1. Name of the medicinal product

Sultolin HFA Inhaler

2. Qualitative and quantitative composition

Salbutamol inhaler is a pressurized metered-dose inhaler delivering 100 micrograms of salbutamol (as Salbutamol Sulfate BP) per actuation.

3. Pharmaceutical form

Aerosol

An easily actuated aerosol having plastic actuator of blue color body and light blue color cap embossed "SQUARE" logo on cap. The canister contains a suspension of Salbutamol Sulphate along with a propellant filled in a metallic can which is fitted with a metering valve; imprinted with Batch no. & code no.

4. Clinical particulars

4.1 Therapeutic indications

Salbutamol inhaler is indicated in adults, adolescents and children aged 4 to 11 years. For babies and children under 4 years of age, see sections 4.2 and 5.1.

Salbutamol inhaler provides short-acting (4 to 6 hour) bronchodilation with fast onset (within 5 minutes) in reversible airways obstruction.

It is particularly suitable for the relief and prevention of asthma symptoms. It 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).

Salbutamol inhaler is particularly valuable as relief medication in mild, moderate or severe asthma, provided that reliance on it does not delay the introduction and use of regular inhaled corticosteroid therapy.

4.2 Posology and method of administration

Salbutamol inhaler is for oral inhalation use only. Salbutamol inhaler may be used with a spacer device by patients who find it difficult to synchronize aerosol actuation with inspiration of breath.

<u>Adults (including the elderly):</u>

For the relief of acute asthma symptoms including bronchospasm, one inhalation (100 micrograms) may be administered as a single minimum

starting dose. This may be increased to two inhalations if necessary. To prevent allergen- or exercise-induced symptoms, two inhalations should be taken 10-15 minutes before challenge.

For chronic therapy, two inhalations up to four

times a day. Pediatric Population

Relief of acute bronchospasm

The usual dosage for children under the age of 12 years: one inhalation (100 micrograms). The dose may be increased to two inhalations if required.

Children aged 12 years and over: Dose as per adult population.

Prevention of allergen or exercise-induced bronchospasm

The usual dosage for children under the age of 12 years: one inhalation (100 micrograms) before challenge or exertion. The dose may be increased to two inhalations if required.

Children aged 12 years and over: Dose as per adult population.

Chronic therapy

The usual dosage for children under the age of 12 years: up to two

inhalations 4 times daily. Children aged 12 years and over: Dose as per

adult population.

The Babyhaler spacer device may be used to facilitate administration to children under 5 years of age.

On-demand use of Salbutamol inhaler should not exceed 8 inhalations in any 24 hours. Reliance on such frequent supplementary use, or a sudden increase in dose, indicates poorly controlled or deteriorating asthma (see section 4.4).

4.3 Contraindications

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

Non-I.V. formulations of salbutamol must not be used to arrest uncomplicated premature labor or threatened abortion.

4.4 Special warnings and precautions for use

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

drug to the lungs. Patients should be warned that they may experience a different taste upon inhalation compared to their previous inhaler.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment, including lung-function testing, as patients are at risk of severe attacks and even death. Physicians should consider using the maximum recommended dose of inhaled corticosteroid and/or oral corticosteroid therapy in these patients.

The dosage or frequency of administration should only be increased on medical advice. If a previously effective dose of inhaled salbutamol fails to give relief lasting at least three hours, the patient should be advised to seek medical advice.

Increasing use of bronchodilators, in particular short-acting inhaled β2-agonists, to relieve symptoms, indicates deterioration of asthma control. The patient should be instructed to seek medical advice if short-acting relief bronchodilator treatment becomes less effective, or more inhalations than usual are required. In this situation the patient should be assessed and consideration given to the need for increased anti-inflammatory therapy (e.g. higher doses of inhaled corticosteroid or a course of oral corticosteroid).

Severe exacerbations of asthma must be treated in the normal way.

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

Salbutamol 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 hypoxia and by concomitant treatment with xanthine derivatives, steroids and diuretics. Serum potassium levels should be monitored in such situations.

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

4.5 Interaction with other medicinal products and other forms of interaction

Salbutamol and non-selective β-blocking drugs such as propranolol, should not usually be prescribed together.

4.6 Fertility, pregnancy and lactation

Pregnancy

Studies in animals have shown reproductive toxicity (see section 5.3). Safety in pregnant women has not been established. No controlled clinical trials with salbutamol have been conducted in pregnant women. Rare reports of various congenital anomalies following intrauterine exposure to salbutamol (including cleft palate, limb defects and cardiac disorders) have been received. Some of the mothers were taking multiple medications during their pregnancies. Salbutamol inhaler should not be used during pregnancy unless clearly necessary.

