# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Asmasal Clickhaler inhalation powder, 95micrograms/inhalation.

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered actuation of 3 mg of inhalation powder contains 114 micrograms of salbutamol sulphate (95 micrograms salbutamol base) and delivers 110 micrograms of salbutamol sulphate (90 micrograms of salbutamol base).

Excipient: : Lactose Monohydrate 2.886 mg per actuation.

For a full list of excipients see section 6.1.

## 3 PHARMACEUTICAL FORM

Inhalation powder.

A plastic inhaler device incorporating an actuating and metering mechanism enclosed within an aluminium foil heat sealed bag.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Asmasal Clickhaler is indicated for the symptomatic treatment of bronchospasm in bronchial asthma and other conditions with associated reversible airways obstruction. Appropriate anti-inflammatory therapy should be considered in line with current practice.

Asmasal Clickhaler may be used when necessary to relieve attacks of acute dyspnoea due to bronchoconstriction.

Asmasal Clickhaler may also be used before exertion to prevent exercise-induced bronchospasm or before exposure to a known unavoidable allergen challenge.

### 4.2 Posology and method of administration

Adults: For the relief of acute bronchospasm and for managing intermittent episodes of asthma, one inhalation may be administered as a single dose; this may be increased to two inhalations if necessary. If the response is inadequate, higher doses than two inhalations can be used. The maximum recommended dose is two inhalations three or four times a day.

To prevent exercise-induced bronchospasm one or two inhalations should be taken 15 minutes before exertion.

One or two inhalations may also be taken before foreseeable contact with allergens.

Elderly: as for adults

Children: One inhalation is the recommended dose for the relief of acute bronchospasm, in the management of episodic asthma or before exercise. If the response is inadequate, higher doses than one inhalation can be used.

On demand use should not exceed four times daily. The bronchodilator effect of each administration of inhaled salbutamol lasts for at least four hours except in patients whose asthma is becoming worse. Such patients should be warned not to increase their usage of the inhaler, but should seek medical advice since treatment with, or an increased dose of an inhaled and/or systemic glucocorticosteroid is indicated.

As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should only be increased on medical advice.

The following instructions for use are included in the Patient Information Leaflet:

1. Remove mouthpiece cover from the inhaler

2. Shake the inhaler well

3. Hold the inhaler upright with thumb on the base and finger on the push button. Press the dosing button down firmly - once only

4. Breathe out as far as is comfortable.
   Note: do not blow into the device at any time.

5. Place mouthpiece in your mouth. Close lips firmly around it (do not bite it)

6. Breathe in through your mouth steadily and deeply, to draw the medicine into your lungs.

7. Hold your breath, take the inhaler from your mouth and continue holding your breath for about 5 seconds.

8. For the second puff, keep the inhaler upright and repeat steps 2-7.

9. Replace the mouthpiece cover.

## 4.3 Contraindications

Asmasal Clickhaler is contra-indicated in patients with intolerance or hypersensitivity to the active ingredient or the excipient.

## 4.4 Special warnings and precautions for use

Bronchodilators should not be the only or main treatment in patients with moderate to 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 the maximum recommended dose of inhaled corticosteroid and/or oral corticosteroid therapy in these patients. Increasing use of bronchodilators, in particular short-acting inhaled beta-2-agonists to relieve symptoms, indicates deterioration of asthma control. If patients find that short-acting bronchodilator treatment becomes less effective or they need more inhalations than usual, they should be warned by the prescriber of the need for consulting immediately. In this situation, patients should be reassessed and consideration given to the need for increased anti-inflammatory therapy (eg. higher doses of inhaled corticosteroids or a course of oral corticosteroids).

Salbutamol should be administered cautiously, especially with systemic therapy, to patients suffering from thyrotoxicosis, myocardial insufficiency, hypertension, known aneurysms, decreased glucose tolerance, manifest diabetes, phaeochromocytoma and concomitant use of cardiac glycosides. Caution should also be applied in patients with myocardial ischemia, tachyarrythmias and hypertrophic obstructive cardiomyopathy.

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.

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

Potentially serious hypokalaemia has resulted from systemic ß2-agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

Salbutamol and non-selective beta-blocking drugs, such as propranolol, should not usually be prescribed together. Caution is also advised in patients using cardiac glycosides.

Potentially serious hypokalaemia has resulted from systemic ß2-agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia.

Patients should be instructed to discontinue salbutamol at least 6 hours before intended anaesthesia with halogenated anaesthetics, wherever possible.

