Formoterol fumarate and Budesonide HFA Inhaler

Foracort-160 Inhaler

COMPOSITION

Each delivered dose (the dose that leaves the mouthpiece) contains as active constituents:

Budesonide BP ..... 160 mcg/inhalation

Formoterol Fumarate Dihydrate Ph. Eur. ..... 4.5 mcg/inhalation

Suspended in Propellant HFA-134a ..... q.s.

DOSAGE FORM

Inhalation aerosol

DESCRIPTION

FORACORT Inhaler is a combination of budesonide, a potent glucocorticoid, and formoterol fumarate, a selective, long-acting beta$_2$-agonist.

Budesonide is a potent glucocorticoid that binds with high affinity to the glucocorticoid receptor. It has a high ratio of topical to systemic activity.

Formoterol is a very potent, long-acting, beta$_2$ adrenoceptor-agonist with a high intrinsic activity and a rapid onset of action.

PHARMACOLOGY

Pharmacodynamics

FORACORT Inhaler contains both budesonide and formoterol; therefore, the mechanisms of action described below for the individual components apply to **FORACORT Inhaler.** These drugs represent two classes of medications (a synthetic corticosteroid and a long-acting, selective beta$_2$-adrenoceptor agonist) that have different effects on the clinical, physiological, and inflammatory indices of asthma.

Budesonide:

Budesonide is an anti-inflammatory corticosteroid that exhibits potent glucocorticoid activity and weak mineralocorticoid activity. In standard *in vitro* and animal models, budesonide has approximately a 200-fold higher affinity for the glucocorticoid receptor and a 1000-fold higher topical anti-inflammatory potency than cortisol.

In glucocorticoid receptor affinity studies, the 22R form of budesonide was two times as active as the 22S epimer. *In vitro* studies indicated that the two forms of budesonide do not interconvert.

Inflammation is an important component in the pathogenesis of asthma. Corticosteroids have a wide range of inhibitory activities against multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in allergic and non-allergic-mediated inflammation. These anti-inflammatory actions of corticosteroids may contribute to their efficacy in asthma.

Studies in asthmatic patients have shown a favorable ratio between topical anti-inflammatory activity and systemic corticosteroid effects over a wide range of doses of budesonide. This is explained by a combination of a relatively high local anti-inflammatory effect, extensive first pass hepatic degradation of orally absorbed drug (85%–95%), and the low potency of formed metabolites.

Formoterol Fumarate:

Formoterol fumarate is a long-acting, selective beta$_2$-adrenergic agonist with a rapid onset of action. Inhaled formoterol fumarate acts locally in the lungs as a bronchodilator. *In vitro* studies have shown that formoterol has over 200-fold greater agonist activity at beta$_2$-receptors than at beta$_1$-receptors. The *in vitro* binding selectivity to beta$_2$-adrenoceptors over beta$_1$-adrenoceptors is higher for formoterol than for salbutamol (5 times), whereas salmeterol has a higher (3 times) beta$_2$-selectivity ratio than formoterol.

Although beta$_2$-receptors are the predominant adrenergic receptors in bronchial smooth muscle and beta$_1$-receptors are the predominant receptors in the heart, there are also beta$_2$-receptors in the human heart, which comprise 10–50% of the total beta-adrenergic receptors. The precise function of these receptors has not been established, but they raise the possibility that even highly selective beta$_2$-agonists may have cardiac effects.

The pharmacological effects of beta$_2$-adrenoceptor agonist drugs, including formoterol, are, at least in part, attributable to the stimulation of intracellular adenyl cyclase, the enzyme that catalyses the conversion of adenosine triphosphate (ATP) to cyclic-3', 5'-adenosine monophosphate (cyclic AMP). Increased cyclic AMP levels cause relaxation of bronchial smooth muscle and inhibit the release of mediators of immediate hypersensitivity from the cells, especially from mast cells.

