PACKAGE INSERT FOR FORATEC HFA:

SCHEDULING STATUS:

S2

PROPRIETARY NAME (AND DOSAGE FORM):

FORATEC HFA (metered dose inhaler)

COMPOSITION:

FORATEC HFA: Each actuation delivers formoterol fumarate 12 mcg. FORATEC HFA contains ethanol 3% as a co-solvent.

PHARMACOLOGICAL CLASSIFICATION:

A 10.2.1 Bronchodilators (inhalants).

PHARMACOLOGICAL ACTION:

Formoterol fumarate is a long-acting beta2-selective adrenergic receptor agonist. Formoterol fumarate exerts a bronchodilator effect which starts within 1 to 3 minutes and is still significant up to 12 hours after inhalation.

Formoterol may suppress the release of histamine and leukotrienes from mast cells in human lung tissue. Some anti-inflammatory properties, such as inhibition of oedema and inflammatory cell accumulation, have been reported in animal experiments.

Pharmacokinetics

Analysis of urinary excretion rates suggests that some formoterol, administered by inhalation, is absorbed, although detection in plasma using current analytical methods has not been shown at therapeutic doses. Plasma protein binding is approximately 50 - 65 %. Formoterol is metabolised via direct glucuronidation and 0-demethylation. The elimination half-life is approximately 2 to 3 hours. Formoterol and its metabolites are completely excreted from the body, with two thirds appearing in the urine and one third in the faeces.

INDICATIONS:

Prophylaxis and treatment of bronchoconstriction in patients with reversible obstructive airways disease, such as bronchial asthma and chronic bronchitis with or without emphysema. Prophylaxis of bronchospasm induced by inhaled allergens, non-specific irritants or exercise challenge.

(FORATEC HFA) may be used in combination with other anti - asthmatic treatments.

CONTRA - INDICATIONS:

- Hypersensitivity to formoterol or mannitol.
- Tachycardia, third degree atrioventricular block, idiopathic subvalvular aortic stenosis, hypertrophic obstructive cardiomyopathy, prolonged Q-T interval (Q-Tc > 0,44 sec) e.g. congenital or drug-induced (see "INTERACTIONS"), and thyrotoxicosis.
- The safe use in children under the age of 6 years has not been established.

WARNINGS:

The longer duration of action of (FORATEC HFA) should not be interpreted as implying that treatment of the underlying condition can be reduced. It is therefore recommended that treatment with inhaled or oral corticosteroids, if indicated should continue unchanged after the introduction of (FORATEC HFA).

Should symptoms persist, or should the requirement for doses of (FORATEC HFA) increase in order to control symptoms, this is usually an indication of a worsening of the underlying condition and warrants a reassessment of therapy.

(FORATEC HFA) should only be administered precisely as recommended in the section "DOSAGE AND DIRECTIONS FOR USE".

Special care and supervision, with particular emphasis on dosage limits, is required when the following conditions may exist (see "CONTRA-INDICATIONS" as well):

- Ischaemic heart disease.
- Myocardial infarction.
- Severe hypertension.
- Cardiac arrhythmias, especially third degree atrioventricular block.
- Severe cardiac decompensation.
- Severe aortic stenosis.

Potentially serious hypokalaemia may result from (FORATEC HFA) therapy. Particular caution is advised in severe asthma as this effect may be potentiated by hypoxia and concomitant treatments (see "INTERACTIONS").

It is recommended that serum potassium levels are monitored in such situations. If paradoxical bronchospasm occurs, (FORATEC HFA) should be discontinued immediately and alternative therapy instituted.

Due to hepatic metabolism, severe hepatic dysfunction may lead to increased exposure.

INTERACTIONS:

Medicines such as quinidine, disopyramide, procainamide, phenothiazines, antihistamines and tricyclic antidepressants may be associated with Q-T interval prolongation and an increased risk of ventricular arrhythmias (see "CONTRA-INDICATIONS").Administration of additional sympathomimetic agents may potentiate the undesirable effects of (FORATEC HFA). Administration of (FORATEC HFA) to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants shouldbe avoided, since the action of Beta$_2$-adrenergic stimulants on the cardiovascular system may be potentiated.

Concomitant treatment with xanthine derivatives, corticosteroids or diuretics may potentiate the hypokalaemic effect of (FORATEC HFA).

