December 2023

SUMMARY OF PRODUCT CHARACTERISTIC (SPC)

1. NAME OF THE MEDICINAL PRODUCT

Butalin (salbutamol 100 mcg aerosol)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each inhalation (actuation) contains 24.0 mg salbutamol sulfate equivalent to 20.0mg salbutamol.
For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Metered dose inhaler aerosol

White and homogeneous suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Butalin is indicated in adults, adolescents and children aged 4 to 11 years.
For babies and children under 4 years of age, see section 4.2 and 5.1.
Butalin is indicated in the management of bronchial asthma, for the relief of wheezing and shortness of breath used on an as required basis. It may be used as necessary to relieve attacks of acute dyspnoea and may be used prophylactically before exertion or to prevent exercise-induced asthma.
Butalin may also be used in the treatment of the reversible component of airways obstruction.

4.2 Posology and method of administration

Posology

Adults:
For the relief of wheezing, shortness of breath and attacks of acute dyspnoea in patients with asthma, or the reversible component of airways obstruction, one or two inhalations may be administered as a single dose.
For prophylaxis of exercise-induced asthma, two inhalations before exercise.
Paediatric 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

Elderly:
No special dosage recommendations are made for elderly patients.
For all patients, the maximum recommended dose should not exceed eight inhalations in 24 hours. With repetitive dosing, inhalations should not usually be repeated more often than every 4 hours.

Method of Administration:
For oral inhalation
Directions for use:

1. Remove the cover from the mouthpiece and shake the inhaler vigorously.
2. Holding the inhaler with the mouthpiece down towards your mouth and putting your thumb under the mouthpiece and your index over the bottom of the canister, breathe out gently (but not fully) and then immediately place the mouthpiece in the mouth and close your lips around it.
3. After starting to breathe in slowly and deeply through your mouth, press the inhaler firmly by using your index to release **Butalin** and continue to breathe in.
4. Hold your breath for 10 seconds, or as long as it is comfortable, before breathing out slowly.
5. If you are to take a second inhalation, you should wait at least 1 minute before repeating steps 2, 3 and 4.
6. After use replace the cover on the mouthpiece.
7. **Cleaning:** Remove the canister, rinse the actuator in warm water, dry, and replace canister.

4.3 Contraindications

- Hypersensitivity to salbutamol or to any of the excipients.
- Salbutamol is contraindicated for use in the management of premature labour and 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 bronchodilators, in particular ß2-agonists to control symptoms, indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Patients with persistent asthma should receive optimal anti-inflammatory basic therapy with corticosteroids.
Sudden and progressive deterioration in asthma control is potentially life threatening and consideration should be given to increasing or starting oral and/or inhaler corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

The patient should be advised to seek medical advice if a previously effective dose ceases to be effective for at least three hours, and/or their asthma seems to be worsening.
The dosage or frequency of administration should only be increased on medical advice.
Patients requiring long-term management with salbutamol should be kept under regular surveillance.
Salbutamol should be administered cautiously to patients with thyrotoxicosis, coronary insufficiency, hypertrophic obstructive cardiomyopathy, arterial hypertension, tachyarrhythmias, in concomitant use of cardiac glycosides or diabetes mellitus.
Potentially serious hypokalaemia has been reported in patients taking 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 treatment with xanthine derivatives, steroids, diuretics, long-term laxatives and by hypoxia. Extra care should therefore be taken if ß2-agonists are used in these groups of patients and it is recommended that serum potassium levels should be monitored in such situations.
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 high doses of salbutamol have been used in emergency situations. This is reversible on reducing the dose of salbutamol (see section 4.9 Overdose).
Unwanted stimulation of cardiac adrenoceptors can occur in patients taking ß2-agonist therapy.
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 ß-agonists. 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.
As with other inhalation therapy, the potential for paradoxical bronchospasm should be considered. If this occurs, the salbutamol inhaler should be discontinued immediately and alternative therapy given. Solutions which are not of neutral pH may rarely cause paradoxical bronchospam in some patients.
Salbutamol and non-selective ß-antagonists such as propranolol should not usually be prescribed together.
In common with other ß-agonists, salbutamol can induce reversible metabolic changes such as increased blood glucose levels. Patients with diabetes 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.
Patients should be warned they may experience a different taste on inhalation compared to their previous inhaler.
Severe exacerbations of asthma must be treated in the normal way.