Pharmacokinetics

In a single-dose study, higher than recommended doses (12 inhalations of 160/4.5 mcg) of the budesonide/formoterol combination dry powder inhaler (DPI) were administered to patients with moderate asthma. For budesonide, peak plasma concentrations of 4.5 nmol/L occurred at 20 minutes following dosing and for formoterol, peak concentrations of 136 pmol/L occurred at 10 minutes following dosing. Approximately 8% of the delivered dose of formoterol was recovered in the urine as unchanged drug. This study also demonstrated that the total systemic exposure to budesonide from the budesonide/formoterol combination DPI was approximately 30% lower than from budesonide DPI alone at the same delivered dose. Following administration of the budesonide / formoterol combination DPI, the half-life of the budesonide component was 4.7 hours and for the formoterol component was 7.9 hours.

In a repeat dose study, the highest recommended dose of the budesonide/formoterol combination DPI (160/4.5 mcg, 2 inhalations twice daily) was administered to patients with moderate asthma and healthy subjects for 1 week. In the asthma patients, peak plasma concentrations of budesonide (1.2nmol/L) and formoterol (28pmol/L) occurred at 21 and 10 minutes, respectively, following dosing. Peak plasma concentrations for budesonide and formoterol were about 30-40% higher in healthy subjects compared to that in the asthma patients. However, the total systemic exposure was comparable to that in the asthma patients.

Following administration of budesonide/formoterol combination DPI (160/4.5 mcg, 2 or 4 inhalations twice daily) for 5 days in healthy subjects, plasma concentrations of budesonide and formoterol generally increased in proportion to the dose. Additionally, in this study, the accumulation index for the group that received 2 inhalations twice daily was 1.32 for budesonide and 1.77 for formoterol.

Special Populations:

Geriatric:

The pharmacokinetics of formoterol/budesonide in geriatric patients has not been specifically studied.

Paediatric:

In a single-dose study in paediatric patients with asthma, 6–11 years of age, plasma concentrations of budesonide were measured following administration of 4 inhalations of budesonide/formoterol combination DPI 160/4.5 mcg. Urine was collected for determination of formoterol excretion. Peak budesonide concentrations of 1.4 nmol/L occurred at 20 minutes post-dose. Approximately 3.5% of the delivered formoterol dose was recovered in the urine as unchanged formoterol. This study also demonstrated that the total systemic exposure to budesonide from the budesonide/formoterol combination DPI was approximately 30% lower than from budesonide DPI alone, which was also evaluated at the same delivered dose.

Gender/Race:

Specific studies to examine the effects of gender and race on the pharmacokinetics of formoterol/budesonide have not been conducted. Population PK analysis of the formoterol/budesonide data indicates that gender does not affect the pharmacokinetics of budesonide and formoterol. No conclusions can be drawn on the effect of race due to the low number of non-Caucasians evaluated for PK.

Renal or Hepatic Insufficiency:

There are no data regarding the specific use of formoterol/budesonide in patients with hepatic or renal impairment. Reduced liver function may affect the elimination of corticosteroids. Budesonide pharmacokinetics was affected by compromised liver function as evidenced by a doubled systemic availability after oral ingestion. The intravenous budesonide pharmacokinetics was, however, similar in cirrhotic patients and in healthy subjects. Specific data with formoterol is not available, but because formoterol is primarily eliminated via hepatic metabolism, an increased exposure can be expected in patients with severe liver impairment.

Drug-Drug Interactions:

A single-dose crossover study was conducted to compare the pharmacokinetics of 8 inhalations of the following: budesonide, formoterol, and budesonide/formoterol administered concurrently. The results of the study indicated that there was no evidence of a pharmacokinetic interaction between the two components of the budesonide/formoterol combination DPI.

Ketoconazole, a potent inhibitor of cytochrome P450 (CYP) isoenzyme 3A4 (CYP3A4), the main metabolic enzyme for corticosteroids, increased plasma levels of orally ingested budesonide. At recommended doses, cimetidine had a slight but clinically insignificant effect on the pharmacokinetics of oral budesonide. Specific drug-drug interaction studies with formoterol have not been performed.

