Foracort Inhaler 160/4.5
(Budesonide 160 mcg/actuation and Formoterol Fumarate Dihydrate 4.5 mcg/actuation Pressurised Inhalation, Suspension)

Composition

Each actuation delivers:
Budesonide BP / Ph. Eur. ……. 160 mcg.
Formoterol Fumarate Dihydrate BP / Ph. Eur. …….... 4.5 mcg

Dosage Form

Pressurised Metered-Dose Inhaler

Description

Foracort Inhaler 160/4.5 is a white to off-white coloured suspension filled in an aluminium aerosol canister fitted into a white polypropylene actuator with a dose counter (120 doses) and a brown polypropylene dust cap. Each inhaler is wrapped in a foil laminate pouch containing a drying agent.

Pharmacology

Pharmacodynamics

Pharmacotherapeutic group: Drugs for obstructive airway diseases: Adrenergics, Inhalants.

ATC-code: R03AK07

Mechanism of action and Pharmacodynamic effects

Budesonide/formoterol (pressurised inhalation, suspension) contains budesonide and formoterol, which have different modes of action and show additive effects in case of obstructive airways diseases.

Budesonide

Budesonide is a glucocorticosteroid which when inhaled has a dose-dependent anti- inflammatory action in the airways, resulting in reduced symptoms and fewer COPD exacerbations, inhaled budesonide has less severe adverse effects than systemic corticosteroids. The exact mechanism responsible for the anti-inflammatory effect of glucocorticosteroids is unknown.

Formoterol

Formoterol is a selective ß2- adrenoceptor agonist that when inhaled results in rapid and long- acting relaxation of bronchial smooth muscle in patients with reversible airways obstruction. The bronchodilating effect sets in rapidly (within 1-3 minutes after inhalation) and has a duration of 12 hours after a single dose.

Pharmacokinetics

Absorption

The fixed-dose combination of budesonide/formoterol, and the corresponding monoproducts have been shown to be bioequivalent with regard to systemic exposure of budesonide/formoterol, respectively. In spite of this, a small increase in cortisol suppression was seen after administration of the fixed-dose combination compared to the monoproducts. The difference is considered not to have an impact on clinical safety.

There was no evidence of pharmacokinetic interactions between budesonide/formoterol. Pharmacokinetic parameters for the respective substances were comparable after the administration of budesonide/formoterol as monoproducts or as the fixed-dose combination. For budesonide, AUC was slightly higher, rate of absorption more rapid and maximal plasma concentration higher after administration of the fixed combination. For formoterol, maximal plasma concentration was similar after administration of the fixed combination. Inhaled budesonide is rapidly absorbed and the maximum plasma concentration is reached within 30 minutes after inhalation. In studies, mean lung deposition of budesonide after inhalation via Turbuhaler ranged from 32% to 44% of the delivered dose. The systemic bioavailability is approximately 49% of the delivered dose. In children 6-16 years of age the lung deposition fall in the same range as in adults for the same given dose, the resulting plasma concentrations were not determined.

Inhaled formoterol is rapidly absorbed and the maximum plasma concentration is reached within 10 minutes after inhalation. In studies the mean lung deposition of formoterol after inhalation via Turbuhaler ranged from 28% to 49% of the delivered dose. The systemic bioavailability is about 61% of the delivered dose.

Distribution and Biotransformation

Plasma protein binding is approximately 50% for formoterol and 90% for budesonide. Volume of distribution is about 4 L/kg for formoterol and 3 L/kg for budesonide. Formoterol is inactivated via conjugation reactions (active O-demethylated and deformylated metabolites are formed, but they are seen mainly as inactivated conjugates). Budesonide undergoes an extensive degree (approximately 90%) of biotransformation on first passage through the liver to metabolites of low glucocorticosteroid activity. The glucocorticosteroid activity of the major metabolites, 6-beta-hydroxy-budesonide and 16-alfa-hydroxy-prednisolone, is less than 1% of that of budesonide. There are no indications of any metabolic interactions or any displacement reactions between formoterol and budesonide.

Elimination

The major part of a dose of formoterol is transformed by liver metabolism followed by renal elimination. After inhalation, 8% to 13% of the delivered dose of formoterol is excreted unmetabolised in the urine. Formoterol has a high systemic clearance (approximately 1.4 L/min) and the terminal elimination half-life averages 17 hours.

