INNOVAIR®

Beclometasone dipropionate 100 mcg
Formoterol fumarate dihydrate 6 mcg

Metered dose inhaler (HFA)
100/6 micrograms per actuation pressurised inhalation solution

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose (ex-valve) dose contains:
100 micrograms of beclometasone dipropionate and 6 micrograms of formoterol fumarate dihydrate. This is equivalent to a delivered dose (ex-actuator) of 84.6 micrograms of beclometasone dipropionate and 5.0 micrograms of formoterol fumarate dihydrate.

PHARMACEUTICAL FORM

Pressurised inhalation solution

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS

ASTHMA

Innovair is indicated in the regular treatment of asthma where use of a combination product (inhaled corticosteroid and long-acting beta2-agonist) is appropriate:

- Patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2- agonist or
- Patients already adequately controlled on both inhaled corticosteroids and long-acting beta2-agonists.

COPD

Symptomatic treatment of patients with severe COPD (FEV_1≥ 30% and < 50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators.

POSOLOGY AND METHOD OF ADMINISTRATION

Innovair is for inhalation use.

Asthma

Innovair is not intended for the initial management of asthma. The dosage of the components of Innovair is individual and should be adjusted to the severity of the disease. This should be considered not only when treatment with combination products is initiated but also when the dose is adjusted. If anindividual patient should require a combination of doses other than those available in the combination inhaler, appropriate doses of beta-2-agonists and/or corticosteroids by individual inhalers should be prescribed.
Beclometasone dipropionate in Innovair is characterised by an extrafine particle size distribution which

results in a more potent effect than formulations of beclometasone dipropionate with a non-extrafine particle size distribution (100 micrograms of beclometasone dipropionate extrafine in Innovair are equivalent to 250 micrograms of beclometasone dipropionate in a non-extrafine formulation). Therefore the total daily dose of beclometasone dipropionate administered in Innovair should be lower than the total daily dose of beclometasone dipropionate administered in a non-extrafine beclometasone dipropionate formulation.
This should be taken into consideration when a patient is transferred from beclometasone dipropionate non-extrafine formulations to Innovair; the dose of beclometasone dipropionate should be lower and will need to be adjusted to the individual needs of patients.

There are two treatment approaches:

A. **Maintenance therapy**: Innovair is taken as regular maintenance treatment with a separate as needed rapid-acting bronchodilator.
B. **Maintenance and reliever therapy**: Innovair is taken as regular maintenance treatment with and as needed in response to asthma symptoms.

A. Maintenance therapy

Patients should be advised to have their separate rapid-acting bronchodilator available for rescue use at all times.

Dose recommendations for adults 18 years and above:

One or two inhalations twice daily.
The maximum daily dose is 4 inhalations.

B. Maintenance and reliever therapy

Patients take their daily maintenance dose of Innovair and in addition take Innovair as needed in response to asthma symptoms. Patients should be advised to always have Innovair available for rescue use.
Innovair maintenance and reliever therapy should especially be considered for patients with:

- Not fully controlled asthma and in need of reliever medication
- Asthma exacerbations in the past requiring medical intervention

Close monitoring for dose related adverse effects is needed in patients who frequently take high numbers of Innovair as-needed inhalations.

Dose recommendations for adults 18 years and older:

The recommended maintenance dose is 1 inhalation twice daily (one inhalation in the morning and one inhalation in the evening).
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.
The maximum daily dose is 8 inhalations.
Patients requiring frequent use of rescue inhalations daily should be strongly recommended to seek medical advice. Their asthma should be reassessed and their maintenance therapy should be reconsidered.

Dose recommendations for children and adolescents under 18 years:

The safety and efficacy of Innovair in children and adolescents under 18 years of age have not been established yet. No data are available with Innovair in children under 12 years of age. Only limited data

are available in adolescents between 12 and 17 years of age. Therefore Innovair is not recommended for children and adolescents under 18 years until further data become available.
Patients should be regularly reassessed by a doctor, so that the dosage of Innovair remains optimal and is only changed on medical advice. The dose should be titrated to the lowest dose at which effective control of symptoms is maintained. When control of symptoms is maintained with the lowest recommended dosage, then the next step could include a test of inhaled corticosteroid alone.
Patients should be advised to take Innovair every day even when asymptomatic.

COPD
Dose recommendations for adults 18 years and above:
Two inhalations twice daily.

Special patient groups:
There is no need to adjust the dose in elderly patients. There are no data available for use of Innovair in patients with hepatic or renal impairment

Method of administration
To ensure proper administration of the drug, the patient should be shown how to use the inhaler correctly by a physician or other health professional. Correct use of the pressurised metered dose inhaler is essential in order that treatment is successful. The patient should be advised to read the Patient Information Leaflet carefully and follow the instructions for use as given in the Leaflet.

