



UNIQUE PHARMACEUTICALS LTD

**COMMON TECHNICAL DOSSIER (CTD) – Module 1**

**ASTHAVENT SYRUP**

## **1.3.1**

# **SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)**

**Enclose in following pages**

# 1 Name of the medicinal product

ASTHAVENT® SYRUP

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

### Each 5 ml contains:

2 mg Salbutamol (as Salbutamol Sulfate BP).

For the full list of excipients, see section 6.1

## 3. PHARMACEUTICAL FORM

Syrup

## 4. Clinical particulars

### 4.1 Therapeutic indications

Asthavent 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. Asthavent syrup can be used in the management of asthma, bronchospasm and/or reversible airways obstruction.

Relief of bronchospasm in bronchial asthma of all types.

Asthavent 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.

Asthavent 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 Contraindications**

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 Asthavent syrup becomes less effective.

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

Patients taking Asthavent 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<sub>2</sub>-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 Asthavent 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.

Asthavent syrup contains 5.844 mg sodium per 5 ml dose, equivalent to 0.29% of the WHO recommended maximum daily intake of 2 g sodium in an adult. Asthavent syrup is sugar free.

Asthavent syrup contains 10.00 mg sodium benzoate per 5 ml dose.

Asthavent syrup contains 0.0000004 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 Interaction with other medicinal products and other forms of interaction

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

#### 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.

##### 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 ( $\geq 1/10$ ), common ( $\geq 1/100$  and  $< 1/10$ ), uncommon ( $\geq 1/1000$  and  $< 1/100$ ), rare ( $\geq 1/10,000$  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 Website: [www.mhra.gov.uk/yellowcard](http://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. Pharmacological Properties**

Pharmacotherapeutic group: Selective beta-2-adrenoreceptor agonists

ATC Code: R03CC02

Salbutamol is a selective beta<sub>2</sub>-adrenoceptor agonist. At therapeutic doses it acts on the beta<sub>2</sub>-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 β<sub>2</sub>-agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of fetuses 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 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 50mg/kg/day orally (i.e. much higher than the normal human dose) 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.

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

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of Excipients:

S. No	Composition	Reference
1.	Sodium Citrate	BP
2.	Citric Acid Monohydrate	BP
3.	Sodium Benzoate	BP
4.	Sodium saccharin	BP
5.	Banana Flavour	BP

### 6.2. Incompatibilities

None known

Asthavent syrup is sugar free. If dilution is required freshly prepared Purified Water BP should be used. The diluted mixture must be protected from light and stored below 25°C.

### 6.3. Shelf life:

3Years

### 6.4. Special precautions for storage

Store at a temperature not exceeding 30°C.

Protect from light.

Asthavent 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 (100ml): Pet bottle 100ml with ROPP cap.

Each labeled bottle is packed into printed inner cartons together with graduated measuring dose cup

And Product leaflet insert.

#### **6.6 Special precautions for disposal and other handling**

Asthavent 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 Asthavent 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 Asthavent syrup with other liquid preparation is not recommended.

### **7. <APPLICANT/MANUFACTURER>**

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