Budesonide is eliminated via metabolism mainly catalysed by the enzyme CYP3A4. The metabolites of budesonide are eliminated in urine as such or in conjugated form. Only negligible amounts of unchanged budesonide have been detected in the urine. Budesonide has a high systemic clearance (approximately 1.2 L/min) and the plasma elimination half-life after i.v. dosing averages 4 hours.

The pharmacokinetics of formoterol in children have not been studied. The pharmacokinetics of budesonide and formoterol in patients with renal failure are unknown. The exposure of budesonide and formoterol may be increased in patients with liver disease.

Linearity/ Non-linearity

Systemic exposure for both budesonide and formoterol correlates in a linear fashion to administered dose.

Indications

Asthma

Foracort is indicated in the regular treatment of asthma where use of a combination (inhaled corticosteroid and long-acting β2 adrenoceptor agonist) is appropriate:

- patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting β2 adrenoceptor agonists, or

- patients already adequately controlled on both inhaled corticosteroids and long-acting β2 adrenoceptor agonists.

Chronic Obstructive Pulmonary Disease (COPD)

Foracort is indicated in adults, aged 18 and older, for the symptomatic treatment of patients with COPD with FEV1 <70% predicted normal (post-bronchodilator) and an exacerbation history despite regular bronchodilator therapy.

Dosage and Method of Administration

Foracort is for oral inhalation only

General information

The patient should be instructed that Foracort must be used regularly even when asymptomatic for optimal benefit.

The medication from Foracort is delivered to the lungs as the patient inhales. Therefore, a correct handling of Foracort is very important. The patients should be instructed accordingly (see *"instruction for use"*).

The patient should be instructed to use Foracort regularly, i.e. in asymptomatic times to get the best therapeutic benefit.

Asthma

The dosage of Foracort should be regularly checked by the doctor, and should be individualised according to disease severity. Initial dose should be adjusted so that effective symptomatic control is obtained. When the desired clinical effect has been achieved, the dose should be titrated to the lowest dose at which effective asthma control is maintained. If so, then the next step could include a test of inhaled corticosteroid alone.

In usual practice when control of symptoms is achieved with the twice daily regimen, titration to the lowest effective dose could include Foracort given once daily, when in the opinion of the prescriber, a long-acting bronchodilator would be required to maintain control.

In case of discontinuance of Foracort therapy, it is recommended to reduce the doses step by step.

Repeated assessments by a doctor at regular intervals are indicated in cases of severe asthma in view of the possible onset of life-threatening situations. Patients suffering from severe asthma show continuous symptoms, frequent exacerbations, PEF values (peak flow values) below 60% of normal with a peak flow variability in excess of 30% and which fail to return to normal despite the administration of a bronchodilator. High-dose inhalation therapy or oral corticosteroid therapy is indicated in these patients. A sudden worsening in symptoms may necessitate an increase in the corticosteroid dose, but only under medical supervision. However, this must not be achieved by administration of the combined product more frequently. In unstable situations, a switch to the individual monoproducts must be considered.

Posology

Asthma

Foracort should be used for a daily maintenance dose and a separate rapid-acting bronchodilator is needed for symptom relief.

Adolescents 12 to 17 years

2 inhalations once to twice daily. During worsening of asthma the dose may temporarily (1 week max.) be increased to a maximum of 4 inhalations twice daily.

Adults (18 years and older)

2 inhalations once or twice daily. In some cases up to a maximum of 4 inhalations twice daily may be required as maintenance dose or temporarily during worsening of asthma.

Equivalence between budesonide/formoterol turbuhaler and budesonide/formoterol (pressurised inhalation, suspension) has been confirmed statistically for doses of twice daily 2 inhalations of 80/4.5 or 160/4.5 µg but has not been proved for all dosages.

A separate inhaler for rescue use is required. Patients should be advised to have their rapid acting bronchodilator available at all times. Increasing use of rescue bronchodilators indicates a worsening of the underlying condition and warrants a reassessment of the asthma therapy.