Innovair inhaler is provided with a counter on the back of the actuator, which shows how many doses are left. For the 120 doses presentation each time the patient press the canister, a puff of medicine is released and the counter counts down by one. Patients should be advised not to drop the inhaler as this may cause the counter to count down.

Testing the inhaler
Before using the inhaler for the first time or if you have not used the inhaler for 14 days or more, the patient should release one actuation into the air to ensure that the inhaler is working properly. After testing the inhaler for the first time, the counter should read 120. Whenever possible, patients should stand or sit in an upright position when inhaling from their inhaler.

Use Innovair with spacer device.
The steps below should be followed:

1. Remove the protective cap off both your puffer and the spacer device.
2. Insert the puffer into the Back piece of the spacer device.
3. Put your lips around the mouthpiece.
4. When you are ready, gently exhale. Start to inhale and press your puffer so that your medicine is sprayed into the spacer. Only press one puff at a time.
5. You will have to wait to take another puff of medicine. Check how many puffs your doctor wants you to take and how long to wait between puffs.

IMPORTANT: patients should not perform steps 2 to 5 too quickly.

After use, patients should close the inhaler with protective cap and check the dose counter.

Patients should be advised to get a new inhaler when the dose counter shows the number 20. They should stop using the inhaler when the counter shows 0 as any puffs left in the device may not be enough to release a full dose.

For patients with weak hands, it may be easier to hold the inhaler with both hands. Therefore the index fingers should be placed on the top of the inhaler canister and both thumbs on the base of the inhaler.

Patients should rinse their mouth or gargle with water or brush the teeth after inhaling.

Cleaning
For the regular cleaning of the inhaler, patients should be remove the cap from the mouthpiece and wipe the outside and inside of the mouthpiece with a dry cloth. They should not remove the canister from the actuator and should not use water or other liquids to clean the mouthpiece.

CONTRAINDICATIONS
Known hypersensitivity to beclometasone dipropionate, formoterol fumarate dihydrate and/or any of the excipients.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Innovair should be used with caution (which may include monitoring) in patients with cardiac arrhythmias, especially third degree atrioventricular block and tachyarrhythmias (accelerated and/or irregular heart beat), idiopathic subvalvular aortic stenosis, hypertrophic obstructive cardiomyopathy, severe heart disease, particularly acute myocardial infarction, ischaemic heart disease, congestive heart failure, occlusive vascular diseases, particularly arteriosclerosis, arterial hypertension and aneurysm.
Caution should also be observed when treating patients with known or suspected prolongation of the QTc interval, either congenital or drug induced (QTc > 0.44 seconds). Formoterol itself may induce prolongation of the QTc interval.

Caution is also required when Innovair is used by patients with thyrotoxicosis, diabetes mellitus, phaeochromocytoma and untreated hypokalaemia.

Potentially serious hypokalaemia may result from beta2-agonist therapy. Particular caution is advised in severe asthma as this effect may be potentiated by hypoxia. Hypokalaemia may also be potentiated by concomitant treatment with other drugs which can induce hypokalaemia, such as xanthine derivatives, steroids and diuretics Caution is also recommended in unstable asthma when a number of “rescue” bronchodilators may be used. It is recommended that serum potassium levels are monitored in such situations.

The inhalation of formoterol may cause a rise in blood glucose levels. Therefore blood glucose should be closely monitored in patients with diabetes.
If anaesthesia with halogenated anaesthetics is planned, it should be ensured that Innovair is not administered for at least 12 hours before the start of anaesthesia as there is a risk of cardiac arrhythmias.

As with all inhaled medication containing corticosteroids, Innovair should be administered with caution in patients with active or quiescent pulmonary tuberculosis, fungal and viral infections in the airways.

It is recommended that treatment with Innovair should not be stopped abruptly.
If patients find the treatment ineffective medical attention must be sought. Increasing use of rescue bronchodilators indicates a worsening of the underlying condition and warrants a reassessment of the asthma therapy. Sudden and progressive deterioration in control of asthma or COPD is potentially life threatening and the patient should undergo urgent medical assessment. Consideration should be given to the need for increase treatment with corticosteroids, either inhaled or oral therapy, or antibiotic treatment if an infection is suspected.
Patients should not be initiated on Innovair 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 Innovair. Patients should be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation on Innovair.

As with other inhalation therapy paradoxical bronchospasm may occur with an immediate increase in wheezing and shortness of breath after dosing. This should be treated immediately with a fast-acting inhaled bronchodilator. Innovair should be discontinued immediately, the patient assessed and alternative therapy instituted if necessary.
Innovair should not be used as the first treatment for asthma.
For treatment of acute asthma attacks patients should be advised to have their rapid-acting bronchodilator available at all times, either Innovair (for patients using Innovair as maintenance and reliever therapy) or a separate rapid-acting bronchodilator (for patients using Innovair as maintenance therapy only).
Patients should be reminded to take Innovair daily as prescribed even when asymptomatic.
The reliever inhalations of Innovair 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 Innovair. Regular review of patients as treatment is stepped down is important. The lowest effective dose of Innovair should be used.

