PROFFESSIONAL INFORMATION FOR ASTHAVENT SYRUP

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE

ASTHAVENT SYRUP (2,0 mg/5 mL Syrup)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL contains Salbutamol sulphate equivalent to salbutamol 2,0 mg.

Contains sugar:	Sucrose 2250,00 mg
	Liquid Sorbitol (70 %) 500,00 mg
Preservative:	Methyl hydroxybenzoate 0,2 % *m/v*
	Propyl hydroxybenzoate 0,02 % *m/v*

For the full list of excipients, see **section 6.1**

3. PHARMACEUTICAL FORM

Syrup

A pink coloured clear solution with a characteristic fruity flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ASTHAVENT SYRUP is indicated as a bronchodilator:

- in the treatment of bronchospasm associated with bronchial asthma
- emphysema
- chronic obstructive bronchitis

4.2 Posology and method of administration

Posology

Adults:

5 mL to 10 mL three to four times daily.

Some patients may require dosages of up to 20 mL.

Children:

2 to 6 years: 2,5 mL to 5 mL three to four times daily.

Over 6 years: 5 mL three to four times daily.

Do not exceed the recommended dose.

Special populations

Elderly Population:

Elderly patients should be given the lower dose initially.

Paediatric population

The safety and efficacy of ASTHAVENT SYRUP in children aged younger than 2 years has not yet been established.

Method of administration

For oral administration

4.3 Contraindications

ASTHAVENT SYRUP is contraindicated in:

- Patients with known hypersensitivity to salbutamol or to any of the excipients used in the formulation of ASTHAVENT SYRUP (see **section 6.1**)**.**
- Concurrent use with beta-blocking medicines.
- Hyperthyroidism.
- Cardiac disease.
- Prevention of premature labour associated with toxaemia of pregnancy or ante partum haemorrhage.
- Threatened abortion during first and second trimesters of pregnancy.

- Concurrent use with monoamine oxidase inhibitors (MAOIs) (see section 4.5).

4.4 Special warnings and precautions for use

Medical advice should be sought if relief from symptoms is not obtained within three hours of taking a previously effective dose, in order that alternative or additional measures may be taken if necessary.

Tolerance may develop in asthmatic patients given salbutamol. If tolerance develops, and the patient's condition worsens, alternative or additional therapy should be instituted. The dosage of salbutamol should not be increased in these cases.

Salbutamol should be avoided or used with care in patients undergoing anaesthesia with any halogenated anaesthetics.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma.

Increasing use of bronchodilators indicates deterioration of asthma control. If patients find that short acting relief bronchodilator treatment becomes less medical attention must be sought.

Salbutamol causes peripheral vasodilation which may result in reflex tachycardia and increased cardiac output.

Constant monitoring of potassium levels in patients with severe asthma is essential, potentially serious hypokalaemia may result from beta-2 agonist therapy.

Hypokalaemia associated with high doses of salbutamol may result in increased susceptibility to digoxin-induced cardiac dysrhythmias.

In common with other β-adrenoceptor agonists, salbutamol can induce reversible metabolic changes

such as increased blood glucose levels.

Diabetes

Administration of beta agonists is associated with a rise of blood glucose. Therefore blood glucose and lactate levels should be monitored in diabetics and diabetic treatment adjusted accordingly to meet the needs of the diabetic during tocolysis. 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.

Cardiovascular effects may be seen with sympathomimetic medications, including ASTHAVENT SYRUP.

Tachyphylaxis with resistance may occur with prolonged use of high dosage.
Care is necessary when treating patients with closed-angle glaucoma, and in those receiving antihypertensive therapy.

It is important to avoid excessive doses as this is thought to be linked to sudden death probably due to the induction of ventricular dysrhythmias.

Salbutamol may be restricted in certain sports as it is considered to be a member of the prohibited group, Beta-2 agonists; competitors should check with the appropriate sports authorities.

ASTHAVENT SYRUP contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.
ASTHAVENT SYRUP contains sucrose and sorbitol.Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take ASTHAVENT SYRUP.

The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

4.5 Interaction with other medicinal products and other forms of interaction

The effects of salbutamol are antagonised by propranolol and other β-adrenoceptor blocking medicines.

An increased risk of dysrhythmias may occur if patients are receiving digoxin, quinidine, or tricyclic antidepressants.

The effects of salbutamol may be altered by reserpine or methyldopa.

Interaction with alpha-and beta-blocking medicines may occur.

Salbutamol may interact with monoamine oxidase inhibitors, and should not be given to patients receiving such treatment or within 14 days after stopping treatment (see section 4.3).

Halogenated anaesthetics

Owing to the additional antihypertensive effect, there is increased uterine inertia with risk of haemorrhage; in addition, serious ventricular rhythm disorders due to increased cardiac reactivity, have been reported on interaction with halogenated anaesthetics. Treatment should be discontinued, whenever possible, at least 6 hours before any scheduled anaesthesia with halogenated anaesthetics (see section 4.4).

