Summary of Product Characteristics

1. Name of Finished Pharmaceutical Product:

AXAMOL (Salbutamol Nebulizer Solution BP 2.5 mg Respules)

2. Qualitative and Quantitative Composition:

a) Qualitative Composition

Product Name: AXAMOL

Generic Name: Salbutamol Nebulizer Solution BP 2.5 mg Respules

Label Claim:

Each 2.5 ml Respules Contains: -

Salbutamol Sulphate BP

Eq. to Salbutamol.....2.5 mg

Water for Injections BP .....q.s.

b) Quantitative Composition

Batch size: 20 Liters

S. No	Name of Ingredients	Reference	Qty./ 2.5 ml	Function of Ingredient
1.	**Salbutamol sulphate Eq. to Salbutamol	BP	6.024 mg≈ 2.5 mg	Active ingredient
2.	Sodium chloride	BP	22.50 mg	Isotonic Agent
3.	Disodium Edetate	BP	1.250 mg	Chelating Agent
4.	Sodium citrate	BP	1.250 mg	Buffering Agent
5.	Citric Acid	BP	0.700 mg	Buffering Agent
6.	* Citric Acid	BP	0.600 mg	pH modifier
7.	Water for injections	BP	q.s. to 2.5 ml	Vehicle

** These material are to be dispensed on 100% assay value

* These material used for pH adjustment

Standard Quantity of Salbutamol Sulphate BP Eq. to Salbutamol=

2.5x70x576.7x1000x100/2.5x239.3x1000x100 = 48.19 gm

3. Pharmaceutical Form

Nebulizer Solution

Salbutamol Nebulizer solution is Clear & colourless solution.

4. Clinical Particulars

4.1 Therapeutic indications

For use in the routine management of chronic bronchospasm unresponsive to conventional therapy and the treatment of acute severe asthma

4.2 Posology and method of administration

Adults: The usual dose is 2.5 mg given up to three to four times a day by a nebulizer. This may be increased to 5 mg up to three to four times a day if necessary.

However, in domiciliary practice the benefits of increasing the dose of nebulized salbutamol sulfate should be weighed against the risk that a deterioration in the patients

underlying condition may be masked. In such circumstances a medical assessment should be considered since alternative therapy may be indicated.

Children: The same dosage as for adults.

Infants: The clinical efficacy of nebulized salbutamol sulfate in infants under 18 months is uncertain. As transient hypoxaemia may occur supplemental oxygen therapy should be considered.

Elderly: The same dosage as for other adults.

Delivery of the aerosol may be by face mask or 'T' piece.

Salbutamol Nebulizer Solution BP 2.5 mg Respules should be used undiluted. However, if a delivery time in excess of 10 minutes is required they should be diluted with Sodium Chloride Injection.

4.3 Contraindications

Hypersensitivity to the active substance salbutamol or to the excipients. Although some forms of salbutamol sulfate have been used in the management of premature labour, Salbutamol Nebulizer Solution should not be used for this purpose. Salbutamol Nebulizer Solution should not be used in threatened abortion

4.4 Special warnings and precautions for use

Salbutamol Nebulizer Solution is for use with a nebulizer under the direction of a physician. The solution must not be injected or administered orally.

In patients with severe or unstable asthma, bronchodilators should not be the only or main treatment. Regular medical assessment is required including lung function testing,

as they are at risk of severe attacks and even death.

Oral corticosteroid therapy and/or inhaled corticosteroids should be considered.

Increasing use of bronchodilators to relieve symptoms indicates deterioration of asthma

control.

In the following cases, salbutamol should only be used with caution and if strictly indicated:

- Serious cardiac disorders, in particular recent myocardial infarction
- Coronary heart disease, hypertrophic obstructive cardiomyopathy and tachyarrhythmia

  (due to the positive ionotropic effect of β2 – agonists) severe and untreated hypertension
- Aneurysm
- Hyperthyroidism
- Diabetes which is difficult to control
- Pheochromocytoma

Daily self-assessment of asthma control following instructions regarding the use of Salbutamol Nebulizer Solution and any other drugs required for the management of asthma is important in order that the course of the disease can be followed and the success of both bronchodilator and anti-inflammatory therapy monitored. The patient should be instructed in the regular measurement of peak expiratory flow rate (PEFR) using a portable peak flow meter.

Patients receiving treatment with Salbutamol Nebulizer Solution at home should be warned that, if asthma control does not improve satisfactorily or deteriorates, or if the short-acting relief bronchodilator treatment becomes less effective, or more inhalations than usual are required, medical advice must be sought in order that the clinical condition can be re-assessed and therapeutic management revised appropriately. In this

situation anti-inflammatory therapy may be required, the dose of anti – inflammatory therapy may need to be increased or a short course of oral glucocorticoids may be needed. Increasing use of bronchodilators and in particular short-acting inhaled beta2 adrenergic agonists to relieve symptoms indicates deterioration of asthma control.

A sudden and increasing deterioration of asthma symptoms can be life threatening. Therefore, medical assistance must be sought immediately.