Chronic Obstructive Pulmonary Disease (COPD)

Adults (18 years and older)

2 inhalations twice daily

General information

Special patient groups

There are no special dosing requirements for elderly patients. There are no data available for use of budesonide/formoterol in patients with hepatic or renal impairment. As budesonide and formoterol are primarily eliminated via hepatic metabolism, an increased exposure can be expected in patients with severe liver cirrhosis.

Paediatric Population

There is no relevant use of Foracort 160 micrograms /4.5 micrograms in children 11 years of age and under or in adolescents 12 to 17 years of age in the symptomatic treatment of COPD.

Switching over of patients who are already receiving oral corticoid therapy (see *Warning and precautions*)

Method of administration

Instructions for use

Before the first use, when the inhaler has not been used for more than one week, or when it has been dropped, shake the inhaler gently and release 2 puffs in the air.

Use

1. Hold the inhaler between thumb and index finger, and shake it gently.
2. Remove the mouthpiece cover.
3. Breathe out deeply, then put the mouthpiece in the mouth and close your lips around it. The container should be hold upright.
4. While breathing in slowly and deeply, press the container firmly to release the medication. Continue to breathe in.
5. Hold the breath for as long as is comfortable. Take the inhaler away, do not press anymore on the container.
6. Shake the inhaler again, and repeat steps 3,4,5.
7. Replace the protective cap.

For cleaning, the protective cap has to be removed, and the mouthpiece cleaned inside and outside with a dry cloth. Do not put the inhaler into water. Clean at least once a week. To minimize the risk of oropharyngeal thrush, rinse the mouth with water after inhaling the prescribed dose.

The arrow pointing at the dose counter of the inhaler points to the number of inhalations (puffs) remaining in your inhaler. The inhaler must be discarded after the counter reaches zero (“0”) even if the inhaler may not feel empty. There will not be enough active substance to be released.

Contraindications

Hypersensitivity to the active substances or to any of the excipient.

Warnings and Precautions

It is recommended that the maintenance dose is tapered when long-term treatment is discontinued and the dosing should not be stopped abruptly. Complete withdrawal of inhaled corticosteroids should not be considered unless it is temporarily required to confirm the diagnosis of asthma.

If patients find the treatment ineffective or exceed the highest recommended dose of budesonide/formoterol, medical attention must be sought (see *Posology and Method of administration*). Sudden and progressive deterioration in control of asthma or COPD 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. For treatment of severe exacerbations, a combination product of inhaled corticosteroid and long acting β2 agonist alone is not sufficient.

Patients should be advised to have their rescue inhaler available at all times.

Patients should be reminded to take their budesonide/formoterol maintenance dose as prescribed even when asymptomatic.

Once asthma symptoms are controlled, consideration may be given to gradually reducing the dose of budesonide/formoterol. Regular review of patients as treatment is stepped down is important. The lowest effective dose of budesonide/formoterol should be used (see *Posology and Method of administration*).

Patients should not be initiated on budesonide/formoterol 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 budesonide/formoterol. Patients should be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation with budesonide/formoterol.

There are no clinical study data on budesonide/formoterol available in COPD patients with a pre-bronchodilator FEV1 >50% predicted normal and with a post-bronchodilator FEV1 <70% predicted normal (see *Pharmacodynamics*).

As with other inhalation therapy, paradoxical bronchospasm may occur, with an immediate increase in wheezing and shortness of breath after dosing. If the patient experiences paradoxical bronchospasm, budesonide/formoterol should be discontinued immediately, the patient should be assessed and an alternative therapy instituted, if necessary. Paradoxical bronchospasm responds to a rapid-acting inhaled bronchodilator and should be treated straightaway (see *Undesirable effects*).

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 Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma, and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children) (see *Undesirable effects*).

Potential effects on bone density should be considered particularly in patients on high doses for prolonged periods that have coexisting risk factors for osteoporosis. 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 budesonide/formoterol 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 budesonide/formoterol therapy.

The benefits of inhaled budesonide therapy would normally minimise the need for oral steroids, but patients transferring from oral steroids may remain at risk of impaired adrenal reserve for a considerable time. Recovery may take a considerable amount of time after cessation of oral steroid therapy and hence oral steroid dependent patients transferred to inhaled budesonide may remain at risk from impaired adrenal function for some considerable time. In such circumstances HPA axis function should be monitored regularly.

