Summary of the Product Characteristics

1. Name of the Medicinal Product

BONAIR HFA Inhaler (Salbutamol Pressurised Inhalation BP)

2. Qualitative and Quantitative Composition

Bonair is a metered dose aerosol inhaler which delivers 100 mcg of Salbutamol per actuation (or metered dose).

Pack size: 12.0 g (200 Metered Dose Inhalation)

Sr. No.	Material Name	Label Claim	Actual input/factor	Quantity per Dose	Qty per Unit	Function/Role
1.	Salbutamol Sulphate BP (Micronised)	100 mcg	120.50 mcg	0.1446 mg*	34.70 mg@	Active Ingredient
2.	Oleic Acid BP	-	-	0.0289 mg	6.94 mg@	Surfactant
3.	Ethanol BP	-	-	5.125 mg	1.23 g@	Solvent
4.	Propellant HFA 134a	-	-	54.875 mg	13.17 g@	Propellant
5.	Aluminium Canisters (19 cc)	-	-	-	01 No.	Primary Packaging Materials.
6.	Metered Valves (50 µl)	-	-	-	01 No.	Primary Packaging Materials.

Note:-

@ We are claiming 2OO MDI's per canister, but practically add 20 % excess for compensation of product loss due to priming/or valve performance checks.

* 20 o/o processing loss for adaptor retention, retention on valve, retention on canister, nonsprayable fraction, and valve performance checks

^ Salbutamol 100 mcg is equivalent to Salbutamol Sulphate 120.50 mcg.

3. Pharmaceutical Form

Pressurised inhaler, suspension.

4. Clinical Particulars

4.1 Therapeutic indications

Symptomatic treatment of reversible bronchoconstriction due to bronchial asthma and chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema.

Prophylaxis of exercise and allergen induced asthma.

Salbutamol is particularly useful for the relief of symptoms of asthma, providing it does not delay the introduction and regular use of inhaled corticosteroid therapy.

4.2 Posology and method of administration

Bonair is for oral Inhalation use only.

Adults (including the elderly):

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.

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

Children under the age of 12 years: 1 inhalation three to four times daily.

4.3 Contraindications

Bonair HFA Inhaler (Salbutamol Pressurised Inhalation BP) is contraindicated in patients with hypersensitivity to any of the active substances or to the excipient.

In the management of premature labour.

In threatened abortion.

4.4 Special warning 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 and the need for reassessment of the treatment.

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.

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, tachyarrhythmia or severe heart failure) who are receiving salbutamol for respiratory disease, should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease.

Hypokalaemia can be potentiated in cases of concomitant treatment with xanthine derivatives, steroids or diuretics, and in hypoxia. The serum potassium level should therefore be monitored in risk patients, especially in the treatment of acute severe asthma with high doses of Salbutamol.

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

Non-selective beta-adrenoreceptor blockers can completely inhibit the effect of salbutamol. In patients with asthma administration of β-receptor blocking drugs is associated with a risk of severe bronchoconstriction. Therefore, Salbutamol and non-selective β-receptor blocking drugs should not usually be prescribed together

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 increased doses of corticosteroids should be considered.

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.

4.5 Interaction with other medicinal products and other forms of interactions

Salbutamol and non-selective β-receptor blocking drugs should not usually be prescribed together. In patients with asthma administration of β-receptor blocking drugs 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 Pregnancy and lactation

Pregnancy
Studies in animals have shown reproductive toxicity. Safety in pregnant women has not been established. Salbutamol should not be used during pregnancy unless clearly necessary.

Lactation
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.

4.7 Effects on ability to drive and use machine

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

4.8 Undesirable effects

Undesirable effects are classified according to organ system and frequency. The frequency range is defined as very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥ 1/10,000, <1/1000) and very rare (<1/10,000) not known (cannot be estimated from the available data).

Very common, common and uncommon undesirable effects have been obtained from clinical trials. Very rare undesirable effects have been obtained from spontaneous post-marketing reports.

Organ system	**Undesirable effects**	**Frequency**
Immune system disorders	Hypersensitivity reactions incl. angioedema, urticaria, bronchospasm, hypotension, collapse	Very rare
Metabolism and nutrition disorders	Hypokalaemia	Rare
Nervous system disorders	Tremor, headache. Hyperactivity, sleep disturbances, hyperexcitability, hallucinations	Common Very rare
Cardiac disorders	Tachycardia	Common

	Palpitations Cardiac arrhythmia (e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles), myocardial ischaemia	Uncommon Very rare
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

Undesirable effects typical of beta$_2$-agonists, such as skeletal muscle tremor and palpitations, can occur especially at the beginning of treatment, and are often dose-dependent.

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

4.9 Overdose

Hypokalaemia 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: Drugs for obstructive airway diseases, selective beta-2-adrenoreceptor agonists.

ATC code: R03AC02

Salbutamol is an adrenergic beta-receptor stimulant with a selective effect on the beta$_2$- receptors of the bronchi, which produces bronchodilatation. The bronchodilator effect occurs within a few minutes after inhalation and reaches its maximum after 30-60 minutes. It generally lasts at least 4 hours. With inhalation the bronchodilator effect is not related to the serum concentration.

Adrenergic beta$_2$-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.

The active substance in Salbutamol is micronised salbutamol sulphate suspended in liquid non-freon-based propellant (norflurane), which does not adversely affect the earth's ozone layer.

5.2 Pharmacokinetic Properties

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 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 metabolized by the lung. 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. Both unchanged drug 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 % 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. Reproductive studies in the rabbit at doses of 50 mg/kg/day orally i.e. (78 times the maximum human oral use) 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-CFC 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

Ethanol
Oleic acid
Propellant HFA 134a

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Pressurised canister. Do not puncture or burn even when apparently empty. Keep away from sunlight and heat. Store below 30°C, protected from moisture. Keep away from eyes. Keep out of reach of children.

Bonair HFA Inhaler (Salbutamol Pressurised Inhalation BP) should be stored horizontal or in an inverted position, with the mouthpiece pointing downwards.

6.5 Nature and contents of container

Pressurised metered-dose preparation for inhalation filled in Aluminium canister crimped with suitable metered-dose valve, labelled with product label, assembled with polypropylene adaptor packed in a folding carton along with Patient Information leaflet.

7. Marketing Authorization Holder

---

8. Marketing Authorization Numbers

---

9. Date of first authorization/renewal of the authorization

---

10. Date of revision of the text
