Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Butovent Pulvinal 200 micrograms/dose inhalation powder

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each actuation provides 200 micrograms of salbutamol.

For excipient see section 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In adults and children over 12 years:
- Symptomatic treatment of asthma attacks.
- Symptomatic treatment of exacerbations of asthma or of chronic obstructive bronchitis with a reversible component.
- Prevention of exercise-induced asthma.

4.2 Posology and method of adminstration

Posology
Adults and children over 12 years:

Treatment of asthma attacks and exacerbations:
as soon as symptoms occur: 1 to 2 inhalations.
If the symptoms persist, the dose may be repeated a few minutes later.

Prevention of exercise-induced asthma: 1 to 2 inhalations 15 to 30 minutes before exercise.

The lowest effective doses of inhaled salbutamol are recommended to be used in the treatment of asthma. In the long term treatment it is recommended instead of regular use, to use inhaled salbutamol when needed.

The daily dose should not exceed 8 inhalations per 24 hours (see section 4.4).

Method of administration.

Inhalation from the device through the mouthpiece.

The physician should ensure that the patient correctly uses the powder inhaler in accordance with the instructions for use reported in the leaflet.
Inhalation powders are suitable for use in patients who show poor hand/lung synchronisation.
This device is a “high resistance” inhaler that requires a peak inspiratory flow rate of at least 28 l/min to insure a satisfactory lung disposition of the powder. Therefore this medicinal product is not suitable for patients with a low peak inspiratory flow rate, such as children under 12 years. This should also be considered when switching between products

within a patient.
When other salbutamol inhalers are replaced by Butovent Pulvinal inhaler, it should be taken into account that the obtained dose can vary between different inhalers and therefore the dose may have to be adjusted.

The drug is delivered into the bronchi when the patient breathes in deeply and naturally through the mouthpiece of the device. The inhalation must be followed by apnoea.

The patient must be advised:

- never to breathe out into the Pulvinal® device
- to re-tighten the cap firmly after use
- never to wash the Pulvinal® device, but to wipe it with a clean, dry cloth.

4.3 Contraindications

This product is contra-indicated in patients with known hypersensitivity to any of the ingredients.

4.4 Special warnings and special precautions for use

Special warnings
Patients should be advised that an immediate medical examination is necessary if the previously usual effective dose is failing to quickly provide the relief usually observed. If patient rapidly increases the use of inhaled short-acting β_2-agonists to relieve symptoms, worsening of asthma is to be feared (especially if peak inspiratory flow rate value falls and/or becomes irregular) and patient may be at risk of severe attacks. Patients should therefore be warned of the need for an immediate examination, without first exceeding the prescribed maximum doses. Therapy should subsequently be reassessed.
In asthmatic adults, a daily anti-inflammatory medication is required as soon as the patient requires inhaled β_2-agonists more than once a week. The patient should be then warned that, even if his asthma control is achieved, the treatment should not be discontinued without any medical advice.

Salbutamol or other bronchodilatating drugs should not be given as the only treatment to patients with moderate to severe or unstable asthma.
Sportsmen and athletes are warned that this medicinal product contains an active ingredient which may produce positive result in anti-doping tests searching for prohibited substances.

Special precautions for use
In the event of bronchial infection or abundant bronchorrhoea, appropriate treatment is necessary to optimise the deposition of the product within the respiratory tract.

At usual doses, when administered by the inhaled route with this device, salbutamol should be given with caution in patients suffering from thyrotoxicosis, coronary failure, congestive cardiomyopathy, ventricular rhythm disorders, arterial hypertension or diabetes mellitus.

4.5 Interaction with other medicinal products and other forms of interaction

- This medicinal product shall be used with caution in case of association with other adrenergic treatments, due to the risk of onset of cardiovascular undesirable events
- Monoamine oxidase inhibitors, tricyclic antidepressants: risk of increased cardiovascular effects
- Beta-blockers, such as propranolol: antagonist effect on the action carried out by salbutamol and the other beta-mimetics
- The simultaneous administration of xanthines, corticosteroids or potassium excreting diuretics may increase hypokalemia

4.6 Pregnancy and lactation

Pregnancy: Data on a large number of exposed pregnancies indicate no adverse effects of salbutamol on pregnancy. Administration of salbutamol during pregnancy should only be considered only if the expected benefit to the mother is greater than any possible risk to the foetus.
When administered during pregnancy, an acceleration in the foetal heart rate may be observed together with tachycardia in the mother. This condition exceptionally persists after birth. Similarly, the values of post-natal glycaemia are only exceptionally altered.
When administered before labour, the peripheral vasodilating effects and the potential inhibiting effect on uterine contractions of β_2-agonists should be taken into account.

Lactation: β_2-agonists pass into maternal milk. Data with respect to passage of salbutamol into breast milk are insufficient. The potential risk for the child is unknown.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The undesirable effects observed with inhaled salbutamol administration given at therapeutic doses are linked to a sympathomimetic activity. They are often mild and generally disappear on continuation of treatment.

Frequent (>1%):
- heart and circulatory effects: peripheral vasodilation might be the cause of a mild reflex tachycardia
- muscular effects: tremors

Less frequent (1-0.1%):
- systemic effects: headache, hypersensitivity reactions (angioedema, urticaria, hypotension and collapse)

Seldom (<0.1%):
- respiratory effects: bronchospasm (see Warnings and Precautions for Use), mouth and throat irritation that can be prevented by rinsing the mouth after product inhalation
- metabolic: hypokalaemia
- muscular: muscular cramps
- central nervous system: restlessness, vertigo

4.9 Overdose

The use of this drug at doses much higher than the recommended doses indicates a worsening of asthma, requiring prompt examination to re-assess the treatment.

The expected symptoms with overdose are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the symptoms listed under section 4.8. “Undesirable Effects”. Particularly hypokalaemia may occur at high doses.
The use of this drug at doses much higher than the recommended doses reflects a deterioration of the respiratory disorder, requiring prompt examination for re-assessment of treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmatherapeutic group: Antiasthmatics, ATC code: R03A C02.

Short-acting inhaled ß$_2$-agonist bronchodilator. Salbutamol is an agonist of the ß-adrenoceptors with a much more selective action on ß$_2$ receptors.
After inhalation, salbutamol exercises a stimulating action on the ß$_2$ receptors of the bronchial smooth muscle, thus ensuring rapid bronchodilation, significant within a few minutes and lasting for 4 to 6 hours.

5.2 Pharmacokinetic properties

After inhalation the plasma concentrations observed at the usual doses are negligible (10-50 times lower than those observed per os or by injection).
A portion of the inhaled dose reaches the lower part of the airways and, after pulmonary resorption, is mainly excreted by renal route partially unchanged and partially as metabolites.
The remaining portion of the inhaled dose is swallowed and then absorbed from the gastrointestinal system into circulation, where it undergoes significant first-pass metabolism.

5.3 Preclinical safety data

Pre-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.
Cleft palate has been reported in mice but not in rats or rabbits after subcutaneous administration.
Findings concerning teratogenicity in rabbits at high systemic exposure levels and the induction of benign mesovarian leiomyomas in rats are not considered of clinical concern.
There is no evidence of carcinogenicity, mutagenicity or teratogenicity in humans.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Keep the dry powder inhaler tightly closed.

6.5 Nature and contents of container

Multidose (reservoir) dry powder inhaler with mouthpiece containing 100 nominal doses of powder.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Chiesi Farmaceutici S.p.A
26/A Via Palermo
43100 PARMA
Italy

8 MARKETING AUTHORISATION NUMBER

PA 584/2/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT