Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ventolin Rotacap 200 micrograms

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule (Rotacap) contains 200 micrograms salbutamol as salbutamol sulphate.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder, hard capsule.

Size 3 hard gelatin capsule with pale blue opaque cap and a clear body containing a small amount of white powder. Each capsule is marked ‘Ventolin 200’, printed in red ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ventolin Rotacaps are indicated in the prophylaxis and treatment of bronchial asthma and other conditions associated with reversible airways obstruction.

4.2 Posology and method of adminstration

Ventolin Rotacaps capsules are for inhalation use only, using a Ventolin Rotahaler inhaler.

Salbutamol has a duration of action of 4 to 6 hours in most patients.

Increasing use of $beta_2$ agonists may be a sign of worsening asthma. Under these conditions a reassessment of the patient's therapy plan may be required and concomitant glucocorticosteroid therapy should be considered.

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

For acute therapy:-

Adults:	200 or 400 micrograms as a single dose.
Children:	200 micrograms as a single dose.

For chronic or prophylactic therapy:-

Adults:	400 micrograms three or four times daily.
Children:	200 micrograms three or four times daily.

4.3 Contraindications

Ventolin Rotacaps are contraindicated in patients with a history of hypersensitivity to sympathomimetics or any component of the preparation.

Although intravenous salbutamol and occasionally salbutamol tablets are used in the management of premature labour uncomplicated by conditions such as placenta praevia, ante-partum haemorrhage or toxaemia of pregnancy, inhaled salbutamol preparations are not appropriate for managing premature labour. Salbutamol presentations should not be used for threatened abortion.

4.4 Special warnings and special precautions for use

The management of asthma should normally follow a stepwise programme, and patient response should be monitored clinically and by lung function tests.

Bronchodilators should not be the only or main treatment in patients with severe or unstable asthma. Patients with severe asthma have constant symptoms and frequent exacerbations, with limited physical capacity, and Peak Expiratory Flow (PEF) values below 60% predicted at baseline with greater than 30% variability, usually not returning entirely to normal after a bronchodilator. These patients will require high dose inhaled (e.g. >1mg/day beclomethasone dipropionate) or oral corticosteroid therapy. With this primary background corticosteroid treatment, Ventolin provides essential rescue medication for a severe asthmatic in treating acute exacerbations. Failure to respond promptly or fully to such rescue medication signals a need for urgent medical advice and treatment.

Increasing use of short-acting inhaled $beta_2$ agonists to control symptoms indicates deterioration of asthma control. Under these conditions, the patient's therapy plan should be reassessed. Sudden and progressive deterioration in asthma control is potentially life-threatening and consideration should be given to starting or increasing corticosteroid therapy. In patients considered at risk, daily peak flow monitoring may be instituted.

In the event of a previously effective dose of inhaled salbutamol failing to give relief lasting at least three hours, the patient should be advised to seek medical advice in order that any necessary additional steps may be taken.

Salbutamol causes peripheral vasodilation which may result in reflex tachycardia and increased cardiac output. Caution should be used in patients with angina, severe tachycardia or 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 concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

Salbutamol should not cause difficulty in micturition because unlike sympathomimetic drugs such as ephedrine, it does not stimulate alpha-adrenoreceptors. However, there have been reports of difficulty in micturition in patients with prostatic enlargement.

Use with caution in diabetic patients as this product may cause an increase in blood sugar level.

A responsible adult should supervise the use of the Rotahaler inhaler in children.

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.

Salbutamol is not contra-indicated in patients under treatment with monoamine oxidase inhibitors (MAOIs), however the effects of salbutamol may be altered by guanethidine, reserpine, methyldopa and tricyclic antidepressants.

Caution should be exercised in its use with anaesthetic agents such as chloroform, cyclopropane, halothane and other halogenated agents.

4.6 Pregnancy and lactation

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.

Salbutamol has been in widespread use for many years in human beings without apparent ill consequence; this indicates its well established use in the management of premature labour. However, 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.

During worldwide marketing experience, rare cases of various congenital anomalies, including cleft palate and limb defects have been reported in the offspring of patients being treated with salbutamol. Some of the mothers were taking multiple medications during their pregnancies.

Because no consistent pattern of defects can be discerned, and baseline rate for congenital anomalies is 2-3%, a relationship with salbutamol use cannot be established.

As salbutamol is probably secreted in breast milk its use in nursing mothers is not recommended unless the expected benefits outweigh any potential risk.

It is not known whether salbutamol in breast milk has a harmful effect on the neonate.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Ventolin Rotacaps may cause a fine tremor of skeletal muscle, usually the hands are most obviously affected. This effect is dose related and is common to all beta-adrenergic stimulants.

Occasionally headaches have been reported.

Peripheral vasodilation and a compensatory small increase in heart rate may occur in some patients.

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

There have been very rare reports of muscle cramps.

As with other inhalation therapy, paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing. This should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator. Ventolin Rotacaps should be discontinued immediately, the patient assessed, and if necessary alternative therapy instituted.

Potentially serious hypokalaemia may result from $beta_2$ agonist therapy.

As with other $beta_2$ agonists, hyperactivity has been reported rarely in children.

Mouth and throat irritation may occur with inhaled salbutamol.

Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles) may occur, usually in susceptible patients.

Tachycardia may occur in some patients.

4.9 Overdose

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

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Selective beta-2-adrenoceptor agonist
ATC code:R03A C02

Salbutamol is a selective $beta_2$ adrenoceptor agonist. At therapeutic doses it acts on the $beta_2$ adrenoceptors of bronchial muscle, with little or no action on the beta- 1 adrenoceptors of the heart.

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-sulphate (phenolic sulphate) 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 administration by the inhaled route, between 10 and 20% of the dose reaches the lower airways. The remainder is retained in the delivery system or is deposited in the oropharynx from 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 sulphate.

The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism to the phenolic sulphate. Both unchanged drug and conjugate are excreted primarily in the urine.

5.3 Preclinical safety data

In common with other potent selective $beta_2$ receptor agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of foetuses were found to have cleft palate, at 2.5mg/kg, 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 foetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. A reproductive study in rabbits revealed cranial malformations in 37% of foetuses at 50mg/kg/day, 78 times the maximum human oral dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 30°C. Keep the container tightly closed.

6.5 Nature and contents of container

Ventolin Rotacaps are supplied in propylene containers with snap on tamper evident polyethylene cap. Each container holds 100 Rotacaps.

6.6 Instructions for use and handling

The Rotacaps must only be inserted in to the Rotahaler immediately prior to use. Failure to observe this instruction will affect the delivery of the drug.

7 MARKETING AUTHORISATION HOLDER

Allen & Hanburys Ltd.
Stockley Park West
Uxbridge
Middlesex, UB11 1BT
England

8 MARKETING AUTHORISATION NUMBER

PA 24/1/3

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15th January 1979

Date of last renewal: 5th August 2003

10 DATE OF REVISION OF THE TEXT

March 2004