Budesonide:

Absorption:

Orally inhaled budesonide is rapidly absorbed in the lungs and peak concentration is typically reached within 20 minutes. After oral administration of budesonide, peak plasma concentration was achieved in about 1-2 hours and the absolute systemic availability was 6–13%, due to extensive first pass metabolism. In contrast, most of the budesonide delivered to the lungs was systemically absorbed. In healthy subjects, 34% of the metered dose was deposited in the lungs (as assessed by the plasma concentration method, and using a budesonide-containing DPI) with an absolute systemic availability of 39% of the metered dose. Peak steady-state plasma concentrations of budesonide administered by DPI in adults with asthma averaged 0.6nmol/L and 1.6nmol/L at doses of 180 mcg and 360 mcg twice daily, respectively.

In asthmatic patients, budesonide showed a linear increase in AUC and C_{max} with increasing dose, after both a single dose and repeated doses of inhaled budesonide.

Distribution:

The volume of distribution of budesonide was approximately 3 L/kg. It was 85–90% bound to plasma proteins. Protein binding was constant over the concentration range (1–100 nmol/L) achieved with, and exceeding, recommended inhaled doses. Budesonide showed little or no binding to corticosteroid-binding globulin. Budesonide rapidly equilibrated with red blood cells in a concentration-independent manner, with a blood/plasma ratio of about 0.8.

Metabolism:

In vitro studies with human liver homogenates have shown that budesonide was rapidly and extensively metabolized. Two major metabolites formed via cytochrome P450 (CYP) isoenzyme 3A4 (CYP3A4)-catalysed biotransformation have been isolated and identified as 16alpha-hydroxyprednisolone and 6beta-hydroxybudesonide. The corticosteroid activity of each of these two metabolites was less than 1% of that of the parent compound. No qualitative differences between the *in vitro* and *in vivo* metabolic patterns were detected. Negligible metabolic inactivation was observed in human lung and serum preparations.

Excretion/Elimination:

Budesonide was excreted in the urine and the faeces in the form of metabolites. Approximately 60% of an intravenous radiolabelled dose was recovered in the urine. No unchanged budesonide was detected in the urine. The 22R form of budesonide was preferentially cleared by the liver with systemic clearance of 1.4 L/min versus 1.0 L/min for the 22S form. The terminal half-life of 2 to 3 hours was the same for both epimers and was independent of dose.

Formoterol Fumarate:

Absorption:

Inhaled formoterol is rapidly absorbed and peak plasma concentrations are typically reached at the first plasma sampling time, within 5–10 minutes after dosing. As with many drug products for oral inhalation, it is likely that the majority of the inhaled formoterol delivered is swallowed and then absorbed from the gastrointestinal tract.

Distribution:

Over the concentration range of 10–500 nmol/L, the plasma protein binding for the RR- and SS-enantiomers of formoterol was 46% and 58%, respectively. The concentrations of formoterol used to assess the plasma protein binding were higher than those achieved in plasma, following inhalation of a single 54 mcg dose.

Metabolism and Excretion:

The metabolism and excretion of formoterol were studied in 4 healthy subjects following simultaneous administration of radiolabelled formoterol via the oral and intravenous routes. In this study, 62% of the radiolabelled formoterol was excreted in the urine while 24% was eliminated in the faeces. The primary metabolism of formoterol is by direct glucuronidation and by O-demethylation, followed by conjugation to inactive metabolites. Secondary metabolic pathways include deformylation and sulphate conjugation. CYP2D6 and CYP2C have been identified as being primarily responsible for O-demethylation.

INDICATIONS

FORACORT Inhaler is indicated in the regular treatment of asthma, where the use of a combination (long-acting, beta$_2$-agonist and inhaled corticosteroid) has been found to be appropriate. It is also indicated in the symptomatic treatment of severe chronic obstructive pulmonary disease (COPD), with a history of repeated exacerbations despite regular therapy with long-acting bronchodilators.

DOSAGE AND ADMINISTRATION

Asthma

Dosage is individual and should be adjusted according to disease severity. When control has been achieved, the dose should be titrated to the lowest effective dose, which could include **FORACORT Inhaler** used once daily.

For **FORACORT** there are two treatment approaches:

A. ***Maintenance Therapy*: FORACORT** is taken as regular maintenance treatment with a separate rapid acting bronchodilator as rescue.

B. ***Single maintenance and reliever therapy*: FORACORT** is taken as regular maintenance and as needed in response to symptoms.

A, Maintenance Therapy: Patients should be advised to have their separate rapid acting bronchodilator available for rescue use at all times.

Adults (18 Years and Older)

1–2 inhalations, twice daily

Maximum dose is 4 inhalations, twice daily

Adolescents (12-17 Years)

1–2 inhalations, twice daily

Children (6-11 Years)

1 inhalation, twice daily

C. Single Maintenance and Reliever Therapy

Patients take a daily maintenance dose of **FORACORT** and in combination take **FORACORT** as needed in response to symptoms. Patients should be advised to always have **FORACORT** available for use.

Adults (18 years and older): The recommended maintenance dosage is 2 inhalations per day as maintenance therapy (either one inhalation twice daily, or two inhalations in either the morning or the evening), although some patients may require two inhalations twice daily.

Patients should take 1 additional inhalation as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation should be taken. Not more than 6 inhalations should be taken on any single occasion.

A total daily dose of more than 8 inhalations is not normally needed; however, a total daily dose of up of 12 inhalations could be used for a limited period. Patients using more than 8 inhalations daily should be strongly recommended to seek medical advice. They should be reassessed and their maintenance therapy should be reconsidered.

Single inhaler as maintenance and reliever therapy is not recommended in children and adolescents.

COPD (Chronic Obstructive Pulmonary Disease)

2 inhalations, twice daily

CONTRAINDICATIONS

FORACORT Inhaler is contraindicated in patients with a history of hypersensitivity to any of the components of the drug product.

WARNINGS AND PRECAUTIONS

It is recommended that the dose is tapered when the treatment is discontinued and should not be stopped abruptly.

If patients find the treatment ineffective, or exceed the highest recommended dose of **FORACORT Inhaler**, medical attention must be sought. Sudden and progressive deterioration in control of asthma is potentially life threatening and the patient should undergo urgent medical assessment. In this situation consideration should be given to the need for increased therapy with corticosteroids e.g, a course of oral corticosteroids, or antibiotic treatment if an infection is present.

Patients should be advised to have their rescue inhaler available at all times, either **FORACORT** (for patients using **FORACORT** as maintenance and reliever therapy) or a separate rapid-acting bronchodilator (for patients using **FORACORT** as maintenance therapy only).

Patients should be reminded to take their **FORACORT** maintenance dose as prescribed, even when asymptomatic. The prophylactic use of **FORACORT**, e.g. before exercise, has not been studied. The reliever inhalations of **FORACORT** should be taken in response to asthma symptoms but are not intended for regular prophylactic use, e.g. before exercise. For such use, a separate rapid-acting bronchodilator should be considered.

Once asthma symptoms are controlled, consideration may be given to gradually reducing the dose of **FORACORT.** Regular review of patients as treatment is stepped down is important. The lowest effective dose of **FORACORT Inhaler** should be used.

Patients should not be initiated on **FORACORT** during an exacerbation, or if they have significantly worsening or acutely deteriorating asthma.

Serious asthma-related adverse events and exacerbations may occur during treatment with **FORACORT**. Patients should be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation with **FORACORT.**

As with other inhalation therapy, paradoxical bronchospasm may occur, with an immediate increase in wheezing after dosing. **FORACORT** should then be discontinued; treatment should be re-assessed and alternative therapy instituted if necessary.

Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur with inhalation treatment than with oral corticosteroids. Possible systemic effects include adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma.

It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroids is regularly monitored. If growth is slowed, therapy should be re-evaluated with the aim of reducing the dose of inhaled corticosteroid. The benefits of the corticosteroid therapy and the possible risks of growth suppression must be carefully weighed. In addition consideration should be given to referring the patient to a paediatric respiratory specialist.

Limited data from long-term studies suggest that most children and adolescents treated with inhaled budesonide will ultimately achieve their adult target height. However, an initial small but transient reduction in growth (approximately 1 cm) has been observed. This generally occurs within the first year of treatment.

Long-term studies with inhaled budesonide in children at mean daily doses of 400 micrograms (metered dose) or in adults at daily doses of 800 micrograms (metered dose) have not shown any significant effects on bone mineral density. No information regarding the effect of formoterol/budesonide at higher doses is available.

If there is any reason to suppose that adrenal function is impaired from previous systemic steroid therapy, care should be taken when transferring patients to **FORACORT** therapy.

