SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

ß REC SYRUP (Salbutamol Oral Solution BP 2mg/5ml)

2. Qualitative and quantitative composition

Each 5ml contains:

Salbutamol Sulfate BP	
Equivalent to Salbutamol	2.0 mg
Colour. Carmoisine	
In Syrup Base	q.s.

3. Pharmaceutical form

Oral Solution
A pink coloured flavoured syrup.

4. Clinical particulars

4.1 Therapeutic indications

Salbutamol is indicated in adults, adolescents and children aged 2 to 12 years.

Salbutamol is a selective β_2-agonist bronchodilator which provides short acting bronchodilation in reversible airways obstruction. Salbutamol is used to rapidly treat asthma, bronchospasm and reversible airways obstruction by widening the airways of the lungs. Salbutamol 2 mg/5ml oral solution is suitable for children and adults who are unable to use an inhaler device.

4.2 Posology and method of administration

For oral administration. Shake the bottle before use. An oral syringe may be used to measure doses less than 5ml.

Adults
The usual adult dose is (4mg) two 5 ml spoonfuls (10ml), 3 or 4 times per day which may be increased to a maximum of (8mg) four 5 ml spoonfuls (20ml), 3 or 4 times per day. The minimum starting dose is (2mg) one 5 ml spoonful (5ml), 3 or 4 times per day.

Elderly
In elderly patients and patients who are unusually sensitive to this class of medicine treatment may be initiated with (2mg) one 5 ml spoonful (5ml), 3 or 4 times per day.

Paediatric population
2- 6 years: the minimum starting dose is 1mg as 2.5 ml of oral solution three times daily. This may be increased to 2mg as 5 ml of oral solution three or four times daily.
6 – 12 years: the minimum starting dose is 2 mg as 5 ml of oral solution three times daily. This may be increased to four times daily.

Over 12 years: the minimum starting dose is 2mg three times daily given as 5 ml oral solution. This may be increased to 4 mg as 10 ml oral solution three or four times daily.

Ventolin is well tolerated by children so that, if necessary, these doses may be cautiously increased to the maximum dose.

4.3 Contraindications

Although intravenous salbutamol and occasionally salbutamol oral solution are used in the management of uncomplicated premature labour, salbutamol presentations should not be used for threatened abortion during the first or second trimester of pregnancy.

Should not be used in patients hypersensitive to any of the product ingredients, see section 6.1.

4.4 Special warnings and precautions for use

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 oral corticosteroid therapy and/or the maximum recommended dose of inhaled corticosteroid in those patients.

Patients should seek medical advice if treatment with Salbutamol 2 mg/5 ml oral solution becomes less effective.

The dosage or frequency of administration should only be increased on medical advice.

Patients taking Salbutamol 2 mg/5 ml oral solution may also be receiving short-acting inhaled bronchodilators to relieve symptoms.

Increasing use of bronchodilators in particular short-acting inhaled $beta_2$-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 they need more inhalations than usual.

In this situation patients should be reassessed and consideration given to the need for increased anti-inflammatory therapy (eg. Higher doses of inhaled corticosteroids or a course of oral corticosteroid). Severe exacerbations of asthma must be treated in the normal way.

Patients should 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.
Salbutamol causes peripheral vasodilation which may result in reflex tachycardia and increased cardiac output. Caution should be used in patients suffering from angina, severe tachycardia or thyrotoxicosis.

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.

Severe exacerbations of asthma must be treated in the usual manner.

Caution should be exercised in its use with anaesthetic agents such as chloroform, cyclopropane, halothane and other halogenated agents.

Salbutamol should not cause difficulty in micturition (urination) because unlike sympathomimetic drugs such as ephedrine, it does not stimulate α-adrenoceptors. However, there have been reports of difficulty in micturition in patients with prostatic enlargement.

Salbutamol should only be used during pregnancy if considered essential by the physician.

Salbutamol does not contain sugars.

This product should not be diluted.

Potentially serious hypokalaemia may result from beta-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. It is recommended that serum potassium levels are monitored is such situations.

In common with other β-adrenoceptor agonists, salbutamol 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 corticosteroids can exaggerate this effect.
This medicinal product contains small amounts of ethanol (alcohol), less than 100mg per 5ml dose.

4.5 Interaction with other medicinal products and other forms of interaction

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

The effects of this product may be altered by guanethidine, reserpine, methyldopa, tricyclic antidepressants.
Salbutamol oral preparations and non-selective beta-blocking drugs, such as propranolol should not usually be prescribed together.

Salbutamol is not contraindicated in patients under treatment with monoamine oxidase inhibitors (MAOIs).