The administration of salbutamol in patients with acute asthma may cause a further reduction of the O2 saturation.

The dose and frequency of inhalation of short-acting beta2 agonists should only be increased following medical advice and if a previously effective dose fails to give the expected relief the patient should be advised to seek medical advice. Exceeding the prescribed dose can be dangerous with resultant cardiac effects, hypokalaemia, taste alteration, nausea, restlessness, sweating, headache, or tremor.

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 ischemia associated with salbutamol.

Patients with underlying severe heart disease (e.g. ischemic 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.

Potentially serious hypokalaemia may result from β2-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, and diuretics. Serum potassium levels should be monitored in such situations.

Due to the hyperglycaemic effects of beta2 – stimulants, additional blood glucose measurements are initially recommended when treatment with Salbutamol Nebulizer Solution is started in diabetic patients.

Inhalation of high doses of salbutamol can increase the blood glucose level. Therefore, blood glucose levels in diabetic patients should be monitored closely.

The use of nebulised salbutamol in combination with nebulised anticholinergic agents has been reported to precipitate acute angle closure glaucoma. This combination should be used with caution, in particular in patients with actual or potential glaucoma. Patients should be warned.

4.5 Interaction with other medicinal products and other forms of interaction

Salbutamol Nebulizer Solution should be used with caution in patients receiving other sympathomimetics.

Salbutamol and non-selective β - receptor blocking drugs should not usually be prescribed together. In patients with asthma administration of β - receptor blocking drugs is associated with a risk of severe bronchoconstriction.

Treatment with salbutamol can lead to hypokalaemia. This effect may be potentiated by the concomitant administration of other drugs, in particular xanthine derivatives, glucocorticoids, diuretics and cardiac glycosides (digoxin). Serum potassium levels should be monitored in these situations.

Tricyclic antidepressants may increase the risk of cardiovascular side effects.

Corticosteroids may increase the risk of hyperglycaemia.

A few cases have been reported where the combination of nebulised salbutamol and ipratropium bromide has given rise to acute angle-closure glaucoma

4.6 Fertility, pregnancy and lactation

Based on preclinical studies and long-term clinical experience, salbutamol has not been shown to have any teratogenic effects. If the mother uses salbutamol during pregnancy, the pulse rate of the foetus may increase. Since salbutamol is passively excreted in breast milk, high doses may induce drug effect in the breast-fed infant.

Although salbutamol is considered the first line treatment to relieve bronchospasm in asthmatic pregnant women, use during pregnancy, especially in the first trimester, and lactation should only be considered once the benefits have been carefully weighed against the risks.

4.7 Effects on ability to drive and use machines

None Known

4.8 Undesirable effects

Up to approximately 10% of patients can be expected to experience adverse reactions. These depend upon the dose and the individual sensitivity. Most commonly reported are: taste alteration (bad, unpleasant and unusual taste) and application site reaction (mouth and throat irritation, burning sensation of the tongue), fine tremor (usually of the hands)

nausea, sweating, restlessness, headache, dizziness and muscle cramps. These undesirable effects may subside on continuation of treatment within 1-2 weeks.

As with other inhalation therapies, in rare cases paradoxical bronchospasm may occur, manifest by an immediate increase in wheezing after dosing. Paradoxical bronchospasm should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator. Salbutamol Nebulizer Solution should be discontinued immediately, the patient should be assessed, and if necessary, alternative therapy instituted. Hypersensitivity reactions such as rash, urticaria, dermatitis, pruritus and erythema have been observed. There have been very rare reports of angioedema (oedema of the face, lips, eyes and throat), bronchospasm, hypotension and collapse.

Tachycardia, with or without peripheral vasodilation, may occur. In common with other beta2 agonists, cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles), palpitations, angina pectoris, and blood pressure effects have been reported in association with the use of salbutamol, usually in susceptible patients. There are reports about stimulating effects on the central nervous system after inhalation of salbutamol which manifest themselves in hyperexcitability, hyperactive behaviour, sleeping disturbances and hallucinations. These observations were predominantly made in children up to 12 years of age.

The table below presents possible adverse drug reaction in system organ class order and sorted by frequency.

Organ System	**Frequency**	**Adverse drug reaction**
Immune system disorders	Very rare (including isolated cases) (<1/10,000)	Hypersensitivity reaction
Metabolism	Rare (>1/10,000, <1/1,000)	Hypokalaemia, hyperglycaemia
Psychiatric disorders	Common (>1/100, <1/10)	Restlessness