The prolonged treatment with high doses of inhaled corticosteroids, particularly higher than recommended doses, may also result in clinically significant adrenal suppression. Therefore, additional systemic corticosteroid cover should be considered during periods of stress such as severe infections or elective surgery. Rapid reduction in the dose of steroids can induce acute adrenal crisis. Symptoms and signs which might be seen in acute adrenal crisis may be somewhat vague but may include anorexia, abdominal pain, weight loss, tiredness, headache, nausea, vomiting, decreased level of consciousness, seizures, hypotension and hypoglycaemia.

Treatment with supplementary systemic steroids or inhaled budesonide should not be stopped abruptly.

During transfer from oral therapy to budesonide/formoterol (pressurised inhalation, suspension) a generally lower systemic steroid action will be experienced which may result in the appearance of allergic or arthritic symptoms such as rhinitis, eczema and muscle and joint pain. Specific treatment should be initiated for these conditions. A general insufficient glucocorticosteroid effect should be suspected if, in rare cases, symptoms such as tiredness, headache, nausea and vomiting should occur. In these cases, a temporary increase in the dose of oral glucocorticosteroids is sometimes necessary.

To minimise the risk of oropharyngeal candida infection (see *Undesirable effects*), 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.

Budesonide/formoterol 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 β2 adrenoceptor agonists. Concomitant treatment of β2 adrenoceptor 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 β2 adrenoceptor 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 β2 adrenoceptor agonists, additional blood glucose controls should be considered in diabetic patients.

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes, which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR), which have been reported after use of systemic and topical corticosteroids.

Paediatric population

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 to the lowest dose at which effective control of asthma is maintained, if possible. 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.

Pneumonia in patients with COPD

An increase in the incidence of pneumonia, including pneumonia requiring hospitalisation, has been observed in patients with COPD receiving inhaled corticosteroids. There is some evidence of an increased risk of pneumonia with increasing steroid dose but this has not been demonstrated conclusively across all studies.

There is no conclusive clinical evidence for intra-class differences in the magnitude of the pneumonia risk among inhaled corticosteroid products.

Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations.

Risk factors for pneumonia in patient with COPD include current smoking, older age, low body mass index (BMI) and severe COPD.

Drug Interactions

Pharmacokinetic interactions

The metabolism of budesonide is primarily mediated by the enzyme CYP3A4. Potent CYP3A4 inhibitors may therefore increase systemic exposure to budesonide. This is of limited clinical importance for short-term (1-2 weeks) treatment with potent CYP3A4 inhibitors but should be taken into consideration during long-term treatment.

If a patient requires long-term concomitant treatment with budesonide/formoterol and a potent CYP3A4 inhibitor, the benefit should be weighed against the increased risk of systemic corticosteroid side effects, patients should be monitored for corticosteroid side effects and/or a reduction of the inhaled corticosteroid dose could be considered.

Pharmacodynamic interactions

Beta-adrenergic blockers can weaken or inhibit the effect of formoterol. Budesonide/formoterol 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) and tricyclic anti-depressants can prolong the QTc-interval and increase the risk of ventricular arrhythmias.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

In addition, L-Dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance towards β2 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 bronchodilating effect.

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

Hypokalaemia may result from beta2-agonist therapy and may be potentiated by concomitant treatment with xanthine derivatives, corticosteroids and diuretics (see *Warning and Precautions*).

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

Paediatric population

Interaction studies have only been performed in adults.

Fertility, Pregnancy and Lactation

Pregnancy

For budesonide/formoterol or the concomitant treatment with formoterol and budesonide, no clinical data on exposed pregnancies are available. Data from an embryo-fetal development study in the rat, using the budesonide/formoterol formulation, showed no evidence of any additional effect from the combination or evidence of any effects attributable to the excipients on the rodent.

There are no adequate data from use of formoterol in pregnant women. In animal studies formoterol has caused adverse effects in reproduction studies at very high systemic exposure levels.

Data in more than 17000 exposed pregnancies indicate no increased teratogenic risk associated with the use of inhaled budesonide. In animal studies glucocorticosteroids have been shown to induce malformations. This is not likely to be relevant for humans given recommended doses.

Animal studies have also identified an involvement of excess prenatal glucocorticoids in increased risks for intrauterine growth retardation, adult cardiovascular disease and permanent changes in glucocorticoid receptor density, neurotransmitter turnover and behaviour at exposures below the teratogenic dose range.

