SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

VENTIMAX CFC FREE 100 µg Metered dose inhaler

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose VENTIMAX CFC FREE contains salbutamol sulphate equivalent to 100 µg salbutamol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Metered dose inhaler

A metered aerosol inhaler, delivering 100 µg of salbutamol per inhalation in a standard pale blue polypropylene actuator with a dark blue polypropylene cap. Each canister provides 200 inhalations.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

VENTIMAX CFC FREE is indicated for use in the treatment of bronchospasm, asthma and chronic obstructive pulmonary disease.

4.2 Posology and method of administration

VENTIMAX CFC FREE is administered by the inhaled route only.

Increasing use of VENTIMAX CFC FREE 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.

One or two inhalations repeated four-hourly if required. The bronchodilator effect of each administration of VENTIMAX CFC FREE lasts for at least four hours and more frequent use should be unnecessary. The patient can readily recognise any reduction in the length of action and should be instructed to consult a doctor if the effect of a previously adequate dose lasts for less than three hours.

VENTIMAX CFC FREE acts rapidly and may be used when necessary to relieve attacks of acute dyspnoea. Doses may be taken prophylactically before exertion to prevent exercise-induced asthma.

4.3. Contraindications

VENTIMAX CFC FREE is contraindicated in patients with a history of hypersensitivity to any of the components.

Thyrotoxicosis.

Concurrent use with beta-blocking medicines.

In managing premature labour (for certain dose indication).

Contraindicated for threatened abortion.

4.4 Special warnings and precautions for use

Patients should be instructed in the proper use of the inhaler and their technique checked, to ensure that the active substance reaches the target areas within the lungs

The management of asthma should normally follow a stepwise programme, and the patient's response should be monitored clinically and by lung function tests. Increasing use of short-acting inhaled bronchodilators, in particular ß2-agonists to control symptoms, indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Asthmatic patients whose conditions deteriorates despite salbutamol

therapy, or where a previously effective dose fails to give relief for at least three hours, should seek medical advice in order that any necessary additional steps may be taken.

Patients must be warned that if either the usual relief is diminished or the usual duration of action is reduced, they should not increase the dose or its frequency of administration but should seek medical advice immediately, so that suitable measure can be taken to combat the condition. The dosage or frequency of administration should only be increased on medical advice

Patients requiring long term management with VENTIMAX CFC FREE Inhaler should be kept under regular surveillance.

Care should be taken when treating acute asthma attacks or exacerbation of severe asthma as increased serum lactate levels and rarely, lactic acidosis have been reported after the use of high doses of VENTIMAX CFC FREE have been used in emergency situations this is reversible on reducing the dose of salbutamol

Fatalities have been reported in association with excessive use of inhaled sympathomimetic medication. The exact cause of death is unknown but cardiac arrest following the unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected. It is important to avoid excessive dosing.

Cardiovascular effects may be seen with sympathomimetic drugs, including VENTIMAX CFC FREE. 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, arrhythmias 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 either respiratory or cardiac in origin.

VENTIMAX CFC FREE should be administered cautiously to patients with thyrotoxicosis, coronary insufficiency, hypertrophic obstructive cardiomyopathy, arterial hypertension, known tachyarrhythmias, concomitant use of cardiac glycosides or diabetes mellitus.

Potentially serious hypokalaemia may result from ß2-agonist therapy mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant.

VENTIMAX CFC FREE should be used with caution in patients known to have received large doses of other sympathomimetic medicine.

In common with other beta-adrenoceptor agonists, VENTIMAX CFC FREE can induce reversible metabolic changes such as increased blood glucose levels. Diabetic patients may be unable to compensate for the increase in blood glucose and the development of ketoacidosis has been reported. Concurrent administration of glucocorticoids can exaggerate this effect.

As with other inhalation therapies, the potential for paradoxical bronchospasm should be considered. If it occurs the preparation should be discontinued immediately, and alternative therapy given. Solutions which are not of neutral pH may rarely cause paradoxical bronchospasm in some patients. VENTIMAX CFC FREE and non-selective beta blocking drugs such as propranolol should not usually be prescribed together.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Severe asthma requires regular medical assessment as the condition is potentially life-threatening. Patients with severe asthma have constant symptoms and frequent exacerbations with limited physical capacity, and *peak expiratory flow* (PEF) values below 60 % predicted at baseline with greater than 30 % variability, usually not returning entirely to normal after a bronchodilator. These patients will require inhaled or oral corticosteroid therapy. With this primary background corticosteroid treatment, VENTIMAX CFC FREE provides essential rescue medication for a severe asthmatic in treating acute exacerbations. Failure to respond promptly or fully to such rescue medication signals a need for urgent medical advice and treatment.

4.5 Interaction with other medicines and other forms of interaction

VENTIMAX CFC FREE should be used with caution in patients undergoing anaesthesia with halothane or other halogenated anaesthetics as ventricular fibrillation may be induced. Patients should be instructed to discontinue salbutamol at least 6 hours before an intended anaesthesia with halogenic anaesthetics, wherever possible. An increased risk of dysrhythmias may also occur if administered concomitantly with cardiac glycosides, quinidine or tricyclic antidepressants.

VENTIMAX CFC FREE should not be given to patients receiving mono-amine oxidase (MAO) inhibitors or within 14 days of termination of mono-amine oxidase inhibitor therapy.

Hypokalaemia occurring with β2-agonist therapy may be exacerbated by treatment with xanthine derivatives, steroids, diuretics, long-term laxatives and by hypoxia.