4.5 Interaction with other medicinal products and other forms of interaction

Propranolol and other non-cardioselective ß-adrenoceptor blocking agents antagonise the effects of salbutamol and should not usually be prescribed together.
Monoamine oxidase inhibitors, tricyclic antidepressants and digoxin increase the risk of cardiovascular effects.
Patients should be instructed to discontinue salbutamol for at least 6 hours before an intended anaesthesia with halogenic anaesthetics, wherever possible.
Hypokalaemia occurring with ß2-agonist therapy may be exacerbated by treatment with xanthines, steroids, diuretics and long-term laxatives.
Because the inhaler contains ethanol there is a theoretical potential for interaction in patients taking disulfiram or metronidazole. The amount of ethanol in the inhaler is small but it may be enough to precipitate a reaction in some sensitive patients.

4.6 Pregnancy and lactation

Pregnancy:
There is no experience of this product in pregnancy and lactation in humans. It should not be used in pregnancy and lactation unless the expected benefit to the mother is thought to outweigh any risk to the foetus or neonate
Propellant 134a:
There is no documented evidence of the use of salbutamol formulated with propellant HFA-134a in pregnant or lactating women.
Salbutamol:
The safe use of inhaled salbutamol during pregnancy has not been established but it has been in widespread use for many years in human beings without apparent ill consequence. 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.
Experience on the use of ß-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 ß2-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.
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.
Salbutamol inhalation is contraindicated in treatment of threatened abortion or premature labour.

4.7 Effects on ability to drive and use machines

It may cause dizziness. If you are affected do not drive or operate machinery.

4.8 Undesirable effects

Based on the MedDRA system organ class and frequencies, adverse events are listed in the table below.
Frequencies are defined as: 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 including isolated reports) and not known (cannot be estimated from the available data).

System organ class	**Frequency**	**Symptom**
Immune system disorders	Very rare	Hypersensitivity reactions (angioedema, urticaria, bronchospasm, hypotension and collapse)
Metabolism and nutrition disorders	Rare	Hypokalaemia (especially in combination with xanthine derivatives, corticosteroids and diuretics) increased serum lactate levels and acidosis lactic
Psychiatric disorders	Common	Tenseness
	Rare	Sleep disturbances and hallucinations (especially in children)
	Very rare	Insomnia
Nervous system disorders	Common	Headache, Dizziness, Tremor muscle
Cardiac disorders	Rare	Palpitations , tachycardia
	Very rare	Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles) especially if used concomitantly with other ß2-agonists
	Not known	Myocardial ischaemia (see section 4.4)
Vascular disorders	Rare	Peripheral vasodilatation
Respiratory, thoracic and mediastinal disorders	Rare	Throat irritation
	Very rare	Paradoxical bronchospasm (with an immediate increase in wheezing after dosing) (As with other inhalation therapy, paradoxical bronchospasm may occur immediately after dosing. If this occurs, the Inhaler should be discontinued immediately and, if needed, an alternative therapy instituted.)
Gastrointestinal disorders	Rare	Mouth irritation, nausea, vomiting, dry mouth, sore mouth
Skin and subcutaneous tissue disorders	Very rare	Pruritus
Musculoskeletal and connective tissue disorders	Uncommon	Myalgia
	Rare	Muscle cramps
	Very rare	Fine tremor (particularly of hands)

Healthcare professionals are asked to report any suspected adverse reactions via:
Pharmacovigilance and Medical Device Section
Drug Department - U.A.E M.O.H
Hotline: 80011111
Email: pv@moh.gov.ae
P.O. Box: 1853 Dubai U.A.E.

