SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SALRES 100 mcg Aerosol Inhaler

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

For each actuation:
Active substance:
It contains 120.50 mcg Salbutamol sulfate equivalent to 100 mcg Salbutamol.

Excipients:
For the full list of excipients, see 6.1.

3. PHARMACEUTICAL FORM

Pressurized metered dose aerosol.
Aerosol as a suspension filled with pressurized propellant gas into aluminum inhaler can.
One actuation valve is supplied with the aluminum can.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

It is used as a relief medication for relief of symptoms by reducing bronchoconstriction in asthma. It should not be used to manage the disease.
In COPD, it is used to reduce symptoms and as relief medication. It is not preferred for regular treatment.

4.2 Posology and method of administration

Posology/frequency and duration of administration:
Duration of action of SALRES is 4 to 6 hours in most patients.
Increasing use of β2 agonists may be a sign of worsening asthma. Under these conditions a reassessment of the patient's therapy plan may be required and concomitant glucocorticosteroid therapy should be considered.

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

Relief of acute bronchospasm:
Adults: 100 or 200 micrograms.

Prevention of allergen or exercise-induced bronchospasm:
Adults: Use of 200 microgram, as necessary, 10-15 minutes before exposure to allergen or exercise.

On demand use of SALRES should not exceed 4 times daily. Reliance on such supplementary use or a sudden increase in dose indicates deteriorating asthma (see section 4.4).

SALRES inhaler should be used to relieve symptoms when they occur, and to prevent them in those circumstances recognized by the patient to precipitate an asthma attack (e.g. before exercise or unavoidable allergen exposure).

Method of administration
SALRES inhaler is administered by the oral inhaled route only.
In patients who find co-ordination of a pressurized metered-dose inhaler difficult a spacer may be used with SALRES.

Additional information on special populations

Renal/Hepatic insufficiency
No data available.

Pediatric population:
Children between 2-12 years: 100 micrograms, the dose may be increased to 200 micrograms if required.
Children aged 12 years and over: Dose as per adult population.

Prevention of allergen or exercise-induced bronchospasm:
Children between 2-12 years: 100 micrograms before exercise or allergen exposure, the dose may be increased to 200 micrograms if required.
Children aged 12 years and over: Dose as per adult population.

For additional information on its use in children below the age of 4 years, see section 5.1.

Children below the age of 5 years may benefit from use of a spacer device with a face mask.

Geriatric population:
No data available.

4.3 Contraindications
SALRES is contra-indicated in patients with history of hypersensitivity to any of its components (see section 6.1).
Non-IV formulations of salbutamol must not be used to arrest uncomplicated premature labor. Salbutamol preparations should not be used for threatened abortion.

4.4 Special warning and precautions for use
The management of asthma should normally follow a stepwise program, and patient response should be monitored clinically and by lung function tests.

Increasing use of short-acting inhaled β2 agonists to control symptoms indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to starting or increasing corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

SALRES should be administered cautiously to patients with thyrotoxicosis.

Potentially serious hypokalemia may result from β2 agonist therapy mainly from parenteral and nebulized 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.

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. SALRES should be discontinued immediately, the patient should be assessed, and if necessary, a different fast-acting bronchodilator instituted for ongoing use.

In the event of a previously effective dose of inhaled SALRES failing to give relief for at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken.

Patients' inhaler technique should be checked to make sure that aerosol actuation is synchronized with inspiration of breath for optimum delivery of the drug to the lungs.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of myocardial ischemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischemic heart disease, arrhythmia or severe heart attack) 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 dyspnea and chest pain, as they may be of either respiratory or cardiac origin.

4.5 Interaction with other medicinal products and other forms of interaction
SALRES and non-selective beta-blocking drugs, such as propranolol, should not usually be prescribed together.
SALRES is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

4.6 Fertility, pregnancy and lactation

General Recommendation
Pregnancy category is “C”.

Women of child-bearing potential/Contraception
There are no data regarding the use of salbutamol in women of child-bearing potential and in women using contraception.

Pregnancy
Animal studies are insufficient with respect to effects on pregnancy /and-or/ embryonal/fetal development/ and-or/ parturition/ and-or/ postnatal development (see section 5.3). The potential risk for humans is unknown.
Administration of drugs during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the fetus. It should not be used during pregnancy unless it

is absolutely necessary.