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 inhaled 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 behavioral effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression.
Therefore, it is important that the patient is reviewed regularly, and the dose of inhaled corticosteroid is reduced to the lowest dose at which effective control of asthma is maintained.

Prolonged treatment of patients with high doses of inhaled corticosteroids may result in adrenal suppression and acute adrenal crisis. Children aged less than 16 years taking/inhaling higher than recommended doses of beclometasone dipropionate may be at particular risk. Situations which could

potentially trigger acute adrenal crisis, include trauma, surgery, infection or any rapid reduction in dosage. Presenting symptoms are typically vague and may include anorexia, abdominal pain, weight loss, tiredness, headache, nausea, vomiting, hypotension, decreased level of consciousness, hypoglycaemia, and seizures. Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.
Care should be taken when transferring patients to Innovair therapy, particularly if there is any reason to suppose that adrenal function is impaired from previous systemic steroid therapy.

Patients transferring from oral to inhaled corticosteroids 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 have received prolonged treatment with or high doses of inhaled corticosteroids may also be at risk. This possibility of residual impairment should always be borne in mind in emergency and elective situations likely to produce stress, and appropriate corticosteroid treatment must be considered. The extent of the adrenal impairment may require specialist advice before elective procedures.

Patients should be advised that Innovair contains a small amount of ethanol (approximately 7 mg per actuation); however at normal doses the amount of ethanol is negligible and does not pose a risk to patients.
Patients should be advised to rinse the mouth or gargle with water or brush the teeth after inhaling the prescribed dose to minimise the risk of oropharyngeal candida infection.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
Pharmacokinetic interactions
Beclometasone dipropionate undergoes a very rapid metabolism via esterase enzymes without involvement of cytochrome P450 system.

Pharmacodynamic interactions
Beta-blockers (including eye drops) should be avoided in asthmatic patients. If beta-blockers are administered for compelling reasons, the effect of formoterol will be reduced or abolished.
On the other hand, concomitant use of other beta-adrenergic drugs can have potentially additiveeffects, therefore caution is required when theophylline or other beta-adrenerigic drugs are prescribed concomitantly with formoterol.
Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, antihistamines, 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 beta2-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 treatment with xanthine derivatives, steroids, or diuretics may potentiate a possible hypokalaemic effect of beta2-agonists .Hypokalaemia may increase the disposition towards arrhythmias in patients who are treated with digitalis glycosides.

Innovair contains a small amount of ethanol. There is a theoretical potential for interaction in particularly sensitive patients taking disulfiram or metronidazole

FERTILITY, PREGNANCY AND LACTATION

There is no experience with or evidence of safety of propellant HFA-134a in human pregnancy or lactation. However studies of the effect of HFA-134a on reproductive function and embryofetal development in animals have revealed no clinically relevant adverse effects.

Pregnancy

There are no relevant clinical data on the use of Innovair in pregnant women. Animal studies using beclometasone dipropionate and formoterol combination showed evidence of toxicity to reproduction after high systemic exposure (see Preclinical safety data). Because of the tocolytic actions of beta2-sympathomimetic agents particular care should be exercised in the run up to delivery. Formoterol should not be recommended for use during pregnancy and particularly at the end of pregnancy orduring labour unless there is no other (safer) established alternative.

Innovair should only be used during pregnancy if the expected benefits outweigh the potential risks.

Lactation

There are no relevant clinical data on the use of Innovair in lactation in humans.

Although no data from animal experiments are available, it is reasonable to assume that beclometasone dipropionate is secreted in milk, like other corticosteroids.

While it is not known whether formoterol passes into human breast milk, it has been detected in the milk of lactating animals.

Administration of Innovair to women who are breast-feeding should only be considered if the expected benefits outweigh the potential risks.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Innovair is unlikely to have any effect on the ability to drive and operate machinery.

UNDESIRABLE EFFECTS

As Innovair contains beclometasone dipropionate and formoterol fumarate dihydrate, the type and severity of adverse reactions associated with each of the compounds may be expected. There is no incidence of additional adverse events following concurrent administration of the two compounds.

Undesirable effects which have been associated with beclometasone dipropionate and formoterol administered as a fixed combination (Innovair) and as single agents are given below, listed by system organ class. Frequencies are defined as: very common (1/10), common (1/100 and <1/10), uncommon (1/1,000 and <1/100), rare (1/10,000 < 1/1,000) and very rare (≤1/10,000).

Common and uncommon ADRs were derived from clinical trials in asthmatic and COPD patients.