4.9 Overdose

Symptoms:
Overdosage may result in skeletal muscle tremor, tachycardia, tenseness, headache, and peripheral vasodilatation.
Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.
Hyperglycaemia, agitation and hyperactivity have also been reported following overdose with salbutamol.
Lactic acidosis has been reported very rarely in patients receiving intravenous or nebulised salbutamol therapy for the treatment of acute asthma exacerbation.
Treatment:
Asthmatic patients: Consideration should be given to discontinuation of treatment. Monitor biochemical abnormalities, particularly hypokalaemia which should be treated with potassium replacement where necessary. ß-adrenoceptor antagonists, even ß1- selective antagonists, are potentially life-threatening and should be avoided.
Non-asthmatic patients: Monitor and correct biochemical abnormalities, particularly hypokalaemia.
The preferred antidote for overdosage with salbutamol is a cardioselective ßadrenoceptor blocking agent but due care and attention should be used in administering beta-blocking drugs in patients with a history of bronchospasm, as these drugs are potentially life-threatening. A non-selective ß-adrenoceptor antagonist (e.g. nadolol, propranolol) will competitively reverse both hypokalaemia and tachycardia (ß1- selective drugs will be largely ineffective).
The treatment of lactic acidosis in cases of salbutamol overdose should be undertaken in a specialist intensive care unit. Salbutamol therapy should be discontinued and appropriate supportive therapy should be commenced to treat the underlying condition.
Lactic acidosis is treated indirectly by correcting the underlying causes and not by any treatment aimed directly at correction of lactic acidosis itself.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: selective ß2-adrenoreceptor agonists
ATC code: R03AC02

Salbutamol is a sympathomimetic agent which has a selective action on ß2-adrenoceptors of bronchial muscle. At therapeutic doses, salbutamol acts on the ß2-adrenoceptors of bronchial muscle with little or no action on the ß2-adrenoceptors of cardiac muscle. Salbutamol provides short acting (4 to 6 hours) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

Special Patient Populations

Children < 4 years of age

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 inhaler has a safety profile comparable to that in children > 4 years, adolescents and adults.

5.2 Pharmacokinetic properties

Salbutamol is readily absorbed from the gastro-intestinal tract, but the systemic absorption of the inhaled drug substance is low. The action of inhaled salbutamol depends on direct stimulation of receptors in the lung.
Onset of action is usually within 10 minutes of inhalation and lasts 4-6 hours in most patients.
Salbutamol is subject to first-pass metabolism in the liver; about half is excreted in the urine as an inactive sulfate conjugate. It does not appear to be metabolised in the lung and therefore its fate following inhalation therapy depends on the delivery method used, which determines the proportion of salbutamol inhaled relative to the proportion inadvertently swallowed. It has been suggested that the slightly extended half-life following inhalation may reflect slow removal of active drug from the lungs.

5.3 Preclinical safety data

Propellant 134a

In animal studies propellant 134a has been shown to have no significant pharmacological effects other than at very high exposure concentrations, when narcosis and a relatively weak cardiac sensitising effect were found. The potency of the cardiac sensitisation was less than that of CFC-11 (trichlorofluoromethane).
In studies to detect toxicity, repeated high dose levels of propellant 134a indicated that safety margins based on systemic exposure would be of the order 2200, 1314 and 381 for mouse, rat and dog with respect to humans.
There are no reasons to consider propellant 134a as a potential mutagen, clastogen or carcinogen judged from in vitro and in vivo studies including long term administration by inhalation in rodents.
The Safety studies with the Salbutamol Sulfate CFC-Free formulation in rat and dog showed few adverse effects. These occurred at high doses and were consistent with the known effects of salbutamol inhalation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Oleic Acid
Absolute alcohol
1,1,1,2-Tetrafluoroethane (HFA, 134a).

6.2 Incompatibilities

None known

6.3 Shelf life

36 months from the date of manufacturing

6.4 Special precautions for storage

Store below 30°C. Do not refrigerate.
Avoid storage in direct sunlight or heat.

6.5 Nature and contents of container

200 Metered doses (actuations) of white suspension in filled and crimped pressurized aluminium containers fitted with aerosol valve, actuator and dust cap, labelled (Upside down) in a printed carton along with a leaflet.

6.6 Special precautions for disposal and other handling

To prevent the inhaler blocking up, it is important to clean it at least once a week.
Cleaning: Remove the canister, rinse the actuator in warm water, dry, and replace canister.
Caution: The canister is pressurized. Do not puncture, break, or burn, even when empty.

7. MARKETING AUTHORISATION HOLDER

Gulf Pharmaceutical Industries - Julphar
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Ras Al Khaimah - United Arab Emirates
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8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Feb 9, 2022

10. DATE OF REVISION OF THE TEXT

December 2023