4.6 Fertility, pregnancy and lactation

Pregnancy
Administration of drugs during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

As with the majority of drugs, there is little published evidence of its safety in the early stages of human pregnancy, but in animal studies there was evidence of some harmful effects on the foetus at very high dose levels.

Breastfeeding
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 known.

4.8 Undesirable effects

a) Summary of the safety profile
The most common side effect of Salbutamol 2mg/5ml oral solution is fine tremor of the hands, which may interfere with precise manual work. Tension, restlessness and a rapid heart beat may also occur. There have been very rare reports of muscle cramps. Hypersensitivity reactions such as angioedema, urticaria, bronchospasm, hypotension and collapse have rarely been reported. Potentially serious hypokalaemia may result from β_2-agonist therapy. Occasional headaches have also been reported. As with other drugs in this class rare reports of hyperactivity in children have been reported.

b) Tabulated list of adverse reactions
Adverse events are listed below by system organ class and frequency. 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. Very common and common events were generally determined from clinical trial data. Rare, very rare and unknown events were generally determined from spontaneous data.

Immune system disorders	
Very rare:	Hypersensitivity reactions including angioedema, urticaria, bronchospasm, hypotension and collapse.
Metabolism and nutrition disorders	
Rare:	Hypokalaemia.
Potentially serious hypokalaemia may result from beta agonist therapy.	
Nervous system disorders	
Very common:	Tremor.
Common:	Headache.
Very rare:	Hyperactivity.
Cardiac disorders	
Common:	Tachycardia, palpitations.
Rare:	Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles
Unknown:	Myocardial ischaemia* (see section 4.4)
Vascular disorders	
Rare:	Peripheral vasodilatation.
Musculoskeletal and connective tissue disorders	
Common:	Muscle cramps.
Very rare:	Feeling of muscle tension.

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

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 Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA yellow Card in the Google play or apple app store.

4.9 Overdose

Symptoms

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 hypokalaemia (see sections 4.4 and 4.8).

Salbutamol overdose may lead to Hypokalaemia (abnormally low potassium concentration in the blood). Serum potassium levels should therefore 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.

Nausea, vomiting and hyperglycaemia have been reported, predominantly in children and when salbutamol overdose has been taken via the oral route.

Treatment

The preferred antidote for overdose with salbutamol sulphate is a cardioselective beta-blocking agent, which should be used with caution in patients with a history of bronchospasm. Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Selective beta-2-adrenoreceptor agonists

ATC Code: R03CC02

As a beta-adrenergic stimulant for relief of bronchospasm such as occurs with asthma, bronchitis, emphysema. It has a highly selective action on the receptors in bronchial muscle and in therapeutic dosage, little or no action on the cardiac receptors.

5.2 Pharmacokinetic properties

Salbutamol is readily absorbed from the gastro-intestinal tract and is subject to first pass metabolism in the liver. Peak plasma concentrations occur within one to four hours after oral administration. After multiple oral doses of salbutamol 4mg four times a day, steady-state plasma concentrations are obtained after 3 days. About half is excreted in the urine as an

inactive sulphate conjugate following oral administration. The bioavailability of orally administered salbutamol is about 50%.

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 foetuses were found to have cleft palate at 2.5mg/kg dose, 4 times the maximum human oral 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 foetal 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 foetuses 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.

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, embryofoetal development, litter size, birth weight or growth rate.

6. Pharmaceutical particulars

6.1 List of excipients

Sr. No.	Raw Material	Pharmacopoeia
1.	Sucrose	BP
2.	Methyl Hydroxybenzoate	BP
3.	Propyl Hydroxybenzoate	BP
4.	Propylene Glycol	BP
5.	Sodium Benzoate	BP
6.	Glycerol	BP
7.	Disodium Edetate	BP
8.	Essence Pineapple	IHS
9.	Colour Carmoisine	IHS
10.	Citric acid	BP
11.	Purified water	BP

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30ºC in dark & dry place. Do not freeze.

6.5 Nature and contents of container

60 ml filled in an Amber Coloured PET Bottle packed in a carton.

6.6 Special precautions for disposal and other handling

No special instructions.

7. Marketing authorisation holder

Kilitch Drugs (India) Limited
37, Ujagar Industrial Estate,
W.T Patil Marg, Deonar,
Mumbai 400 088,Maharashtra, India.
Website- www.kilitch.com

8. Marketing Authorisation Number (S) issued by Ethiopian FDA

06883/07956/REN/2021

9. Date of First Authorisation/Renewal of the Authorisation

28-11-2021

10. Date of Revision of the Text

05/07/2023