Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Salbutamol CFC-Free Inhaler 100 micrograms per metered dose, pressurised inhalation, suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One metered dose contains 100 micrograms of salbutamol (equivalent to 120 micrograms of salbutamol sulphate). This is equivalent to a delivered dose of 90 micrograms of salbutamol (equivalent to 108 micrograms of salbutamol sulphate).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Pressurised inhalation suspension

Pressurised inhalation suspension supplied in an aluminium canister with a metering valve and a plastic actuator and dust cap.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Salbutamol CFC-Free Inhaler is indicated in adults, adolescents and children. For babies and children under 4 years of age, see sections 4.2 and 5.1.
Salbutamol CFC-Free Inhaler is indicated for the relief and prevention of bronchial asthma and conditions associated with reversible airways obstruction.

Salbutamol CFC-Free Inhaler can be used as relief medication in the management of mild, moderate or severe asthma, provided that its use does not delay the introduction and use of regular inhaled corticosteroid therapy, where necessary.

4.2 Posology and method of administration

Salbutamol CFC-Free Inhaler is for oral inhalation use only.
Posology

Adults (including the elderly) and adolescents (children 12 years and over):
For the relief of acute bronchospasm, one inhalation (100 micrograms) increasing to two inhalations (200 micrograms), if necessary.

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

Maximum daily dose: two inhalations (200 micrograms) up to four times a day.

Paediatric Population:
Babies and young children using Salbutamol CFC-Free Inhaler may benefit from the use of a paediatric spacer device with a face mask (for example the BABYHALER™). (See Section 5.1),

- *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 (200 micrograms) if required.

Children aged 12 years and over: One or two inhalations (100 or 200 micrograms).

On demand use of Salbutamol CFC Free Inhaler should not exceed four times daily. Reliance on such supplementary use or a sudden increase in dose indicates deteriorating asthma (see Section 4.4*).*

- *Prevention of recognised 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 (200 micrograms) if required.

Children aged 12 years and over: Two inhalations (200 micrograms) before challenge or exertion.

- *Chronic therapy:*

The usual dosage for children under the age of 12 years: Up to two inhalations (200 micrograms) four times daily.
Children aged 12 years and over: Up to two inhalations (200 micrograms) four times daily.

Patients with impaired renal or hepatic function:
No dosage adjustment is required.

For all patients, on-demand use of Salbutamol CFC-Free Inhaler should not exceed a total of 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).

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

For patients requiring a spacer device the Volumatic™ and the Babyhaler™ have shown to be compatible with Salbutamol CFC free pressurised inhalation suspension.

4.3 Contraindications

The use of salbutamol is contraindicated in the management of premature labour and threatened abortion.

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

4.4 Special warnings and precautions for use

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

Treatment of asthma normally follows a gradually adjusted programme and the patient's therapeutic response must be monitored both clinically and with lung function tests.
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 β_2-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).

Patients requiring long-term management with bronchodilators should be kept under regular surveillance.

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 ischaemia associated with salbutamol. 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.

Salbutamol CFC Free Inhaler must be administered with caution to patients with thyrotoxicosis.

Potentially serious hypokalaemia may result from β_2-agonist therapy, mainly from parenteral and nebulised 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 most inhaled medications in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.

Paediatric population
A responsible adult should supervise the use of the inhaler in children.

4.5 Interaction with other medicinal products and other forms of interactions

Propranolol and other non-cardioselective ß-adrenoreceptor blocking agents antagonise the effects of salbutamol, and should not usually be prescribed together.

Concomitant administration of xanthine derivatives, diuretics or steroids may lead to severe hypokalaemia (see section 4.4 Special Warnings and Precautions for Use).

Caution should be exercised during the concurrent use of anaesthetic agents such as cyclopropane, chloroform, halothane and other halogenated agents.

Salbutamol is not contraindicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).
The effects of salbutamol may be altered by guanethidine, reserpine, methyldopa and tricyclic antidepressants.

Because Salbutamol CFC-Free Inhaler contains ethanol there is a theoretical potential for interaction in patients taking disulfiram or metronidazole. The amount of ethanol in Salbutamol CFC-Free is small but it may be enough to precipitate a reaction in some sensitive patients.

4.6 Fertility, pregnancy and lactation

Pregnancy:
In animal studies, administration of salbutamol at very high doses resulted in some harmful effects on the foetus (see section 5.3). The safety of salbutamol in pregnant women has not been established. No controlled clinical trials with salbutamol have been conducted in pregnant women.

During worldwide marketing of salbutamol containing products, rare reports of various congenital anomalies (including cleft palate, limb defects and cardiac disorders) have been reported in the offspring of patients being treated with salbutamol. No consistent pattern of defects has been discerned and a relationship with salbutamol use has not been established. Salbutamol CFC-Free Inhaler should not be used during pregnancy unless clearly necessary.