## 4.6 Fertility, pregnancy and lactation

Pregnancy: Administration of salbutamol during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the fetus. As with the majority of drugs there is little published evidence of its safety in the early stages of pregnancy, but in animal studies, there was evidence of some harmful effects in the fetus at very high dose levels.

Lactation: Salbutamol may be secreted in breast milk. 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.

## 4.7 Effects on ability to drive and use machines

Individual reactions, especially at higher doses, may be such that patients' ability to drive or use machines may be affected, particularly so at the beginning of treatment and in conjunction with alcohol.

The possible side effects of salbutamol such as transient muscle cramps and tremor may necessitate caution when using machines.

## 4.8 Undesirable effects

The side effects are dose dependent and due to the direct mechanism of ß2-agonists.

Hypersensitivity reactions include angioedema and urticaria, bronchospasm, hypotension and collapse and have been reported very rarely.

*Blood and the lymphatic system disorders:* potentially serious hypokalaemia may result from systemic ß2-agonist therapy. Special precautions should be taken in patients using ß2 -agonists with hypokalaemia because of the increased risk of tachycardia and arrhythmias. Hypokalaemia may be potentiated by concomitant therapy with corticosteroids, diuretics and xanthines.

*Psychiatric disorders:* nervousness, feeling of tenseness. As with other ß2 agonists, hyperactivity in children has been reported rarely.

*Nervous system disorders:* mild tremor, headache, dizziness.

*Cardiac disorders:* tachycardia, angioedema, hypotension, cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles) and myocardial ischemia (*see section 4.4, Special warnings and precautions for use*) have been reported in association with ß2 agonists, usually in susceptible patients.

*Respiratory, thoracic and mediastinal disorders:* as with other inhalation therapy, the potential for paradoxical bronchospasm should be kept in mind. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted.

*Gastrointestinal disorders:* nausea

*Skin and subcutaneous tissue disorders:* urticaria.

*Musculoskeletal, connective tissue and bone disorders:* there have been rare reports of transient muscle cramps

*General disorders and administration site conditions:* oral and pharyngeal irritation can occur.

## 4.9 Overdose

An overdose should be treated symptomatically.

The preferred antidote for overdosage with salbutamol is a cardioselective beta-blocking agent but beta-blocking drugs should be used with caution in patients with a history of bronchospasm.

If hypokalaemia occurs potassium replacement via the oral route should be given. In patients with severe hypokalaemia intravenous replacement may be necessary.

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.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

ATC Code: R03A C02

Salbutamol is a beta-adrenergic stimulant which has a selective action on bronchial ß2-adrenoceptors at therapeutic doses. Following inhalation, salbutamol exerts a stimulating action on ß2 receptors on bronchial smooth muscles, and thus ensures rapid bronchodilation which becomes significant within a few minutes and persists for 4 to 6 hours.

The drug also causes vasodilation leading to a reflex chronotropic effect and widespread metabolic effects, including hypokalaemia.

## 5.2 Pharmacokinetic properties

Following treatment with salbutamol by inhalation, only approximately 10% or less of the drug is deposited in the airways and the remainder is swallowed. Pre-systemic metabolism of salbutamol is considerable and occurs primarily in the gastrointestinal tract and by conjugation to form an inactive sulphate ester. The systemic clearance for salbutamol is 30 l/hr. Salbutamol is eliminated both through excretion of unchanged drug in urine and through metabolism mainly via sulphate conjugation. The elimination half-life varies between 3 and 7 hours. Salbutamol is well absorbed from the gastrointestinal tract.

## 5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity. Findings concerning teratogenicity in rabbits at high systemic exposure and the induction of benign mesovarian leiomyomas in rats are not considered of clinical concern.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Lactose monohydrate (which contains milk protein).

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

3 years in unopened foil pouch. 6 months when removed from foil pouch.

## 6.4 Special precautions for storage

Do not store above 30°C. Store in the original package.

## 6.5 Nature and contents of container

A plastic inhaler device incorporating an actuating and metering mechanism enclosed within an aluminium foil heat sealed bag. Each device contains 750mg of powder - sufficient for 200 actuations.

## 6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Instructions for use are included in the patient information leaflet. These are also included in *see section 4.2, Posology and method of administration*.

# 7 MARKETING AUTHORISATION HOLDER

RPH Pharmaceuticals AB
Lagervagen 7
136 50 Haninge
Sweden

## 8 MARKETING AUTHORISATION NUMBER

PA 1638/011/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First date of authorisation: 17 April 1998

Date of last renewal: 08 May 2007

## 10 DATE OF REVISION OF THE TEXT

May 2011