Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

HFA-134a Beclometasone Dipropionate 100 micrograms Autohaler.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose delivers Beclometasone Dipropionate 100 micrograms ex-valve into the mouthpiece of the actuator.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Pressurised inhalation, solution.
Pressurised aluminium container closed with a metering valve and inserted into a breath-actuated mauve (cap) and grey (mouthpiece) plastic actuator.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prophylactic anti-inflammatory treatment of reversible obstructive airway disease.

4.2 Posology and method of adminstration

NOTE: The recommended total daily dose of beclometasone dipropionate extrafine aerosol from HFA-134a Beclometasone Dipropionate is lower than that for current beclometasone dipropionate CFC product and should be adjusted to the individual patient.

HFA-134a Beclometasone Dipropionate is for inhalation use only.

ADULTS STARTING AND MAINTENANCE DOSE:

For mild to moderate asthma : 50 micrograms to 200 micrograms twice daily.

In more severe cases : doses up to 400 micrograms twice daily.

The maximum recommended daily dose in adults is 800 micrograms.
When patients' symptoms remain under satisfactory control, the dose can be gradually reduced to the minimum effective dose to maintain control.

CHILDREN AGED FIVE YEARS AND OVER – STARTING AND MAINTENANCE DOSE:

For mild asthma: 50 micrograms twice daily.

Children with well controlled asthma on doses of up to 400 micrograms per day of CFC containing beclometasone dipropionate may be titrated to a dose of 50 micrograms twice daily of HFA-134a Beclometasone Dipropionate.

During periods of deterioration in asthma control, the dose may be increased to 100 micrograms twice daily. The dose should be reduced to the minimum needed to maintain effective control of asthma.

The maximum recommended daily dose in children is 200 micrograms.

The same total daily dose in micrograms from either HFA-134a Beclometasone Dipropionate 50 micrograms or HFA-134a Beclometasone Dipropionate 100 micrograms aerosol provides the same clinical effect.

To be effective inhaled HFA-134a Beclometasone Dipropionate must be used on a regular basis.

Patients should be instructed on the proper use of their inhaler, including rinsing out their mouth after use. Patients should be advised that HFA-134a Beclometasone Dipropionate may have a different taste and feel than a CFC inhaler.

For normal hygiene, the mouthpiece of your Autohaler should be cleaned weekly with a clean, dry tissue or cloth. DO NOT WASH OR PUT ANY PART OF YOUR INHALER IN WATER.

Comparative clinical studies have demonstrated that asthma patients achieve equivalent pulmonary function and control of symptoms with HFA-134a Beclometasone Dipropionate at lower total daily doses than CFC beclometasone dipropionate aerosol inhalers.

Special patient groups: No special dosage recommendations are made for elderly or patients with hepatic or renal impairment.

4.3 Contraindications

Hypersensitivity to Beclometasone Dipropionate or any other ingredient in HFA-134a Beclometasone Dipropionate.

4.4 Special warnings and special precautions for use

HFA-134a Beclometasone Dipropionate is not indicated for immediate relief of asthma attacks or status asthmaticus.

Individual patients may vary in their sensitivity to the systemic effects of inhaled steroids.

Beclometasone, like other inhaled steroids, is absorbed into the systemic circulation from the lungs. Beclometasone and its metabolites may exert detectable suppression of adrenal function. However, within the dose range 100-800 micrograms daily, clinical studies with HFA-134a Beclometasone Dipropionate have demonstrated mean values for adrenal function and responsiveness within the normal range.

If the prescribed dose of HFA-134a Beclometasone Dipropionate is no longer effective or symptoms get worse, the patient must seek medical attention for review of maintenance therapy.

Like other corticosteroids, caution is necessary in patients with active or latent pulmonary tuberculosis.

In patients who have been transferred from oral steroids to inhalation therapy, systemic steroid therapy may need to be re-instated rapidly during periods of stress or where airways obstruction or mucus prevents absorption from the inhalation.

Patients who have received systemic steroids for long periods of time or at high doses, or both, need special care and subsequent management when being transferred to inhaled steroid therapy. Recovery from impaired adrenocortical function, caused by prolonged systemic steroid therapy, is slow.

The patient’s asthma should be in a stable state before being given inhaled steroids in addition to the usual maintenance dose of systemic steroid.

Withdrawal of the systemic steroids should be gradual, starting after about seven days by reducing the daily oral dose by 1 - 2.5mg prednisolone, or equivalent, at intervals not less than one week. Adrenocortical function should be monitored regularly.

Most patients can be successfully transferred to inhaled steroids with maintenance of good respiratory function, but special care is necessary for the first months after the transfer, until the hypothalamic-pituitary-adrenal (HPA) system has sufficiently recovered to enable the patient to cope with emergencies such as trauma, surgery or serious infections.

It may be advisable to provide such patients with a supply of oral steroid to use in such emergencies. The dose of inhaled steroids should be increased at this time and then gradually reduced to the maintenance level after the systemic steroid has been discontinued.