Lactation:
Salbutamol may be secreted in breast milk. Its effect on breast-fed neonates is not known as there are insufficient data available, 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.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

The following adverse events have been reported with inhaled salbutamol (frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports).

Organ system	Undesirable effects	Frequency
Immune system disorders	Hypersensitivity reactions including angioedema, urticaria,	Very rare

	bronchospasm, hypotension and collapse	
Metabolism and nutrition disorders	Hypokalaemia	Rare
Nervous system disorders	Tremor, headache Tension, anxiety, nervousness. Hyperactivity	Common Rare Very rare
Cardiac disorders	Tachycardia Palpitations Cardiac arrhythmias Myocardial ischaemia* (see section 4.4)	Common Uncommon Very rare Unknown
Vascular disorders	Peripheral vasodilatation	Rare
Respiratory, thoracic and mediastinal disorders	Paradoxical bronchospasm **	Very rare
Gastrointestinal disorders	Irritation of the mouth and throat	Uncommon
Musculoskeletal and connective tissue disorders	Muscle cramps	Uncommon

* reported spontaneously in post-marketing data therefore frequency 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 CFC-Free Inhaler 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:
Pharmacovigilance Section, Health Products Regulatory Authority, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2. Tel: +353 1 6764971 Fax: +353 1 6762517, Website: www.hpra.iee-mail: Medsafety@hpra.ie

4.9 Overdose

The most common signs and symptoms of overdose with salbutamol are the same as those which may occur during salbutamol treatment:
- Cardiovascular symptoms such as vasodilatation, warm red face, tachycardia, palpitations, hypotension or hypertension, a constricting feeling in the chest.

- Central nervous system symptoms such as headache, tremor, agitation, restlessness, hallucinations, anxiety, insomnia, increased sweating, nausea and vomiting.

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

The preferred antidote for overdosage with salbutamol is a cardioselective β-blocking agent, but β-blocking drugs should be used with caution in patients with a history of bronchospasm.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Selective beta-2-adrenoceptor agonists.
ATC Code: R03 AC02

Salbutamol is a selective β_2-adrenoceptor agonist. At therapeutic doses it acts on the β_2-adrenoceptors of bronchial muscle providing short acting (4-6 hour) bronchodilatation with a fast onset (within 5 minutes) in reversible airways obstruction.

Pediatric Population
Children < 4 years of age:
Paediatric clinical studies conducted at the recommended dose in patients younger than 4 years with bronchospasm associated with reversible obstructive airways disease, show that inhaled salbutamol has a safety profile comparable to that in children older than 4 years, adolescents and adults.

5.2 Pharmacokinetic properties

When salbutamol is taken by the inhalation route only about 10% - 20% of the dose is deposited in the lower airways, with the remainder either being retained in the delivery system or swallowed.

The fraction that reaches the airways does not appear to be metabolised by the lung. It is absorbed into the pulmonary tissues and circulation where it is metabolised by the liver and excreted primarily in the urine, partly unchanged and partly as the inactive phenolic sulphate. The fraction that is swallowed is absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism to the phenolic sulphate.

Most of a dose of salbutamol is excreted within 72 hours. The elimination half life is 4-6 hours when given intravenously. Salbutamol is bound to plasma proteins to the extent of 10%.

5.3 Preclinical safety data

The CFC-free propellant gas HFA134a caused no toxicological effects in various animal studies.

Like other potent selective β_2-receptor agonists, salbutamol administered subcutaneously at high doses has been documented to have teratogenic effects in mice.

Preclinical data on salbutamol reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity. Foetal abnormalities in reproduction studies in mice and rabbits at high systemic exposure and the induction of benign mesovarian leiomyomas in certain strains of rats are not considered of clinical concern.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Oleic acid
Ethanol
Norflurane (HFA-134a)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Aluminium alloy canister sealed with a metering valve and fitted with a plastic actuator and a dust cap. Each canister contains 200 metered doses.

6.6 Special precautions for disposal and other handling

As the canister is pressurised, it should not be broken, punctured or burnt even when apparently empty.
The canister contains a pressurised liquid. Do not expose to temperatures higher than 50 °C. Do not pierce the canister.

Instructions for use are given in the Patient Information Leaflet which should be read by the patient before use.

7 MARKETING AUTHORISATION HOLDER

Valeas SPA Industria Chimica e Farmaceutica
Via Vallisneri 10
20133 Milano
Italy

8 MARKETING AUTHORISATION NUMBER

PA1987/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 26th May 2016

10 DATE OF REVISION OF THE TEXT

December 2017