System Organ Class	Adverse Reaction	Frequency
Infections and Infestations	Pharyngitis, oral candidiasis	Common
	Influenza, oral fungal infection, pharyngeal and oesophageal candidiasis, vaginal candidiasis, gastroenteritis, sinusitis, rhinitis, pneumonia*	Uncommon

Blood and the lymphatic system disorders	Granulocytopenia	Uncommon
	Thrombocytopenia	Very rare
Immune system disorders	Dermatitis allergic	Uncommon
	Hypersensitivity reactions, including erythema, lips, face, eye and pharyngeal oedema	Very rare
Endocrine disorders	Adrenal suppression	Very rare
Metabolism and nutrition disorders	Hypokalaemia, hyperglycaemia	Uncommon
Psychiatric disorders	Restlessness	Uncommon
	Psychomotor hyperactivity, sleep disorder, anxiety, depression, aggression, behavioural changes (predominantly in children)	Unknown
Nervous system disorders	Headache	Common
	Tremor, dizziness,	Uncommon
Eye disorders	Glaucoma, cataract	Very rare
Ear and labyrinth disorders	Otosalpingitis	Uncommon
Cardiac disorders	Palpitations, electrocardiogram QT corrected interval prolonged, electrocardiogram change, tachycardia, tachyarrhythmia, atrial fibrillation*	Uncommon
	Ventricular extrasystoles, angina pectoris	Rare
Vascular disorders	Hyperaemia, flushing	Uncommon
Respiratory, thoracic and mediastinal disorders	Dysphonia	Common
	Rhinitis, cough, productive cough, throat irritation, asthmatic crisis	Uncommon
	Bronchospasm paradoxical	Rare
	Dyspnoea, exacerbation of asthma	Very rare
Gastrointestinal disorders	Diarrhoea, dry mouth, dyspepsia, dysphagia, burning sensation of the lips, nausea, dysgeusia	Uncommon
Skin and subcutaneous tissue disorders	Pruritus, rash, hyperhidrosis, urticaria	Uncommon
	Angioneurotic oedema	Rare

Musculoskeletal, connective tissue and bone disorders	Muscle spasms, myalgia	Uncommon
	Growth retardation in children and adolescents	Very rare
Renal and urinary disorders	Nephritis	Rare
General disorders and administration site conditions	Oedema peripheral	Very rare
Investigations	C-reactive protein increased, platelet count increased, free fatty acids increased, blood insulin increased, blood ketone body increased, blood cortisol decrease*	Uncommon
	Blood pressure increased, blood pressure decreased	Rare
	Bone density decreased	Very rare

*One related non serious case of pneumonia was reported by one patient treated with Innovair in a pivotal clinical trial in COPD patients. Other adverse reactions observed with Innovair in COPD clinical trials were: reduction of blood cortisol and atrial fibrillation.

As with other inhalation therapy, paradoxical bronchospasm may occur (see Special Warnings and Precautions for Use).
Among the observed adverse reactions those typically associated with formoterol are:
hypokalaemia, headache, tremor, palpitations, cough, muscle spasms and prolongation of QTc interval.
Adverse reactions typically associated with the administration of beclometasone dipropionate are:
oral fungal infections, oral candidiasis, dysphonia, throat irritation. Dysphonia and candidiasis may be relieved by gargling or rinsing the mouth with water or brushing the teeth after using the product. Symptomatic candidiasis can be treated with topical anti-fungal therapy whilst continuing the treatment with Innovair.
Systemic effects of inhaled corticosteroids (e.g. beclometasone dipropionate) may occur particularly when administered at high doses prescribed for prolonged periods, these may include adrenal suppression, decrease in bone mineral density, growth retardation in children and adolescents, cataract and glaucoma.
Hypersensitivity reactions including rash, urticaria pruritus, erhythema and oedema of the eyes, face,lips and throat may also occur.

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 national reporting system.

OVERDOSE

Inhaled doses of Innovair up to twelve cumulative actuations (total beclometasone dipropionate 1200 micrograms, Formoterol 72 micrograms) have been studied in asthmatic patients. The cumulative treatments did not cause abnormal effect on vital signs and neither serious nor severe adverse events were observed.

Excessive doses of formoterol may lead to effects that are typical of beta$_2$-adrenergic agonists: nausea, vomiting, headache, tremor, somnolence, palpitations, tachycardia, ventricular arrhythmias, prolongation of QTc interval, metabolic acidosis, hypokalaemia, hyperglycaemia.

In case of overdose of formoterol, supportive and symptomatic treatment is indicated. Serious cases should be hospitalized. Use of cardioselective beta-adrenergic blockers may be considered, but only subject to extreme caution since the use of beta-adrenergic blocker medication may provoke bronchospasm. Serum potassium should be monitored.

Acute inhalation of beclometasone dipropionate doses in excess of those recommended may lead to temporary suppression of adrenal function. This does not need emergency action as adrenal function is recovers in a few days, as verified by plasma cortisol measurements. In these patients treatment should be continued at a dose sufficient to control asthma.

Chronic overdose of inhaled beclometasone dipropionate: risk of adrenal suppression monitoring of adrenal reserve may be necessary. Treatment should be continued at a dose sufficient to control asthma.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Adrenergics and other drugs for obstructive airway diseases.