During worldwide marketing experience, rare cases of various congenital anomalies, including cleft palate and limb defects have been reported in the offspring of patients being treated with salbutamol. Some of the mothers were taking multiple medications during their pregnancies. Because no consistent pattern of defects can be discerned, and baseline rate for congenital anomalies is 2-3%, a relationship with salbutamol use cannot be established.

Breast-feeding
As salbutamol is probably secreted in breast milk its use in nursing mothers is not recommended unless the expected benefits outweigh any potential risk. It is not known whether salbutamol in breast milk has a harmful effect on the neonate.

Fertility
There is no information on the effects of salbutamol on human fertility. There were no adverse effects on fertility in animals.

4.7 Effects on ability to drive and use machines
No data available.

4.8 Undesirable effects
Following adverse effects are given according to system organ classification and frequency.
Classification of frequency:

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

Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown events were generally determined from spontaneous data.

Immune system disorders
Very rare: Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse

Metabolism and nutrition disorders
Rare: Hypokalemia. Potentially serious hypokalemia may result from β2 agonist therapy.

Nervous system disorders
Common: Tremor, headache
Very rare: Hyperactivity

Cardiac disorders
Common: Tachycardia
Uncommon: Palpitations
Very rare: Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardias and extrasystoles

Unknown: Myocardial ischemia* (see section 4.4)
*reported spontaneously in post-marketing data therefore frequency regarded as unknown

Vascular disorders
Rare: Peripheral vasodilatation

Respiratory, thoracic and mediastinal disorders
Very rare: Paradoxical bronchospasm

Gastrointestinal disorders
Uncommon: Mouth and throat irritation

Musculoskeletal, connective tissue and bone disorders
Uncommon: Muscle cramps

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 to Turkey Pharmacovigilance Center (TÜFAM). (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; phone number: +90 800 314 00 08; fax: +90 312 218 35 99)

4.9 Overdose
The most common signs and symptoms of overdose with SALRES are transient beta agonist pharmacologically mediated events, including tachycardia, tremor, hyperactivity and lactic acidosis (see sections 4.4 and 4.8).
Hypokalemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.
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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Andrenergics, inhalants. Selective β2-andrenoreceptor agonists
ATC code: R03AC02

Mechanism of action
Salbutamol is selective β2 adrenoceptor agonist. At therapeutic doses it acts on the β2-adrenoceptors of bronchial muscle, with little or no action on the β1 adrenoceptors of cardiac muscle.

Pharmacodynamic effects
Salbutamol is a selective β2-adrenoceptor agonist. At therapeutic doses it acts on the β2-adrenoceptors of bronchial muscle providing short acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

Special patient populations

Children <4 years of age:

Pediatric clinical studies conducted at the recommended dose (SBO20001, SBO30001, SBO30002), in patients <4 years with bronchospasm associated with reversible obstructive airways disease, show that Salbutamol Inhaler has a safety profile comparable to that in children ≥4 years, adolescents and adults.

5.2 Pharmacokinetic properties

General properties

Absorption:

After administration by the inhaled route between 10-20% 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 metabolized by the lung.

Distribution:

Salbutamol is bound to plasma proteins to the extent of 10%.

Biotransformation:

On reaching the systemic circulation it becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged drug 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.

Elimination:

Both unchanged drug and conjugate are excreted primarily in the urine. Salbutamol administered intravenously has a half-life 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 feces are a minor route of excretion. The majority of a dose of salbutamol given intravenously, orally or by inhalation is excreted within 72 hours.

Characteristics in patients

No data available.

5.3 Preclinical safety data

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 2.5 mg/kg, 4 times the maximum human oral dose. 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 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. A reproductive study in rabbits revealed cranial malformations in 37% of fetuses at 50 mg/kg/day, 78 times the maximum human oral dose.