Propranolol and other non-cardio selective β-adrenoreceptor blocking agents antagonise the effects of salbutamol and should not usually be prescribed together.

Because of the content of ethanol, there is theoretical potential for interaction in patients taking disulfiram or metronidazole.

4.6 Fertility, pregnancy and lactation

Pregnancy

VENTIMAX CFC FREE inhalation is contraindicated in treatment of threatened abortion or premature labour.

Experience on the use of beta-sympathomimetics during early pregnancy indicates no harmful effect at the doses ordinarily used for inhalation therapy. High systemic doses at the end of pregnancy can cause inhibition of labour and may induce β2-specific foetal/neonatal effects like tachycardia and hypoglycaemia. Inhalation therapy at recommended doses is not expected to induce these harmful side effects at the end of pregnancy.

Breastfeeding

Salbutamol may be secreted in breast milk. It is not known whether salbutamol has a harmful effect on the neonate.

Fertility

There is no information on the effects of salbutamol on human fertility.

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

Based on the MedDRA system organ class and frequencies, adverse events are listed in the table below.

System Organ Class	**Frequency**	**Description**
Immune system disorders	Less frequent	Hypersensitivity reactions (including angioedema, urticaria, bronchospasm, hypotension and collapse).
Metabolism and nutrition disorders	Less frequent	Hypokalaemia Increased serum lactate levels and lactic acidosis.
Psychiatric disorders	Frequent	Tenseness
	Less frequent	Sleep disturbances and hallucinations (especially in children) Hyperactivity in children Insomnia
Nervous system disorders	Frequent	Tremor muscle, Headache, dizziness
Cardiac disorders	Frequent	Palpitations, Tachycardia
	Less frequent	Cardiac arrhythmia including atrial fibrillation, supraventricular tachycardia and extrasystoles – especially if used concomitantly with other β2-agonists.

	Frequency unknown	Myocardial ischaemia (see section 4.4)
Vascular disorders	Less frequent	Peripheral vasodilation
Respiratory, thoracic and mediastinal disorders	Less frequent	Throat irritation Paradoxical Bronchospasm, (with an immediate increase in wheezing after dosing)
Gastrointestinal disorders	Less frequent	Mouth irritation, nausea and/or vomiting, dry mouth, sore mouth.
Skin and subcutaneous tissue disorders	Less frequent	Pruritus
Musculoskeletal, connective tissue and bone disorders	Less frequent	Myalgia, Muscle cramps, fine tremor (particularly of hand)

As with other inhalation therapies, paradoxical bronchospasm may occur immediately after dosing. VENTIMAX CFC FREE Inhaler should be discontinued immediately, the patient reassessed and treated immediately with another presentation or a different fast-acting inhaled bronchodilator.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Overdosage may result in skeletal muscle tremor, tachycardia, tenseness, headache and peripheral vasodilatation. The preferred antidote for overdosage with salbutamol is a cardioselective ß-adrenoceptor blocking agent. Beta-blocking drugs should be used with caution in patients with a history of bronchospasm, as these drugs are potentially

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

Hyperglycaemia and agitation have also been reported following overdose with salbutamol.

Treatment is supportive and symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A.10.2.1 Medicines acting on respiratory system. Inhalants.

ATC code: R03AC02

Mechanism of action

At therapeutic doses Salbutamol is a beta-adrenergic stimulant which acts on the β2-adrenoceptors of bronchial muscle with little or no action on the β1-adrenoceptors of cardiac muscle.

Pharmacodynamic effects

Salbutamol provides short acting (4 – 6 hour) bronchodilatation with a fast onset (within 5 minutes) in reversible airways obstruction.

Paediatric Population

Paediatric clinical studies conducted at the recommended dose (SB020001. SB030001. SB030002) in patients < 4 years with bronchospasm associated with reversible obstructive airways disease, show that Salbutamol CFC-Free Inhaler has a safety profile comparable to that in children > 4 years, adolescents and adults.

5.2 Pharmacokinetic properties

VENTIMAX CFC FREE Inhaler has been shown to be therapeutically equivalent to salbutamol metered dose inhaler formulated with chlorofluorocarbon (CFC) propellants.

Absorption

Salbutamol is readily absorbed from the gastro-intestinal tract.

Distribution

Salbutamol is subject to first pass metabolism in the liver, about half is excreted in the urine as an inactive sulfate conjugate following oral administration (the rest being unchanged salbutamol). Salbutamol does not appear to be metabolised in the lung, therefore its behaviour following inhalation depends upon the delivery method used which determines the proportion of inhaled salbutamol relative to the proportion inadvertently swallowed.

Elimination

The plasma half-life has been estimated to range from about two to seven hours, the longer values have followed aerosol inhalation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous ethanol (99,5 %),

hydrofluoroalkane -134a (HFA 134a).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store at or below 25 °C. Avoid storage in direct sunlight or heat. Do not refrigerate (2-8 °C). Protect from freezing. The canister should not be punctured, broken or burnt even if it is apparently empty.

6.5 Nature and contents of container

A metered aerosol inhaler, delivering 100 µg of salbutamol per inhalation in a standard pale blue polypropylene actuator with a dark blue polypropylene cap. Each canister provides 200 inhalations.

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. HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd.

Block K West, Central Park

400, 16th Road, Halfway House

Midrand, 1685

8. REGISTRATION NUMBER(S)

36/10.2.1/0393

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 05 June 2014

10. DATE OF REVISION OF THE TEXT

21/12/2021