SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ventolin Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 2 mg Salbutamol (as Salbutamol Sulfate BP).

Excipient with known effect:
5.6 mg sodium per 5 ml dose,
10.0 mg sodium benzoate per 5 ml dose,
0.00003325 mg benzyl alcohol per 5 ml dose,
1.9 mg propylene glycol per 5 ml dose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Salbutamol is a selective beta-2 adrenoceptor agonist providing short-acting (4-6 hour) bronchodilation in reversible airways obstruction. Ventolin syrup can be used in the management of asthma, bronchospasm and/or reversible airways obstruction.

Relief of bronchospasm in bronchial asthma of all types.

Ventolin syrup is suitable oral therapy for children and adults who are unable to use an inhaler device.

4.2 Posology and method of administration

Posology

Adults

The minimum starting dose is 2mg three times a day given as 5ml syrup. The usual effective dose is 4mg (10ml syrup) three or four times a day, which may be increased to a maximum of 8mg (20ml syrup) three or four times a day if adequate bronchodilation is not obtained.

Elderly

In elderly patients or in those known to be unusually sensitive to beta-adrenergic stimulant drugs, it is advisable to initiate treatment with the minimum starting dose.

Paediatric Population

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

6 - 12 years: the minimum starting dose is 2mg as 5ml syrup 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 5ml syrup. This may be increased to 4mg as 10ml syrup 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.

For lower doses the syrup may be diluted with freshly prepared purified water BP.

Method of administration

Route of administration: oral

4.3 Contra-indications

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

Non-i.v. formulations of salbutamol must not be used to arrest uncomplicated premature labour or threatened abortion.

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 Ventolin syrup becomes less effective.

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

Patients taking Ventolin syrup may also be receiving short-acting inhaled bronchodilators to relieve symptoms.

The management of asthma should normally follow a stepwise programme, and patient response should be monitored clinically and by lung function tests.

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 (e.g. 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 with Ventolin oral preparations is diminished or the usual duration of action reduced, they should not increase the dose or its frequency of administration, but should seek medical advice.

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 should be administered cautiously to patients suffering from thyrotoxicosis.

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, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in 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.

Ventolin Syrup contains 5.6 mg sodium per 5 ml dose, equivalent to 0.28% of the WHO recommended maximum daily intake of 2 g sodium in an adult.
Ventolin syrup is sugar free.
Ventolin Syrup contains 10.00 mg sodium benzoate per 5 ml dose.
Ventolin Syrup contains 1.9 mg of propylene glycol in each 5 ml dose.
Ventolin Syrup contains 0.00003325 mg benzyl alcohol in each dosage unit.
Benzyl alcohol may cause allergic reactions. Patients with liver or kidney disease and pregnant or breastfeeding patients should be advised that large amounts of benzyl alcohol can build up in the body and may cause metabolic acidosis.

4.5 Interactions with other medicinal products and other forms of interaction

Ventolin syrup and non-selective beta-blocking drugs, such as propranolol, should not usually be prescribed together.

4.6 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.

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.

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

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

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).

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.

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

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

Salbutamol is a selective beta-$_2$ adrenoceptor agonist. At therapeutic doses it acts on the beta-$_2$ adrenoceptors of bronchial muscle providing short acting (4-6 hours) bronchodilation in reversible airways obstruction.

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-sulfate (phenolic sulfate) which is also excreted primarily in the urine. The faeces are a minor route of excretion. The majority 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%.

After oral administration, salbutamol is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulfate. Both unchanged drug and conjugate are excreted primarily in the urine. 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

Sodium citrate
Citric acid monohydrate
Hydroxypropyl methylcellulose
Sodium benzoate
Benzyl alcohol
Propylene glycol (present in orange flavour IFF 17.42.8187)

Saccharin sodium
Sodium chloride
Orange flavour IFF 17.42.8187
Purified water

6.2 Incompatibilities

None known

Ventolin syrup is sugar free. Dilution of Ventolin syrup with syrup BP or sorbitol solution is not recommended as this may result in the precipitation of the cellulose thickening agent. If dilution is required freshly prepared Purified Water BP should be used. The diluted mixture must be protected from light and stored below 25ºC.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C.

Protect from light.

Ventolin syrup may be diluted with freshly Purified Water BP. The diluted mixture must be protected from light and stored below 25°C. Discard after 28 days.

6.5 Nature and contents of container

Amber glass bottle.

Closure (150ml): plastic tamper evident, child resistant or plastic child

resistant or ROPP aluminium (lacquered internally and externally) with either

PVdC faced EPE or LDPE faced PVdC/EPE OR LLDPE/PVdC

PVC/LLDPE/EPE (single or double faced) wad.

Pack size: 150ml.

6.6 Special precautions for disposal and other handling

Ventolin syrup may be diluted with Purified Water BP (50%v/v). The resulting mixture should be protected from light and used within 28 days.

A 50% v/v dilution of Ventolin syrup has been shown to be adequately preserved against microbial contamination. However, to avoid the possibility of introducing excessive microbial contamination, the Purified Water used for dilution should be recently prepared or alternatively it should be boiled and cooled immediately before use.

Admixture of Ventolin syrup with other liquid preparation is not recommended.

7 MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

PL 10949/0088

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16/11/2023