ATC-code: R03 AK07.

Mechanisms of action and pharmacodynamic effects

Innovair contains beclometasone dipropionate and formoterol, which have different modes of action. In common with other inhaled corticosteroids and beta2-agonists combinations, additive effects are seen in terms of reduction of asthma exacerbations.

Beclometasone dipropionate

Beclometasone dipropionate given by inhalation at recommended doses has a glucocorticoid antiinflammatory action within the lungs, resulting in reduced symptoms and exacerbations of asthma with less adverse effects than when corticosteroids are administered systemically.

Formoterol

Formoterol is a selective beta$_2$-adrenergic agonist that produces 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.

ASTHMA

Clinical trial for Innovair maintenance therapy

In clinical trials in adults, the addition of formoterol to beclometasone dipropionate improved asthma symptoms and lung function and reduced exacerbations.

In a 24-week study the effect on lung function of Innovair was at least equal to that of the free combination of beclomeasone dipropionate and formoterol, and exceeded that of beclometasone dipropionate alone.

Clinical efficacy for Innovair maintenance and reliever therapy

In a 48-week parallel group study involving 1701 asthma patients, the efficacy of Innovair administered as maintenance (1 inhalation BID) and reliever therapy (up to a total of 8 puffs per day) was compared to Innovair administered as maintenance therapy (1 inhalation BID) plus as needed salbutamol, in adult patients with un-controlled moderate to severe asthma. The results demonstrated that Innovair used as maintenance and reliever therapy significantly prolonged the time to first severe exacerbation (*) when compared with Innovair used as maintenance plus as needed salbutamol ($p< 0.001$ for both ITT and PP population). The rate of severe asthma exacerbations per patients/year, was significantly reduced in the maintenance and reliever therapy group compared to salbutamol group: 0,1476 vs 0,2239 respectively (statistically significant reduction: $p<0.001$). Patients in the Innovair maintenance and reliever group achieved a clinically meaningful improvement in asthma control.

The mean number of inhalations/day of reliever medication and the proportion of patients using reliever medication decreased similarly in both groups.

Note*: severe exacerbations were defined as deterioration in asthma resulting in hospitalization or emergency room treatment, or resulting in the need for systemic steroids for more than 3 days.

In another clinical study, a single dose of Innovair 100/6 mcg provided a quick bronchodilation effect and a rapid relief from dyspnea symptoms similar to that of salbutamol 200 mcg/dose in asthmatic patients when metacholine challenge is used to induce bronchocostriction.

COPD

In two 48-weeks studies, the effects on lung function and the rate of exacerbation (defined as courses of oral steroids and/or course of antibiotics and/or hospitalisations) in patients with severe COPD (30% <FEV1%<50%) was evaluated.

One pivotal trial showed a significant improvement in lung function (primary endpoint change in pre- dose FEV1) compared to formoterol after 12 weeks of treatment (adjusted mean difference between Innovair and formoterol: 69 ml) as well as at each clinic visit during the whole treatment period (48 weeks). The study demonstrated that the mean number of exacerbations per patient/year (exacerbation rate, co-primary endpoint) was statistically significantly reduced with Innovair as compared with formoterol treatment (adjusted mean rate 0.80 compared with 1.12 in the formoterol group, adjusted ratio 0.72, $p<0.001$) over 48 weeks treatment period in a total of 1199 patients with severe COPD. In addition, Innovair statistically significantly prolonged the time to first exacerbation compared to formoterol. The superiority of Innovair versus formoterol was also confirmed in terms of exacerbation rate in subgroups of patients taking (around 50% in each treatment arm) or not Tiotropium Bromide as concomitant medication.

The other pivotal study, which was a three arm, randomised, parallel group study in 718 patients, confirmed the superiority of Innovair versus formoterol treatment in terms of change in pre-dose FEV1 at the end of treatment (48 weeks) and demonstrated the non-inferiority of Innovair compared to budesonide/formoterol fixed dose combination on the same parameter.

PHARMACOKINETIC PROPERTIES

The systemic exposure to the active substances beclometasone dipropionate and formoterol in the fixed combination Innovair have been compared to the single components.

In a pharmacokinetic study conducted in healthy subjects treated with a single dose of Innovair fixed combination (4 puffs of 100/6 micrograms) or a single dose of beclometasone dipropionate CFC (4 puffs of 250 micrograms) and Formoterol HFA (4 puffs of 6 micrograms), the AUC of beclometasone dipropionate main active metabolite (beclometasone-17-monopropionate), and its maximal plasma concentration were, respectively, 35% and 19% lower with the fixed combination, than with non-extrafine beclometasone dipropionate CFC formulation, in contrast, the rate of absorption was more rapid (0.5 vs 2h) with the fixed combination compared to non-extrafine beclometasone dipropionate CFC alone.
For formoterol, maximal plasma concentration was similar after administration of the fixed or the extemporary combination and the systemic exposure was slightly higher after administration of Innovair than with the extemporary combination.