The benefits of inhaled budesonide therapy would normally minimize the need for oral steroids, but patients transferring from oral steroids may remain at risk of impaired adrenal reserve for a considerable time. Patients, who have required high dose emergency corticosteroid therapy in the past or prolonged treatment with high doses of inhaled corticosteroids, may also be at risk. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

To minimize the risk of oropharyngeal candida infection, the patient should be instructed to rinse their mouth out with water after inhaling the maintenance dose. If oropharyngeal thrush occurs, patients should also rinse their mouth with water after the as-needed inhalations.

FORACORT Inhaler should be administered with caution in patients with thyrotoxicosis, phaeochromocytoma, diabetes mellitus, untreated hypokalaemia, hypertrophic obstructive cardiomyopathy, idiopathic subvalvular aortic stenosis, severe hypertension, aneurysm or other severe cardiovascular disorders, such as ischaemic heart disease, tachyarrhythmias or severe heart failure.

Caution should be observed when treating patients with prolongation of the QTc-interval. Formoterol itself may induce prolongation of the QTc-interval.

The need for, and dose of inhaled corticosteroids should be re-evaluated in patients with active or quiescent pulmonary tuberculosis, fungal and viral infections in the airways.

Potentially serious hypokalaemia may result from high doses of beta$_2$-agonists. Concomitant treatment of beta$_2$-agonists with drugs which can induce hypokalaemia or potentiate a hypokalaemic effect, e.g. xanthine-derivatives, steroids and diuretics, may add to a possible hypokalaemic effect of the beta$_2$-agonist. Particular caution is recommended in unstable asthma with variable use of rescue bronchodilators, in acute severe asthma as the associated risk may be augmented by hypoxia and in other conditions when the likelihood for hypokalaemia adverse effects is increased. It is recommended that serum potassium levels are monitored during these circumstances.

As for all beta$_2$-agonists, additional blood glucose controls should be considered in diabetic patients.

Drug Interactions

Pharmacokinetic interactions:

The metabolic conversion of budesonide is impeded by substances metabolized by CYP P450 3A4 (e.g. itraconazole, ritonavir). The concomitant administration of these potent inhibitors of CYP P450 3A4 may increase plasma levels of budesonide. The concomitant use of these drugs should be avoided unless the benefit outweighs the increased risk of systemic side-effects. In patients using potent CYP3A4 inhibitors, **FORACORT** maintenance and reliever therapy is not recommended.

Pharmacodynamic interactions:

Beta-adrenergic blockers can weaken or inhibit the effect of formoterol. **FORACORT Inhaler** should therefore not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons.

Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, antihistamines (terfenadine), monoamine oxidase inhibitors and tricyclic antidepressants can prolong the QTc-interval and increase the risk of ventricular arrhythmias.

In addition L-Dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance towards beta$_2$-sympathomimetics.

Concomitant treatment with monoamine oxidase inhibitors including agents with similar properties such as furazolidone and procarbazine may precipitate hypertensive reactions.

There is an elevated risk of arrhythmias in patients receiving concomitant anaesthesia with halogenated hydrocarbons.

Concomitant use of other beta-adrenergic drugs can have a potentially additive effect.

Hypokalaemia may increase the disposition towards arrhythmias in patients who are treated with digitalis glycosides.

Budesonide and formoterol have not been observed to interact with any other drugs used in the treatment of asthma.

Renal Impairment

There are no data regarding the specific use of the budesonide/formoterol combination DPI in patients with renal impairment.

Hepatic Impairment

There are no data regarding the specific use of the budesonide/formoterol combination DPI in patients with hepatic impairment. Reduced liver function may affect the elimination of corticosteroids. Budesonide pharmacokinetics was affected by compromised liver function as evidenced by a doubled systemic availability after oral ingestion. The intravenous budesonide pharmacokinetics was, however, similar in cirrhotic patients and in healthy subjects. Specific data with formoterol is not available, but since formoterol is primarily eliminated via hepatic metabolism, an increased exposure can be expected in patients with severe liver impairment.

