known
Nervous system disorders	Tremor, headache	Common
	Hyperactivity, sleep disturbances	Very rare
Cardiac Disorders	Tachycardia	Common
	Palpitations	Uncommon
	Cardiac arrhythmia (e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles)	Very rare
	Myocardial ischaemia* (see section 4.4)	Not known
Vascular disorders	Peripheral vasodilatation	Rare
Respiratory, thoracic and mediastinal disorders	Paradoxical bronchospasm**	Very rare
Gastrointestinal Disorders	Irritation in mouth and throat	Uncommon
Musculoskeletal and connective tissue disorders	Muscle cramps	Common

* Reported spontaneously in post-marketing data therefore frequency regarded as unknown.
** As with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with an alternative presentation or a

different fast-acting inhaled bronchodilator. Salbutamol should be discontinued immediately, the patient assessed, and, if necessary, alternative therapy instituted.

Undesirable effects typical of beta2-agonists, such as skeletal muscle tremor and palpitations, can occur especially at the beginning of treatment, and are often dose-dependent.

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

Symptoms of an overdose
In case of overdose, the adverse reactions already named may appear very rapidly and possibly to an increased extent.

Typical symptoms are:
headache, seizures, tachycardia, palpitations, arrhythmias, agitation, excitation, dyssomnia, chest pain and severe tremor, particularly affecting hands, but also the whole body.

Gastrointestinal complaints including nausea can occur, particularly after oral intoxication.

Psychotic reactions have uncommonly been observed after excessive salbutamol doses.

In association with overdose of salbutamol, displacements of potassium into the intracellular space may occur with the consequence of hypokalaemia as well as hyperglycaemia.

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 tachypnoea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

Therapeutic measures in case of an overdose
Treatment of overdoses with beta-sympathomimetics is mainly symptomatic. The following measures can be recommended:

- Gastric lavage should be considered if large quantities of the medicinal product have been swallowed inadvertently. Activated charcoal and laxatives may have a positive influence on undesired absorption.
- Cardiac symptoms may be treated with a cardioselective beta-blocker, but an elevated risk that bronchospasticity occurs in patients with bronchial asthma is to be borne in mind.
- ECG monitoring is indicated for cardiac supervision.
- In case of more pronounced hypotension, volume substitution (e.g. plasma substitutes) is recommended.

The development of hypokalaemia must be expected, hence appropriate monitoring of the electrolyte balance and, if necessary, substitutions are to be recommended while heeding a possible preceding treatment with other medicinal products that can induce hypokalaemia, hyperlipidemia, ketonemia.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Respiratory system, Drugs for obstructive airway diseases. Selective beta-2-adrenoreceptor
agonists.
ATC code: R03AC02

Mechanism of action and pharmacodynamic effects

Salbutamol is an adrenergic beta-receptor stimulant with a selective effect on the beta2- receptors of the bronchi, which produces bronchodilatation in reversible airway obstruction. The bronchodilator effect occurs within a few minutes after inhalation and reaches its maximum after 30-60 minutes. It has a short-term bronchodilating effect of 4-6 hours. With inhalation the bronchodilator effect is not related to the serum concentration.
Adrenergic beta2-stimulants have also been shown to increase the reduced mucociliary clearance that occurs in obstructive pulmonary disease, and thus facilitate the coughing up of viscous secretion.

Special Populations
Children <4 years of age
Paediatric clinical studies conducted in patients <4 years with bronchospasm associated with reversible obstructive airway disease, showed that salbutamol pressurised inhalation, suspension was well tolerated and had a safety profile comparable to that in children over 4 years, adolescents and adults.

5.2 Pharmacokinetic properties

Salbutamol administered intravenously has a halflife of 4 to 6 hours and is cleared partly renally and partly by metabolism to the inactive 4'-O-sulphate (phenolic sulphate) which is also excreted primarily in the urine. The faeces are a minor route of excretion.

After administration by the inhaled route between 10 and 20% of the dose reaches the lower airways. The remainder is retained in the delivery system or is deposited in the oropharynx from where it is swallowed. The fraction deposited in the airways is absorbed into the pulmonary tissues and circulation, but is not metabolised by the lung. On reaching the systemic circulation it becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged substance and as the phenolic sulphate.

The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulphate. Both unchanged substance and conjugate are excreted primarily in the urine. Most of a dose of salbutamol given intravenously, orally or by inhalation is excreted within 72 hours. Salbutamol is bound to plasma proteins to the extent of 10%.

5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction. The observed effects in the preclinical studies were related to the beta-adrenergic activity of salbutamol.

In common with other potent selective β2-receptor agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of fetuses were found to have cleft palate at 2.5mg/kg, 4 times the maximum human oral dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50mg/kg/day orally throughout pregnancy resulted in no significant fetal

abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. Reproductive studies in the rabbit at doses of 50mg/kg/day orally (i.e. 78 times the maximum human oral dose) have shown fetuses with treatment related changes; these included open eyelids (ablepharia), secondary palate clefts (palatoschisis), changes in ossification of the frontal bones of the cranium (cranioschisis) and limb flexure.

The non- chlorofluorocarbon propellant, HFA 134a, has been shown to have no toxic effect at very high vapour concentrations, far in excess of those likely to be experienced by patients, in a wide range of animal species exposed daily for periods of two years.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propellant gas:
Norflurane (tetrafluoroethane or HFC-134a)
This medicine contains fluorinated gases.

Each inhaler contains 17.57 g of HFC-134a corresponding to 0.027 tonne CO_2 equivalent (global warming potential = 1430).

6.2 Incompatibilities

None known.

6.3 Shelf life

2 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

Replace the cap on the mouthpiece and press firmly into position.

Store the inhaler in an inverted position, with the mouthpiece pointing downward.

The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C.

Do not freeze. Store in the outer carton in order to protect from direct sunlight.

Do not pierce or burn the canister, even when empty.

6.5 Nature and contents of container

This medicine is a white to off white pressurised inhalation suspension in aluminium canister with metering valve and fitted in white colour polypropylene homopolymer actuator with green colour dust cap.

Pack size(s):
1 canister x 200 metered actuations
2 canisters x 200 metered actuations
3 canisters x 200 metered actuations

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Clean the inhaler once a week, at least. If the inhaler does block up, the same cleaning instructions should be followed.

1. The metal canister should be pulled out of the plastic case of the inhaler and the mouthpiece cover should be removed.
2. The plastic case and the mouthpiece cover should be rinsed in warm water. Do not attempt to remove any build-up of medicine around the mouthpiece with a sharp object, such as a pin. A mild detergent may be added to the water, then rinse thoroughly with clean water before drying. The metal canister should not be put into water.
3. The plastic case and the mouthpiece cover should be left to dry in a warm place. Excessive heat should be avoided.
4. Put back the canister and mouthpiece cover.

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

7. HOUDER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

Sandoz B.V.
Hospitaaldreef 29
1315 RC Almere
Nederland

8. NUMMER(S) VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

RVG 134489

9. DATUM VAN EERSTE VERLENING VAN DE VERGUNNING/VERLENGING VAN DE VERGUNNING

Datum van eerste verlening van de vergunning: 4 september 2025

10. DATUM VAN HERZIENING VAN DE TEKST