Nervous system disorders	Common (>1/100, <1/10)	Fine tremor, dizziness
	Rare (>1/10,000, <1/1,000)	Hyperactive behaviour
	Very rare (including isolated cases) (<1/10,000)	Hyperexcitability, sleeping disturbances, hallucinations
Cardiac disorders	Rare (>1/10,000, 1/1,000)	Tachycardia, cardiac arrhythmia (atrial fibrillation, supraventricular tachycardia, extrasystoles), palpitations, angina pectoris, blood pressure effects (lowering or increase)
	Unknown*	Myocardial ischemia
Vascular disorders	Rare (>1/10,000, <1/1,000)	Peripheral vasodilation
	Very rare (including isolated cases) (<1/10,000)	Collapse
Respiratory, thoracic and mediastinal disorders	Rare (>1/10,000, 1/1,000)	Paradoxical bronchospasm
Gastrointestinal disorders	Common (>1/100, <1/10)	Nausea, taste alteration
Skin and subcutaneous tissue disorders	Common (>1/100, <1/10)	Pruritus, rash, erythema, urticaria, angioedema
Musculoskeletal disorders	Rare (>1/10,000, 1/1,000)	Muscle cramps
General disorders and administration site condition	Common (>1/100, <1/10)	Headache, application site reaction (mouth and throat irritation, burning sensation of the tongue)

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

4.9 Overdose

The risk of overdose with Salbutamol Nebulizer Solution is rather unlikely, if used according to the instructions.

Symptoms of an overdose

In the case of an overdose, the above-mentioned undesirable effects occur very quickly and with increased severity.

Typical symptoms are: tachycardia, palpitations, arrhythmia, restlessness, sleep disturbances, chest pain and vigorous tremor, especially on hands but also on the whole body. Nausea, dizziness, increased systolic blood pressure and decreased diastolic blood pressure may also be observed.

Occasionally, psychotic reactions were observed after excessive doses of salbutamol.

In the case of a salbutamol overdose there can increasingly be a shift of potassium into the intracellular space resulting in hypokalaemia, as well as hyperglycaemia, hyperlipidaemia, and hyperketonaemia.

Increased serum lactate levels and rarely, lactic acidosis, have been reported following therapy with salbutamol, particularly after high dose administration. Symptoms include deep, rapid breathing, cold and blue coloured fingers and toes, inability to concentrate and general malaise.

Management of an overdose

Treatment after an overdose of a β-sympathomimetic is mainly symptomatic. The following measures may be considered, depending upon the individual circumstances:

- If large amounts of the drug are swallowed, irrigation of the stomach should be considered. Activated charcoal and laxatives can have favourable effects on the undesired absorption of the β-sympathomimetic.
- For the cardiac symptoms of overdosage with salbutamol a cardioselective betablocking agent may be considered, but beta-blocking drugs should only be used with caution and be avoided as far as possible in patients with a history of bronchospasm.

  ECG monitoring is indicated in such patients.
- In the case of fairly pronounced lowering of the blood pressure, volume substitution (e.g. plasma expanders) is recommended.
- If hypokalaemia develops, electrolyte balance should be monitored and, if appropriate, electrolytes may need to be administered.

5. Pharmacological properties

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Broncholytic/antiasthmatic/ β2-sympathomimetic

ATC code: R03AC02

Salbutamol is a selective beta2-adrenoceptor agonist. At therapeutic doses it acts on the beta2-adrenoceptors of bronchial muscle to provide bronchodilation. With its fast

onset of action (within 5 minutes) it is particularly suitable for the management and prevention of attacks in asthma. Salbutamol has a duration of action of 4 to 6 hours in most patients.

5.2 Pharmacokinetic properties

Absorption and metabolism of salbutamol in lungs and gastrointestinal tract differ.

After inhalation, between 10 and 20 % of the active substance reaches the lower airways. The remainder is retained in the delivery system or is deposited in the oropharynx where it is swallowed. The fraction deposited in the airways is absorbed into the pulmonary tissues and circulation, but is not metabolised by the lung. On reaching the systemic circulation it becomes accessible to hepatic metabolism and is excreted, primarily in the urine, as unchanged drug and as the phenolic sulfate.

The swallowed portion of an inhaled dose 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. Approximately 90% of an oral dose is excreted in urine and 10% in faeces. 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.

Most 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%.

5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction. Effects seen in toxicity studies were related to the beta-adrenergic activity of salbutamol.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium chloride, Disodium Edetate, Sodium citrate, Citric acid, Water for Injections

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months from the date of manufacturing.

6.4 Special precautions for storage

Store below 30ºC. Protect from light. Do not refrigerate or freeze.

6.5 Nature and contents of container

4 x 5 x 2.5 ml LDPE Respule wrapped in a foil pouch packed in a Unit Carton, along with the pack insert.

6.6 Special precautions for disposal and other handling

The product should be used with a respirator or nebuliser only, under the direction of a physician. It is not to be injected or administered orally.

Remove a strip of combipack respules from the carton.

Use afresh respule for each dose.

1. Tear one respule from the combipack.
2. To open the respule twist off the cap as shown in the figure.
3. Squeeze the content into the reservoir of the nebulising chamber
4. Discard the respule after use.

Shake well before use.

Keep out of reach of reach of children

7. Manufacturer and Marketing

Authorization Holder

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8. Marketing authorization number(s)

FDA-HMP-MA-0480

9. Date of first authorization/renewal of the authorization

24.08.2023

10. Date of revision of the text

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