There was no evidence of pharmacokinetic or pharmacodynamic (systemic) interactions between beclometasone dipropionate and formoterol.

A lung deposition study conducted in stable COPD patients, healthy volunteers and asthmatic patients, demonstrated that on average 33% of the nominal dose is deposited into the lung of COPD patients compared to 34% in healthy subjects and 31% in asthmatic patients. Beclometasone 17- monopropionate and formoterol plasma exposures were comparable across the three groups during the24 hours following the inhalation. The total exposure of beclometasone dipropionate was higher in COPD patients compared to the exposure in asthmatic patients and healthy volunteers.

Beclometasone dipropionate
Beclometasone dipropionate is a pro-drug with weak glucocorticoid receptor binding affinity that is hydrolysed via esterase enzymes to an active metabolite beclometasone-17-monopropionate which has a more potent topical anti-inflammatory activity compared with the pro-drug beclometasone dipropionate.

Absorption distribution and metabolism
Inhaled beclometasone dipropionate is rapidly absorbed through the lungs; prior to absorption there is extensive conversion to its active metabolite beclometasone-17-monopropionate via esterase enzymes that are found in most tissues. The systemic availability of beclometasone-17-monopropionate arises from lung (36%) and from gastrointestinal absorption of the swallowed dose. The bioavailability of swallowed beclometasone dipropionate is negligible however, pre-systemic conversion to beclometasone-17-monopropionate results in 41% of the dose being absorbed as the active metabolite.
There is an approximately linear increase in systemic exposure with increasing inhaled dose.
The absolute bioavailability following inhalation is approximately 2% and 62% of the nominal dose for unchanged beclometasone dipropionate and beclometasone-17-monopropionate respectively.
Following intravenous dosing, the disposition of beclometasone dipropionate and its active metabolite are characterised by high plasma clearance (150 and 120L/h respectively), with a small volume of distribution at steady state for beclometasone dipropionate (20L) and larger tissue distribution for its active metabolite (424L).
Plasma protein binding is moderately high.
Elimination

Faecal excretion is the major route of beclometasone dipropionate elimination mainly as polar metabolites. The renal excretion of beclometasone dipropionate and its metabolites is negligible. The terminal elimination half-lives are 0.5 h and 2.7 h for beclometasone dipropionate and beclometasone-17-monopropionate respectively.

Special populations

As beclometasone dipropionate undergoes a very rapid metabolism via esterase enzymes present in intestinal fluid, serum, lungs and liver, to originate the more polar products beclometasone-21-monopropionate, beclometasone-17-monopropionate, and beclometasone hepatic impairment is not expected to modify the pharmacokinetics and safety profile of beclometasone dipropionate.

The pharmacokinetics of beclometasone dipropionate in patients with renal impairment has not been studied. As beclometasone dipropionate or its metabolites were not traced in the urine, an increase in systemic exposure is not envisaged in patients with renal impairment.

Formoterol

Absorption and distribution

Following inhalation, formoterol is absorbed both from the lung and from the gastrointestinal tract. The fraction of an inhaled dose that is swallowed after administration with an metered dose inhaler (MDI) may ranges between 60% and 90%, At least 65% of the fraction that is swallowed is absorbed from the gastrointestinal tract.Peak plasma concentrations of unchanged drug occur within 0.5 to 1 hours after oral administration. Plasma protein binding of formoterol is 61-64% with 34% bound to albumin. There was no saturation of binding in the concentration range attained with therapeutic doses. The elimination half-life determined after oral administration is 2-3 hours. Absorption of formoterol is linear following inhalation of 12 to 96 µg of formoterol fumarate.

Biotransformation

Formoterol is widely metabolized and the prominent pathway involves direct conjugation at the phenolic hydroxyl group. Glucuronide acid conjugate is inactive. The second major pathway involves O-demethylation followed by conjugation at the phenolic 2'-hydroxyl group. Cytochrome P450 isoenzymes CYP2D6, CYP2C19 and CYP2C9 are involved in the O-demethylation of formoterol. Liver appears to be the primary site of metabolism. Formoterol does not inhibit CYP450 enzymes at therapeutically relevant concentrations.

Elimination

The cumulative urinary excretion of formoterol after single inhalation from a dry powder inhaler increased linearly in the 12 – 96 µg dose range. On average, 8% and 25% of the dose was excreted as unchanged and total formoterol, respectively. Based on plasma concentrations measured following inhalation of a single 120 µg dose by 12 healthy subjects, the mean terminal elimination half-life was determined to be 10 hours. The (R,R)- and (S,S)-enantiomers represented about 40% and 60% of unchanged drug excreted in the urine, respectively. The relative proportion of the two enantiomers remained constant over the dose range studied and there was no evidence of relative accumulation of one enantiomer over the other after repeated dosing.