In an oral fertility and general reproductive performance study in rats at doses of 2 and 50 mg/kg/day, with the exception of a reduction in number of weanlings surviving to day 21 post partum at 50 mg/kg/day, there were no adverse effects on fertility, embryofetal development, litter size, birth weight or growth rate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
HFA 134a Pharma Grade

6.2 Incompatibilities
None reported.

6.3 Shelf life
36 months.

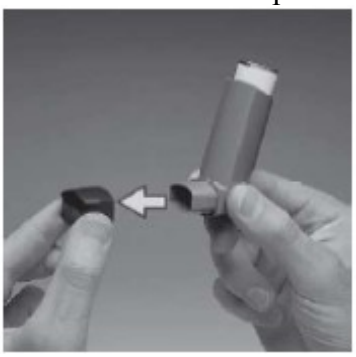
6.4 Special precautions for storage
It should be kept at room temperature below 30°C. It should be protected from frost and direct sun light.
Replace the mouthpiece cover firmly when not in use.
As with most of other inhaled medicines, the therapeutic effect of this medicine may decrease when aerosol tube is too cold.
Aerosol tube should not be broken, punctured or burnt even when empty.

6.5 Nature and contents of container
SALRES 100 mcg metered dose aerosol for inhalation is presented in aluminum can of 200 doses with metering valve in cardboard box with Package Leaflet.

6.6 Special precautions for disposal and other handling
Instructions for use of SALRES:

Testing the inhaler:
- When using the inhaler for the first time, test that it is working. Remove the mouthpiece cover by gently squeezing the sides of cover. To make sure that it works, shake it well, release 1-2 puffs into the air.
- If you have not used the inhaler for 5 days or more shake it well and release two puffs into the air to make sure that it works.

Using the inhaler:
1. Remove the mouthpiece cover by gently squeezing the sides of the cover.



2. Check inside and outside of the inhaler including the mouthpiece to make sure that the mouthpiece is clean and free of objects.

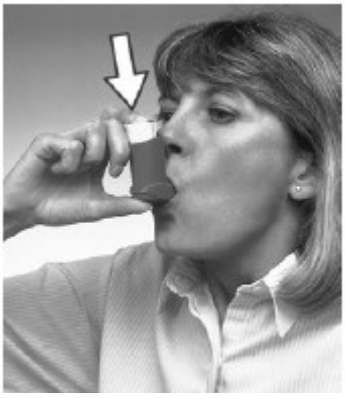
3. Shake the inhaler well to ensure that any loose objects are removed and that the contents of the

inhaler are evenly mixed.

4. Hold the inhaler upright between fingers and thumb with your thumb on the base, below the mouthpiece.

5. Breathe out as far as is comfortable and then place the mouthpiece in your mouth between your teeth and close your lips around it but do not bite it.

6. Breathe in through your mouth. Just after starting to breathe in, press down on the top of the canister to release a puff of medicine. Do this while still breathing in steadily and deeply.



7. Hold your breath, take the inhaler from your mouth and your finger from the top of the inhaler. Continue holding your breath for a few seconds, or as long as is comfortable.

8. If your doctor has told you to take 2 doses, keep the inhaler upright and wait about half a minute before you take another puff by repeating steps 3 to 7.

9. After use always replace the mouthpiece cover straight away to keep out dust. Replace the cover by firmly pushing and clicking into position.

IMPORTANT:
Do not rush Stages 5, 6 and 7. It is important that you start to breathe in as slowly as possible just before operating your inhaler.

Practice in front of a mirror for the first few times. If you see 'mist' coming from the top of the inhaler or the sides of your mouth you should start again from stage 2.

Young children may need help and their parents may need to operate the inhaler for them.
Encourage the child to breathe out and operate the inhaler just after the child starts to breathe in. Practice the technique together. You may find the face mask of spacer device useful if you have to give SALRES to a baby or a child under 5 – speak to your doctor if you think you might need one of these.

Older children or people with weak hands may find it easier to hold the inhaler with both hands. Put the two forefingers on top of the inhaler and both thumbs on the bottom below the mouthpiece.

Cleaning your inhaler:
To stop your inhaler blocking, it is important to clean it at least once a week.

To clean your inhaler:
- Remove the metal aerosol tube from the plastic casing.
- Remove the mouthpiece cover.
- Rinse the plastic casing under warm running water.
- Dry the plastic casing thoroughly inside and out (e.g. in the night).
- Replace the metal aerosol tube and the mouthpiece cover.

Do not put the metal aerosol tube in water.

Any unused product or waste material should be disposed of in accordance with local disposal regulations.

7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. 34303 No: 1
Küçükçekmece / İSTANBUL / TURKEY

8. MARKETING AUTHORIZATION NUMBER

245/60

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 12.10.2012
Date of last renewal :

10. DATE OF REVISION OF THE TEXT