Hypokalaemia may increase the susceptibility to cardiac arrhythmias in patients treated with digitalis (see "WARNINGS"). Beta-adrenergic blockers (including eye drops) should not be used in asthmatics as their use involves the risk of provoking an attack of bronchospasm. They can also weaken or inhibit the effect of (FORATEC HFA).

PREGNANCY AND LACTATION:

The safety of (FORATEC HFA) during pregnancy and lactation has not been established. Its use in pregnancy should therefore be avoided until further evidence is available. It is not known whether formoterol passes into human breast milk. Mothers taking (FORATEC HFA) should refrain from breast-feeding their infants.

DOSAGE AND DIRECTIONS FOR USE:

Directions for use of the (FORATEC HFA) in the Dry Powder inhaler device: Please refer to the enclosed patient leaflet.

The inhalation capsules are to be used with the dry powder inhaler device provided.

The following dosages are recommended in adults, including elderly patients, and in children aged 6 years and over:

Regular maintenance and prophylactic therapy:

One inhalation capsule twice daily, in the morning and in the evening.

In the exceptional case where an acute attack occurs, one or two additional capsules may be inhaled.

In such cases the maximum daily dose is 48 mcg or 4 capsules.

For maintenance therapy, no more than two capsules in 12 hours should be inhaled. If the maximum daily maintenance dose of 24 meg does not control symptoms, medical advice should be sought and therapy, e.g. inhaled steroids, reassessed.

Prophylaxis against exercise-induced bronchospasm or before exposure to a known unavoidable allergen challenge:

One inhalation capsule of 12 mcg should be inhaled about 15 minutes beforehand.
To ensure proper administration, the patient should be instructed by a doctor or other health care professional on the use of the dry powder inhaler device. The capsules should be removed from the container immediately before use.

The use of (FORATEC HFA) inhalation capsules in children aged 6 years and over should depend on the ability of the individual child to use the dry powder inhaler device correctly (including inhalation technique). The dry powder inhaler device should only be used under the supervision of adults.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

SIDE EFFECTS:

Nervous System Disorders:

Frequently:

Tremor, headache, agitation and dizziness (tremor tends to be transient and diminishes with regular therapy).

Less frequently:

Anxiety, nervousness and insomnia.

Eye disorders:

Less frequently:

Conjunctival irritation and eyelid oedema.

Cardiovascular disorders

Less frequently:

Palpitations (palpitations tend to be transient and diminish with regular therapy).

Tachycardia.

Respiratory disorders:

Less frequently:

Aggravated bronchospasm and oropharyngeal irritation.

Gastrointestinal disorders:

Less frequently:

Nausea and taste perversion.

Skin and subcutaneous tissue disorders:

Less frequently:

Pruritus and exanthema.

Musculoskeletal disorders:

Less frequently:

Muscle cramps and myalgia.

Special Precautions:

Due to the hyperglycaemic effect of beta$_2$-stimulants, additional blood glucose control is initially recommended when FORATEC HFA therapy is commenced in diabetic patients.

If adverse reactions such as tremor or agitation occur, they may affect the patient's ability to drive a vehicle or operate machinery.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms: Nausea, vomiting, headache, tremor, somnolence, palpitations, tachycardia, ventricular arrhythmias, metabolic acidosis, hypokalaemia, hyperglycaemia, hypotension

Treatment: Supportive and symptomatic.

The use of cardioselective beta-blockers may be considered. However, such therapy must be administered with extreme caution since the use of a beta-blocker involves the risk of provoking an attack of bronchospasm.

IDENTIFICATION

FORATEC HFA: White homogenous suspension aerosol for inhalation, in propellant HFA – 134a supplied in a pressurized container.

PRESENTATION:

FORATEC HFA: A pressurized aluminium canister which delivers 12 formoterol fumarate with each actuation. Each canister provides 120 metered dose inhalations.

STORAGE INSTRUCTIONS:

Store this medicine in a cool dry place at or below 25°C. Protect from excessive heat, freezing and moisture. The canister is pressurized. It should not be broken, punctured or burnt, even when apparently empty.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

40/10.2.1/0413

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

CIPLA MEDPRO (PTY) LTD

,Parc du Cap

Mispel Street, Belville,

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DATE OF PUBLICATION OF THIS PACKAGE INSERT:

To be allocated