Anti-diabetics

The use of salbutamol and other beta-agonists are associated with a rise of blood glucose which may be interpreted as an attenuation of anti-diabetic therapy; therefore individual anti-diabetic therapy may need to be adjusted.

Potassium depleting medicine

Owing to the hypokalaemic effect of beta-agonists, concurrent administration of serum potassium depleting medicine known to exacerbate the risk of hypokalaemia, such as diuretics, digoxin, methyl xanthines (e.g. theophylline) and corticosteroids, should be administered cautiously after careful evaluation of the benefits and risks with special regard to the increased risk of cardiac arrhythmias arising as a result of hypokalaemia.

4.6 Fertility, pregnancy and lactation

Pregnancy:

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

Breastfeeding:

As salbutamol is probably secreted in breast milk its use in nursing mothers requires careful consideration.

Fertility:

No data available.

4.7 Effects on ability to drive and use machines

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that salbutamol does not adversely affect their ability to do so safely (see section 4.8).

4.8 Undesirable effects

Tabulated summary of adverse reactions

The following adverse reactions have been classified according to the following categories, frequent, less frequent and frequency unknown.

System organ class	Adverse Reaction
Immune system disorders	**Less frequent:** Hypersensitivity reactions including paradoxical bronchospasm, angioedema, urticaria, hypotension, and collapse.
Metabolism and nutrition disorders	**Less frequent:** Decreased appetite, altered metabolism including disturbances of glucose metabolism, lactic acidosis, hypokalaemia
Psychiatric disorders	**Less frequent:** Fear, anxiety, restlessness, insomnia, confusion, irritability, psychotic states, nervous tension.
Nervous system disorders	**Frequent:** Tremor of skeletal muscle (particularly in the hands), headache **Less frequent:** Myoclonus
Cardiac disorders	**Less frequent:** Palpitations, anginal pain, tachycardia, cardiac arrhythmias, hypotension with dizziness, cardiac dysrhythmias, myocardial ischaemia.
Vascular disorders	**Less frequent:** Vascular constriction which can give rise to hypertension, peripheral vasodilation
Respiratory, thoracic and mediastinal disorders	**Less frequent:** Dyspnoe, pulmonary oedema
Gastrointestinal disorders	**Less frequent:** Nausea, vomiting, hypersalivation

Musculoskeletal and connective tissue disorders	**Less frequent:** Muscle cramps
Renal and urinary disorders	**Less frequent:** Difficulty in micturition, urinary retention.
General disorders and administrative site conditions	**Less frequent:** Asthenia, increased sweating, fainting and flushing

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8 and to Cipla Medpro (Pty) Ltd at drugsafetysa@cipla.com or telephone 080 222 6662 (toll free)

4.9 Overdose

See sections 4.4 and 4.8.

Symptoms

Fine tremor of skeletal muscles, tachycardia, palpitations, hyperactivity, peripheral vasodilatation and metabolic effects including hypokalaemia have been reported.

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.

Treatment

The preferred antidote for overdosage with salbutamol is a cardioselective beta blocking medicine, but beta blocking medicines should be used with caution in patients with a history of bronchospasm.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification

A 10.2.2 Medicines acting on respiratory system. Bronchodilators. Other.

Pharmacotherapeutic group

Selective beta-2-adrenoreceptor agonists

ATC code: R03CC02

Mechanism of action

Salbutamol acts by stimulating beta-2-adrenergic receptors in the lungs to relax bronchial smooth muscle, thereby relieving bronchospasm associated with bronchial asthma, emphysema and chronic bronchitis. Because of this action, salbutamol increases vital capacity, decreases residual volume and reduces airway resistance.

5.2 Pharmacokinetic properties

Absorption

Salbutamol is readily absorbed from the gastrointestinal tract.

Distribution

The peak plasma concentration of salbutamol and its metabolites is 5,1 to 11,7 ng/mL at 2,5 to 3 hours after an oral dose of 4 mg.

Biotransformation

Salbutamol does not cross the blood brain barrier to a significant extent, but it crosses the placental barrier. The plasma half-life of salbutamol has been estimated to range from 4 to 6 hours.

Elimination

Salbutamol is excreted in urine in about 24 hours, with 50 % being excreted within 4 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Citric Acid Monohydrate
- Colour Carmoisine Supra
- Liquid Sorbitol 70 %
- Methyl Hydroxybenzoate (Methyl Parahydroxybenzoate)
- Orange four flavour
- Propyl Hydroxybenzoate (Propyl Parahydroxybenzoate)
- Purified Water
- Sodium Citrate Dihydrate
- Sodium Chloride
- Sucrose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

18 months

6.4 Special precautions for storage

- Store at or below 25 °C.
- Protect from light.

- Keep in original packaging

6.5 Nature and contents of container

Carton containing a 100 mL amber PET bottle.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBER(S)

30/10.2.2/0200

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

February 1996

10. DATE OF REVISION OF THE TEXT

08 March 2023

Botswana: S2 BOT0200535

Namibia: NS1

06/10.2.1/0077