Summary of Product Characteristics

1. Name of the medicinal product:
MUCO-ASTHALIN® syrup

2. Qualitative and quantitative composition
Each 5 ml (tea spoonful) contains – Terbutaline Sulphate BP 2.5 mg

For a full list of excipients, see section 6.1

3. Pharmaceutical form: Syrup
Description: Reddish-pink, clear syrup with pleasant aroma

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For bronchodilation – Terbutaline is a selective beta$_2$-adrenergic agonist recommended for the relief and prevention of bronchospasm in bronchial asthma and other bronchopulmonary disorders in which bronchospasm is a complicating factor.

4.2 Posology and method of administration
As directed by the Physician OR

Use in bronchospasm – Adults 15 years and above – 5mg (10ml) 3 times daily.

Adults should not receive more than 15mg (30ml) of the drug daily. If disturbing adverse effects occur, dosage may be reduced to 2.5mg (5ml) 3 times daily.

Children 12 to 15 years of age – 2.5mg (5ml) 3 times daily; dosage should not exceed 7.5mg (15ml) daily.

Children under 12 years: It is contraindicated in children under the age of 12 years. Do not exceed the stated dose

4.3 Contraindications
Muco-Asthalin Syrup should not be used as a tocolytic agent in patients with pre-existing ischaemic heart disease or those patients with significant risk factors for ischaemic heart disease. It is also contraindicated for any condition of the mother or foetus in which prolongation of the pregnancy is hazardous, e.g. severe toxaemia, anti-partum haemorrhage, intra-uterine infection, severe pre-eclampsia, abruptio placentae, threatened abortion during the 1st and 2nd trimester, or cord compression. It should not be used in patients with a history of hypersensitivity to any of the ingredients.

4.4 Special warnings and precautions for use:
As for all beta$_2$-agonists caution should be observed in patients with thyrotoxicosis. Cardiovascular effects may be seen with sympathomimetic drugs, including Muco-Asthalin. Due to the positive inotropic effect of beta$_2$-agonists, these drugs should not be used in patients with hypertrophic cardiomyopathy. It should be used with caution in tocolysis and supervision of cardiorespiratory function, including ECG monitoring, should be considered. Treatment should be discontinued if signs of myocardial ischaemia (such as chest pain or ECG changes) develop. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin. Due to the hyperglycemic effects of beta$_2$-agonists, additional blood glucose controls are recommended initially in diabetic patients. Potentially serious hypokalemia may result from beta$_2$-agonist therapy. Particular caution is recommended in acute severe asthma as the associated risk may be augmented by hypoxia.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This product may cause allergic reactions (possibly delayed) due to Sodium propyl hydroxybenzoate and Sodium methyl hydroxybenzoate.

If a previously effective dosage regimen no longer gives the same symptomatic relief, the patient should urgently seek further medical advice. Keep out of reach of children.

4.5 Interaction with other medicinal products and other forms of interaction:

Beta-blocking agents (including eye drops), especially the non-selective ones such as propranolol, may partially or totally inhibit the effect of beta-stimulants. Therefore Muco-Asthalin preparations and non-selective beta-blockers should not normally be administered concurrently. Muco-Asthalin should be used with caution in patients receiving other sympathomimetics.

Hypokalemia may result from $beta_2$-agonist therapy and may be potentiated by concomitant treatment with xanthine derivatives, corticosteroids and diuretics.

Halothane anaesthesia should be avoided during $beta_2$-agonists treatment, since it increases the risk of cardiac arrhythmias. Other halogenated anaesthetics should be used cautiously together with $beta_2$-agonists.

4.6 Pregnancy and lactation:

Although no teratogenic effects have been observed in animals or in patients, Muco-Asthalin should only be administered with caution during the first trimester of pregnancy. Terbutaline is secreted in breast milk, but effect on the infant is unlikely at therapeutic doses. Transient hypoglycaemia has been reported in newborn preterm infants after maternal $beta_2$-agonist treatment.

4.7 Effects on ability to drive and use machines:

None known.

4.8 Undesirable effects:

The most common adverse effects of terbutaline sulfate are dose related and characteristic of sympathomimetic agents. The principal adverse effects of oral or subcutaneous terbutaline are an increase in heart rate, changes in blood pressure, nervousness, tremor, palpitation, and dizziness. Headache, nausea, vomiting, anxiety, restlessness, lethargy, drowsiness, weakness, flushes, sweating, chest discomfort, muscle cramps, and tinnitus have also been reported. Seizures, hypersensitivity vasculitis, and elevations in liver enzymes have been reported rarely in patients receiving terbutaline sulfate. Seizures did not recur following discontinuance of the drug. Immediate hypersensitivity reactions and exacerbations of bronchospasm have been reported in patients receiving terbutaline.