After oral administration (40 to 80 µg), 6% to 10% of the dose was recovered in urine as unchanged drug in healthy subjects; up to 8% of the dose was recovered as the glucuronide.

A total 67% of an oral dose of formoterol is excreted in urine (mainly as metabolites) and the remainder in the faeces. The renal clearance of formoterol is 150 ml/min.

Special populations

Hepatic/Renal impairment: the pharmacokinetics of formoterol has not been studied in patients with hepatic or renal impairment.
However, as formoterol is primarily eliminated via hepatic metabolism, an increased exposure can be expected in patients with severe liver cirrhosis.

PRECLINICAL SAFETY DATA

The toxicity observed in animal studies with beclometasone dipropionate and formoterol, given in combination or separately, consisted mainly of effects associated with exaggerated pharmacological activity. They are related to the immuno-suppressive activity of beclometasone dipropionate and to the known cardiovascular effects of formoterol evident mainly in dogs. Neither increase in toxicity nor occurrence of unexpected findings were observed upon administration of the combination.

Reproduction studies in rats showed dose-dependent effects. The combination was associated with reduced female fertility and embryofetal toxicity. High doses of corticosteroids to pregnant animals are known to cause abnormalities of fetal development including cleft palate and intra-uterine growth retardation, and it is likely that the effects seen with the beclometasone dipropionate/formoterol combination were due to beclometasone dipropionate. These effects were noted only with high systemic exposure to the active metabolite beclometasone-17-monoproprionate (200 fold the expected plasma levels in patients). Additionally, increased duration of gestation and parturition, an effect attributable to the known tocolytic effects of beta$_2$-sympathomimetics, was seen in animal studies. These effects were noted when maternal plasma formoterol levels were below the levels expected in patients treated with Innovair .
Genotoxicity studies performed with a beclometasone dipropionate /formoterol combination do not indicate mutagenic potential. No carcinogenicity studies have been performed with the proposed combination. However animal data reported for the individual constituents do not suggest any potential risk of carcinogenicity in man.

Preclinical data on the CFC free propellant HFA-134a reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

PHARMACEUTICAL PARTICULARS

LIST OF EXCIPIENTS

Norflurane (HFA-134a)
Ethanol anhydrous
Hydrochloric acid

INCOMPATIBILITIES

Not applicable.

SHELF LIFE

17 months.

SPECIAL PRECAUTIONS FOR STORAGE

Prior to dispensing to the patient:
Store in a refrigerator (2-8°C) (for a maximum of 15 months).
After dispensing:
Do not store above 30°C (for a maximum of 2 months).

The canister contains a pressurised liquid. Do not expose to temperatures higher than 50°C. Do not pierce the canister.

NATURE AND CONTENTS OF CONTAINER
The inhalation solution is contained in a pressurised aluminium container sealed with a metering valve and fitted into a polypropylene plastic actuator which incorporates a mouthpiece and is provided with a plastic protective cap.

Dus, 1 Canister With Dose Counter @ 120 Actuations

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING
For pharmacies:
Enter the date of dispensing to the patient on the pack.
Ensure that there is a period of at least 2 months between the date of dispensing and the expiry date printed on the pack.

PRESCRIPTION ONLY MEDICINE

Reg. No. DKI1460600568A1

Manufactured by :
Chiesi Farmaceutici S.p.A.
Via San Leonardo 96
43122 Parma
Italy

Imported by :
PT. Tunggal Idaman Abdi
Jakarta – Indonesia

Marketed by:
PT. Zambon Indonesia
Jakarta – Indonesia

INNOVAIR®

Beclometasone dipropionate 100 mcg
Formoterol fumarate dihydrate 6 mcg

Metered dose inhaler (HFA)
100/6 micrograms per actuation pressurised inhalation solution

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Innovair pressurized inhalation solution, mengandung 100/6 mikrogram beklometason dipropionat /formoterol fumarat dihidrat per aktuasi, untuk digunakan pada orang dewasa.
Bacalah informasi dalam leaflet ini dengan seksama sebelum Anda mulai menggunakan obat ini. Karena mengandung informasi penting untuk Anda

- Simpanlah leaflet ini. Suatu saat Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker maupun perawat Anda.
- Obat ini diresepkan hanya untuk Anda. Jangan memberikan kepada orang lain. Hal ini dapat membahayakan mereka, bahkan jika mereka memiliki gejala penyakit yang sama seperti Anda.
- Jika terdapat efek samping segera sampaikan kepada dokter, apoteker maupun perawat Anda.
- Termasuk efek samping yang mungkin terjadi dan tidak disebutkan dalam leaflet.