During pregnancy, budesonide/formoterol should only be used when the benefits outweigh the potential risks. The lowest effective dose of budesonide needed to maintain adequate asthma control should be used.

Breastfeeding

A clinical pharmacology study has shown that inhaled budesonide is excreted in breast milk. However, budesonide was not detected in nursing infant blood samples. Based on pharmacokinetic parameters, the plasma concentration in the child is estimated to be less than 0.17% of the mother’s plasma concentration. Consequently, no effects due to budesonide are anticipated in breast-fed children whose mothers are receiving therapeutic doses of budesonide/formoterol. It is not known whether formoterol passes into human breast milk. In rats, small amounts of formoterol have been detected in maternal milk. Administration of budesonide/formoterol 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.

Fertility

There is no data available on the potential effect of budesonide on fertility. Animal reproduction studies with formoterol have shown a somewhat reduced fertility in male rats at high systemic exposure.

Effect on The Ability to Drive and Use Machines

Budesonide/ formoterol has no or negligible influence on the ability to drive and use machines

Undesirable Effects

Since budesonide/formoterol (pressurised inhalation, suspension) 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 β2 adrenoceptor agonist therapy, such as tremor and palpitations. These tend to be mild and usually disappear within a few days of treatment.

Adverse reactions, which have been associated with budesonide or formoterol, are given below, listed by system organ class (SOC) and frequency. Frequency are defined as: very common (≥1/10), common (≥1/100) to <1/10), uncommon (≥1/1000 to < 1/100), rare (≥1/10000 to < 1/1000) and very rare (<1/10000).

Table 1

SOC	**Frequency**	**Adverse Drug Reaction**
Cardiac disorders	Common	Palpitations
	Uncommon	Tachycardia
	Rare	Cardiac arrhythmias e.g. atrial fibrillation, supraventricular tachycardia, extrasystoles
	Very rare	Angina pectoris. Prolongation of QTC- interval
Endocrine disorders	Very rare	Cushing's syndrome, adrenal suppression, growth retardation, decrease in bone mineral density
Gastrointestinal disorders	Uncommon	Nausea
Immune system disorders	Rare	Immediate and delayed hypersensitivity reactions, e.g., exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction
Infections and infestations	Common	Candida infections in the oropharynx Pneumonia (in COPD patients)
Metabolic and nutrition disorders	Rare	Hypokalaemia
	Very rare	Hyperglycaemia
Musculoskeletal connective tissue and bone disorders	Uncommon	Muscle cramps
Nervous system disorders	Common	Headache, tremor
	Uncommon	Dizziness
	Very rare	Taste disturbances
Psychiatric disorders	Uncommon	Aggression, psychomotor hyperactivity, anxiety, sleep disorders
	Very rare	Depression, behavioural changes (predominantly in children)
Respiratory, thoracic and mediastinal disorders	Common	Mild irritation in the throat, coughing, hoarseness
	Rare	Bronchospasm
Skin and subcutaneous tissue disorders	Uncommon	Bruises

Vascular disorders	Very rare	Variations in blood pressure
Eye disorders	Uncommon	Vision blurred (see *Warnings and Precautions*)
	Very rare	Cataract and glaucoma

Candida infection in the oropharynx is due to drug deposition. Advising the patient to rinse the mouth out with water after each maintenance dose will minimise the risk. Oropharyngeal Candida infection usually responds to topical anti-fungal treatment without the need to discontinue the inhaled corticosteroid. If oropharyngeal thrush occurs, patients should also rinse their mouth with water after the as-needed inhalations.

As with other inhalation therapy, paradoxical bronchospasm may occur very rarely, affecting less than 1 in 10,000 people, with an immediate increase in wheezing and shortness of breath after dosing. Paradoxical bronchospasm responds to a rapid-acting inhaled bronchodilator and should be treated straightaway. Budesonide/formoterol should be discontinued immediately, the patient should be assessed and an alternative therapy instituted if necessary (see *Warning and Precautions*).

Systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. Increased susceptibility to infections and impairment of the ability to adapt to stress may also occur. Effects are probably dependent on dose, exposure time, concomitant and previous steroid exposure and individual sensitivity.