Adverse effects with usual oral or subcutaneous doses are generally transient and usually do not require treatment; however, the increase in heart rate may persist for a relatively long time. ECG changes, including flattening of the T wave, prolongation of the QTc interval, and ST-segment depression, have been reported with b-agonist therapy; the clinical importance of these findings is unknown.

4.9 Overdose:

Symptoms **–** Headache, anxiety, tremor, nausea, tonic cramp, palpitations, tachycardia, arrhythmia. A fall in blood pressure sometimes occurs. Laboratory findings; hypokalaemia, hyperglycaemia and lactic acidosis sometimes occur.

Treatment – Mild and moderate cases: Reduce the dose. Severe cases: Gastric lavage, administration of activated charcoal. Determination of acid-base balance,

blood sugar and electrolytes, particularly serum potassium levels. Monitoring of the heart rate and rhythm and blood pressure. Metabolic changes should be corrected. A cardioselective beta-blocker (e.g. metoprolol) is recommended for the treatment of arrhythmias causing haemodynamic deterioration. The beta blocker should be used with care because of the possibility of inducing bronchoconstriction: use with caution in patients with a history of bronchospasm. If the $beta_2$-mediated reduction in the peripheral vascular resistance significantly contributes to the fall in blood pressure, a volume expander should be given.

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

Terbutaline is a selective $beta_2$ -adrenergic stimulant having the following pharmacological effects: -

In the lung: bronchodilation; increase in mucociliary clearance; suppression of oedema and anti-allergic effects.

In skeletal muscle: stimulates Na^+/K^+transport and also causes depression of subtetanic contractions in slow-contracting muscle. In the CNS: low penetration into the blood-brain barrier at therapeutic doses, due to the highly hydrophilic nature of the molecule.

5.2 Pharmacokinetic properties:

Basic parameters results with oral administration of therapeutic doses, Renal clearance (CLR) – 1.925ml/min (nales) and 2.32ml/min (females).

The plasma concentration/time curve after iv administration is characterized by a fast distribution phase, an intermediate elimination phase and a late elimination phase.

Terminal half-life T½ has been determined after single and multiple dosing (mean values varied between 16-20 h).

Bioavailability – Food reduces bioavailability following oral dosing (10% on average). Fasting values of 14-15% have been obtained.

Metabolism – The main metabolite after oral dosing is the sulphate conjugate and also some glucoronide conjugate can be found in the urine.

5.3 Preclinical safety data:

The major toxic effect of Terbutaline, observed in toxicological studies in rats and dogs at exposures in excess of maximum human exposure, is focal myocardial necrosis. This type of cardiotoxicity is a well-known pharmacological manifestation seen after the administration of high doses of $beta_2$-agonists.

In rats, an increase in the incidence of benign uterine leiomyomas has been observed. This effect is looked upon as a class-effect observed in rodents after long term exposure to high doses of $beta_2$-agonists

6. Pharmaceutical particulars:

6.1 List of Excipients:

Sucrose, Sodium Citrate, Sodium Methyl Hydroxybenzoate, Sodium Propyl Hydroxybenzoate, Anhydrous Citric Acid, Glycerol, Strawberry Liquid Flavour, Colour Amaranth Powder, and Purified water.

6.2 Incompatibilities:

None known.

6.3 Shelf life:

2 years when stored under recommended conditions.

6.4 Special precautions for storage:
Store in a dry place below 30˚C. Protect from light.
Keep the medicine out of reach of children.

6.5 Nature and contents of container:
Bottle: 100ml USP Type III amber colored glass bottle with aluminium white Roll-on-pilfer-proof (ROPP) cap with white colored polypropylene wad.

Supplied with dose measuring device: Plastic/Polypropylene measuring cup with graduation mark of 2.5, 5.0, 7.5 and 10.0 ml.

6.6 Special precautions for disposal:
No special requirement.

7. Marketing Authorization Holder:
Shelys Pharmaceuticals Limited,
Plot No. 696, New Bagamoyo Road, Mwenge,
P.O. Box 32781, Dar es Salaam, Tanzania.

8. Marketing Authorization Number(s):
TAN 22 HM 0151

9. Date of first registration/renewal of the registration:
11/04/2022

10. **Date of revision of the text:**