Discontinuation of systemic steroids may cause exacerbation of allergic diseases such as atopic eczema and rhinitis. These should be treated as required with antihistamine and topical therapy.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Pregnancy and lactation

HFA-134a Beclometasone Dipropionate

There is no experience of this product in pregnancy and lactation in humans, therefore the product should only be used if the benefits outweigh any potential risk to the patient.
An inhalation reproductive study with this product in rats did not exhibit any teratogenic effects.

Hydrofluoroalkane 134a (HFA-134a)

Studies of HFA-134a administered to pregnant and lactating rats and rabbits have not revealed any special hazard.

Beclometasone Dipropionate

There is inadequate evidence of safety in human pregnancy. In animals, systemic administration of relatively high doses can cause abnormalities of foetal development including growth retardation and cleft palate. There may therefore be a very small risk of such effects in the human foetus.

However, inhalation of Beclometasone Dipropionate into the lungs avoids the high level of exposure that occurs with administration by systemic routes.

The use of Beclometasone Dipropionate in pregnancy requires that the possible benefits of the drug be weighed against the possible hazards. The drug has been in widespread use for many years without apparent ill consequence.

It is probable that Beclometasone is excreted in milk. However, given the relatively low doses used by the inhalation route, the levels are likely to be low. In mothers breast feeding their baby the therapeutic benefits of the drug should be weighed against the potential hazards to mother and baby.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

When taking any inhaled medicine containing Beclometasone Dipropionate, an occasional incidence of hoarseness; a rare occurrence of either post inhalation bronchospasm or candidiasis of throat and mouth, may occur. Patients may find it helpful to rinse out their mouth after using their inhaler to reduce the risk of candidiasis and hoarseness.
For Beclometasone Dipropionate extrafine aerosol, a rare incidence of nausea has been reported.

4.9 Overdose

Acute overdosage is unlikely to cause problems. The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of HPA function. Specific emergency action need not be taken. Treatment with HFA-134a Beclometasone Dipropionate should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two.

If gross excessive doses of Beclometasone Dipropionate were taken over a prolonged period a degree of atrophy of the adrenal cortex could occur in addition to HPA suppression. In this event the patient should be treated as steroid dependent and transferred to a suitable maintenance dose of a systemic steroid such as prednisolone. Once the condition is stabilised, the patient should be returned to HFA-134a Beclometasone Dipropionate by the recommended dose above.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

HFA-134a Beclometasone Dipropionate contains beclometasone dipropionate in solution in HFA-134a propellant resulting in an extrafine aerosol. The aerosol droplets are on average much smaller than the beclometasone dipropionate particles delivered by CFC-suspension formulations or dry powder formulations of beclometasone dipropionate. The extrafine particle fraction will be 60%±20% of the drug particles ≤3.3 microns per shot, ex-actuator.

Radio-labelled deposition studies have demonstrated that the majority of drug (>55% ex-actuator) is deposited in the lung and <35% ex-actuator is deposited in the oropharynx. These delivery characteristics result in equivalent therapeutic effects at lower total daily doses of HFA-134a Beclometasone Dipropionate, compared with CFC beclometasone dipropionate formulations.

Inhaled Beclometasone Dipropionate is now well established in the management of asthma. It is a synthetic glucocorticoid and at up to the maximum recommended daily dose exerts a topical, anti-inflammatory effect on the lungs, without significant systemic activity.

5.2 Pharmacokinetic properties

In a single dose pharmacokinetic study in children, a dose of 200 micrograms of HFA-134a Beclometasone Dipropionate delivered without a spacer achieved comparable AUC (17-BMP) levels as a dose of 400 micrograms of a CFC aerosol via a spacer.

Pharmacokinetic studies with HFA-134a Beclometasone Dipropionate have not been carried out in any other special populations.

5.3 Preclinical safety data

Hydrofluoroalkane 134a

Statements from CPMP:

1. In animal studies, HFA-134a has been shown to have no significant pharmacological effects other than at very high exposure concentrations, then narcosis and a relatively weak cardiac sensitising effect were found. The potency of the cardiac sensitisation was less than that of CFC-11 (trichlorofluoromethane).

2. In studies to detect toxicity, repeated high dose levels of HFA-134a indicated that safety margins based on systemic exposure would be of the order 2200, 1314 and 381 for mouse, rat and dog with respect to humans.

3. There are no reasons to consider HFA-134a as a potential mutagen, clastogen or carcinogen judged from *in vitro* and *in vivo* studies including long-term administration by inhalation in rodents.

HFA-134a Beclometasone Dipropionate

Safety studies with this product in rat and dog showed few, if any, adverse effects other than those normally associated with general steroid exposure including lymphoid tissue alterations such as reduction in thymus, adrenal and spleen weights.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Norflurane (hydrofluoroalkane 134a)
Ethanol Anhydrous.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 30°C. Storage in direct sunlight or heat should be avoided.
The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C. Do not pierce the canister or dispose of it by burning.

6.5 Nature and contents of container

Pressurised aluminium container closed with a metering valve containing either 100 or 200 metered doses and supplied with a plastic breath-actuated actuator.

6.6 Instructions for use and handling

None

7 MARKETING AUTHORISATION HOLDER

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Loughborough
Leicestershire LE11 1EP
England

8 MARKETING AUTHORISATION NUMBER

PA 57/68/4

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 26th July 2004

10 DATE OF REVISION OF THE TEXT

August 2004