Pregnancy

There are no adequate data from use of formoterol and budesonide in pregnant women. Administration of **FORACORT Inhaler** in pregnant women should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus. The lowest effective dose of budesonide needed to maintain adequate asthma control should be used.

Lactation

Budesonide is excreted in breast milk. However, at therapeutic doses no effects on the suckling child are anticipated. It is not known whether formoterol passes into human breast milk. Administration of **FORACORT Inhaler** to women who are breastfeeding should only be considered if the expected benefit to the mother is greater than any possible risk to the child.

Paediatric Use

The growth of paediatric patients receiving orally inhaled corticosteroids, including **FORACORT Inhaler**, should be monitored. If a child or adolescent on any corticosteroid appears to have growth suppression, the possibility that he/she is particularly sensitive to this effect should be considered. The potential growth effects of prolonged treatment should be weighed against the clinical benefits obtained. To minimize the systemic effects of orally inhaled corticosteroids, including **FORACORT Inhaler**, each patient should be titrated to the lowest strength that effectively controls his/her asthma.

Geriatric Use

No overall differences in safety were observed between these patients and younger patients. As with other products containing beta$_2$-agonists, special caution should be observed when using **FORACORT Inhaler** in geriatric patients who have concomitant cardiovascular disease that could be adversely affected by beta$_2$-agonists. Based on available data for formoterol and budesonide or its active components, no adjustment of dosage of **FORACORT Inhaler** in geriatric patients is warranted.

UNDESIRABLE EFFECTS

Since **FORACORT Inhaler** contains both budesonide and formoterol, the same pattern of undesirable effects as reported for these substances may occur. No increased incidence of adverse reactions has been seen following concurrent administration of the two compounds. The most common drug related adverse reactions are pharmacologically predictable side-effects of beta$_2$-agonist therapy, such as tremor and palpitations. These tend to be mild and usually disappear within a few days of treatment.

Following are some common, uncommon and rare adverse events that occurred in the groups receiving formoterol/budesonide were derived from clinical trial data:

Cardiac disorders: Palpitations, Tachycardia, Cardiac arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia, extrasystoles, Angina pectoris.

Endocrine disorders: Signs or symptoms of systemic glucocorticosteroid effects e.g. adrenal suppression, growth retardation, decrease in bone mineral density, cataract and glaucoma.

Gastrointestinal disorders: Nausea.

Immune system disorders: Immediate and delayed hypersensitivity reactions, e.g. exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction.

Infections and infestations: Candida infections in the oropharynx.

Metabolic and nutrition disorders: Hypokalemia, Hyperglycemia.

Musculoskeletal, connective tissue and bone disorders: Muscle cramps.

Nervous system disorders: Headache, tremor, Dizziness, Taste disturbances.

Psychiatric disorders: Agitation, restlessness, nervousness, sleep disturbances, Depression, behavioural disturbances (mainly in children).

Respiratory, thoracic and mediastinal disorders: Mild irritation in the throat, coughing, hoarseness, Bronchospasm.

Skin and subcutaneous tissue disorders: Bruises.

Vascular disorders: Variations in blood pressure.

As with other inhalation therapy, paradoxical bronchospasm may occur in very rare cases.

Treatment with beta$_2$-agonists may result in an increase in blood levels of insulin, free fatty acids, glycerol and ketone bodies.

OVERDOSAGE

An overdose of formoterol would likely lead to effects that are typical for beta$_2$-adrenergic agonists: tremor, headache, palpitations. Symptoms reported from isolated cases are tachycardia, hyperglycaemia, hypokalaemia, prolonged QTc-interval, arrhythmia, nausea and vomiting. Supportive and symptomatic treatment may be indicated. A dose of 90 micrograms administered during three hours in patients with acute bronchial obstruction raised no safety concerns.

Acute overdosage with budesonide, even in excessive doses, is not expected to be a clinical problem. When used chronically in excessive doses, systemic glucocorticosteroid effects, such as hypercorticism and adrenal suppression, may appear.

If **FORACORT Inhaler** therapy has to be withdrawn due to overdose of the formoterol component of the drug, provision of appropriate inhaled corticosteroid therapy must be considered.

PACKAGING INFORMATION

Foracort-160 Inhaler

Each sales pack is available as a canister containing 120 metered doses.

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