Treatment with β2 adrenoceptor agonists may result in an increase in blood levels of insulin, free fatty acids, glycerol and ketone bodies.

Paediatric population

It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroids is regularly monitored (see *Warning and Precautions*).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the local reporting system.

Overdose

An overdose of formoterol would likely lead to effects that are typical for β2 adrenoceptor 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 and when given three times daily as a total of 54 micrograms/day for 3 days to stable asthmatics 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 budesonide/formoterol therapy has to be withdrawn due to overdose of the formoterol component of the drug, provision of appropriate inhaled corticosteroid therapy must be considered.

Incompatibility

Not applicable.

Shelf-Life

Unopened product: 2 years.
After opening the foil wrapper: Use within 3 months.

Storage and Handling Instruction

Store below 30°C.
Use this product within 3 months after opening of laminated pouch

Packaging Information

Each inhaler unit comes in a sealed aluminium pouch with 3g silica gel bag. Each sealed pouch comes in a box with a package insert.

Pack size

Each inhaler delivers 120 actuations.

Product Registration Holder

Cipla Malaysia Sdn Bhd
Suite 1101, Amcorp Tower,
Amcorp Trade Centre, 18 Persiaran Barat,
46050 Petaling Jaya, Selangor, Malaysia

Manufacturer

Cipla Limited - Unit II Plot No. 9 and 10, Indore Special
Economic Zone, Phase II, Pithampur, District Dhar Pincode: 454775
Madhya Pradesh, India

Last Updated: May 2026

INSTRUCTIONS FOR USE/ HANDLING

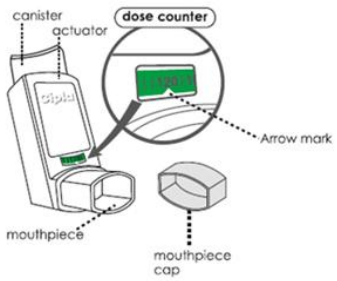
Please read the complete instructions carefully before you start to take your medication.

Application

Before your first application, note the last date you can use the metered dose inhaler. This is 3 months from the moment the protective foil was opened.

Preparation of the metered dose inhaler

Take the metered dose inhaler out of the protective foil before using it for the first time and throw the foil away. Your metered dose inhaler is ready to use, please do not disassemble it (figure 1). Before using the metered dose inhaler for the first time, if you have not used it for more than a week, or if it has been dropped, gently shake it and release two puffs into the air (see figure 2).



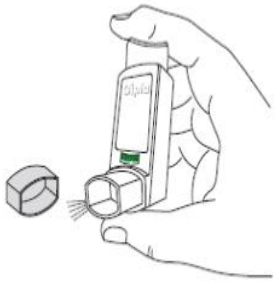


Figure 1 Figure 2 Figure 3

Method of administration

1. Shake the metered dose inhaler gently.
2. Remove the protective mouthpiece cap by gently squeezing and pulling it out.
3. Hold the metered dose inhaler upright between your thumb and index finger (figure 2). Exhale as strongly as possible holding the mouthpiece in your mouth between your teeth and wrapping your lips around it (figure 3).
4. Begin breathing slowly and deeply through your mouth while pressing firmly on the container (figure 2, 3).
5. Continue to inhale and hold your breath for approximately 10 seconds or as long as it is comfortable. Then take the metered dose inhaler out of your mouth and stop pressing down on the container.
6. Shake the container again and repeat points 3 to 5.
7. After application, put the protective cap back on.
8. Rinse your mouth with water to prevent any drug residue.

Routine care for mouthpiece

The mouthpiece must be cleaned regularly, at least once a week. Proceed as follows:

1. Remove the protective cap.
2. Wipe the inside and outside of the mouthpiece with a clean, dry cloth.
3. Put the protective cap back on.
4. Do not try to disassemble the metered dose inhaler.

Never put the metered dose inhaler in water!

How do you know when your metered inhaler device no longer have doses available?

Your inhaler device has a counter that shows how many doses are still available. The counter, indicated by a small arrow, starts at 120. Each time you inhale a dose or spray it into the air, the arrow will move towards “0”. If the arrow points to “0”, you must use a new metered dose inhaler, even if the metered dose inhaler does not yet appear to be empty. You would no longer inhale the correct dose.