Breast-feeding

As salbutamol is probably secreted in breast milk, its use in nursing mothers requires careful consideration. It is not known whether salbutamol has a harmful effect on the neonate, and so its use should be restricted to situations where it is felt that the expected benefit to the mother is likely to outweigh any potential risk to the neonate.

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

None reported.

4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000) and very rare (<1/10,000) including isolated reports. Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown events were generally determined from spontaneous data.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via national Pharmacovigilance Electronic Reporting Systems.

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 *beta2* 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 tachycardia and extrasystoles).
Unknown*:*	Myocardial ischemia* (see section 4.4)

Vascular disorders

Rare:	Peripheral vasodilatation.

Respiratory, thoracic and mediastinal disorders

Very rare:	Paradoxical bronchospasm.

Gastrointestinal disorders

Uncommon:	Mouth and throat irritation.

Musculoskeletal and connective tissue disorders

Uncommon:	Muscle cramps.

* reported spontaneously in post-marketing data therefore frequency regarded as unknown

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events**,** including tachycardia, tremor, hyperactivity and metabolic effects including hypokalemia (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: Adrenergic, inhalants. Selective beta-2-

andrenoreceptor agonists ATC code: R03AC02

Salbutamol is a selective β2-adrenoceptor agonist with effects on smooth and skeletal muscle. These include bronchodilation, relaxation of uterine muscle and tremor. Binding of a β-stimulant to the receptor unit activates to generate cyclic AMP from ATP. Cyclic AMP inhibits actin-myosin linkagethus causing relaxation of smooth muscle. Salbutamol also has an anti-allergic effect on mast cells causing inhibition of release of bronchoconstrictor mediators including histamine, neutrophil chemotactic factor (NCF) and prostaglandin D2 (PGD2). All of these events contribute to the effectiveness of Salbutamol as inhibitor of the early asthmatic response, indicative of their ability to provide symptomatic relief in asthma. As such they are the first line treatment used on an "as required" basis for the reversal of acute asthma attacks.

5.2 Pharmacokinetic properties

In general, only 10% or less of an inhaled drug from a pressurized aerosol is deposited in the airways and the reminder is swallowed. No significant metabolism is done by the lungs. The reminder drug that is swallowed has a considerable presystolic metabolism. The major metabolite is a sulphate conjugate, salbutamol 4-O-sulfate which is probably formed in the bowel mucosa and is inactive. Because of its gradual absorption from the bronchi, systemic levels of salbutamol are low after inhalation of recommended dose. Peak plasma concentration occurs within 2-4 hours. The proportion of circulating drug that is protein bound is approximately 10%. After inhalation via conventional aerosol, the pattern of excretion is similar to that after oral treatment. Approximately 72% of the inhaled dose are excreted within 24 hours in the urine and consist of 28% of unchanged drug and 44% as metabolite. About 4% of the dose are excreted in feces. Salbutamol has an average elimination half-life of 3.8 hours. The plasma half-life of salbutamol has been estimated to range from about 2 to as much as 7 hour.

5.3 Preclinical safety data

In common with other potent selective β2-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 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. much higher than the normal human 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. Reformulation of the Salbutamol inhaler has not altered the known toxicological profile of salbutamol.

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.

The non-CFC propellant, HFA 134a, has been shown to have no toxic effect at very high vapor 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

Absolute
Ethanol Oleic
Acid
Norflurane {1,1,1,2-Tetrafluoroethane (HFA 134a)}

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

Suspension along with HFA 134a filled in 19 ml aluminium canister and sealed with 50 mcl aluminium metering valve. The can is labeled containing the information of product name, strength and other get up similar to standard. Batch no; Mfg. date and Exp. dates are over printed on the label. Over printed on the inner cartoon. The checked inhaler will be wrapped with clear poly pouch.

Each pack contains 1 inhaler.

6.6 Special precautions for disposal and other handling

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

7. Marketing authorization holder

Square Pharmaceuticals Ltd.
Square Centre
48, Mohakhali C.A, Dhaka – 1212,
Bangladesh

8. Market authorization number

H2005/562

9. Date of first registration

25/07/2010

10. Date of revision of the text

19/07/2026

Ref:

https://www.medicines.org.uk/emc/product/850/smpc

http://www.squarepharma.com.bd/downloads/Sultolin%20100.pdf