Apa yang ada di dalam leaflet ini :

1. Apakah itu Innovair dan digunakan untuk apa?

Innovair adalah larutan inhalasi bertekanan tinggi yang mengandung dua zat aktif yang dihirup melalui mulut dan dilepaskan langsung ke paru-paru Anda.
Kedua zat aktif yang dimaksud adalah beklometason dipropionat dan formoterol fumarat dihidrat.
Beklometason dipropionat termasuk dalam golongan kortikosteroid dan memiliki peran sebagai anti inflamasi (anti-peradangan), menurunkan pembengkakan dan iritasi pada paru-paru.
Formoterol fumarat dihidrat termasuk golongan bronkodilator kerja panjang yang dapat merelaksasi otot-otot di saluran napas dan memperluas saluran napas sehingga membuat Anda lebih mudah untuk menghirup udara masuk dan keluar dari paru-paru Anda.
Kombinasi dua zat aktif ini membuat Anda bernapas lebih mudah, membantu meringankan gejala seperti sesak napas, mengi dan batuk pada penderita asma serta membantu mencegah gejala asma bernafas lebih mudah.

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Kedua zat aktif ini bersama-sama membuat nafas lebih mudah, dengan cara meringankan gejala seperti sesak nafas, mengi dan batuk pada asma atau PPOK dan juga membantu pencegahan gejala pada asma.

ASMA
Innovair diindikasikan untuk pengobatan rutin pada penderita asma dewasa diantaranya :

- Asma yang tidak terkontrol dengan menggunakan kortikosteroid inhalasi bronkodlator kerja singkat dengan dosis sesuai yang diperlukan atau
- Asma yang memiliki respon yang baik terhadap pengobatan dengan kortikosteroid maupun bronkodilator kerja panjang

PPOK
Innovair juga dapat digunakan pada pengobatan Penyakit Paru Obstruktif Kronik (PPOK) pada pasien dewasa. PPOK merupakan penyakit gangguan pernafasan jangka panjang pada paru-paru dimana utamanya disebabkan oleh merokok.

2. Sebelum Anda menggunakan Innovair

Jangan gunakan Innovair.
Jika Anda alergi atau merasa alergi terhadap satu atau lebih bahan aktif Innovair atau jika Anda alergi terhadap obat-obatan lain atau inhaler yang digunakan untuk mengobati asma atau salah satu komponen dalam Innovair (tercantum pada bagian 6 : isi kemasan dan Informasi lainnya), hubungi dokter Anda untuk meminta saran lebih lanjut.

Peringatan dan tindakan pencegahan.
Konsultasikan dengan dokter, apoteker atau perawat Anda sebelum menggunakan Innovair:

- Jika Anda memiliki masalah pada jantung, seperti angina (nyeri jantung, nyeri di dada), mengalami serangan jantung (infark miokard), gagal jantung, penyempitan pembuluh darah sekitar jantung (penyakit jantung koroner), kelainan katup jantung atau kelainan jantung lainnya yang Anda ketahui atau jika Anda memiliki kondisi yang dikenal sebagai kerusakan hipertrofik kardiomiopati (juga dikenal sebagai HOCM, suatu kondisi dimana otot jantung abnormal).
- Jika Anda mengalami penyempitan arteri (juga dikenal sebagai arteriosklerosis), jika tekanan darah Anda tinggi atau jika Anda tahu bahwa Anda memiliki aneurisma (suatu penonjolan yang abnormal dari dinding pembuluh darah).
- Jika Anda memiliki gangguan irama jantung seperti peningkatan atau tidak teraturnya ritme jantung, denyut nadi cepat atau palpitasi atau jika Anda telah diberitahu bahwa detak jantung Anda abnormal.
- Jika Anda memiliki kelenjar tiroid yang terlalu aktif.
- Jika Anda memiliki kadar kalium dalam darah rendah.
- Jika Anda memiliki penyakit hati atau ginjal.

- Jika menderita diabetes (jika Anda menghirup dosis tinggi formoterol maka glukosa darah Anda dapat meningkat dan karena itu Anda mungkin harus melakukan beberapa tes darah tambahan untuk memeriksa kadar gula darah Anda pada saat Anda mulai menggunakan inhaler selama pengobatan.
- Jika Anda memiliki tumor pada kelenjar adrenal (dikenal sebagai phaeochromocytoma).
- Jika Anda sedang menggunakan obat bius. Tergantung pada jenis anestesi, mungkin Anda perlu untuk berhenti menggunakan Innovair setidaknya 12 jam sebelum anestesi.
- Jika Anda sedang, atau pernah, diobati untuk tuberkulosis (TB) atau jika Anda memiliki infeksi virus atau jamur pada area dada Anda.
- Jika Anda harus menghindari alkohol untuk alasan apapun

Jika salah satu gejala diatas Anda derita, informasikan kepada dokter sebelum Anda menggunakan Innovair.
Jika Anda memiliki masalah medis atau alergi atau jika Anda tidak yakin apakah Anda dapat menggunakan Innovair, sampaikan kepada dokter, perawat atau apoteker sebelum menggunakan produk ini.
Pengobatan dengan beta-2-agonist seperti formoterol yang terkandung dalam Innovair dapat menyebabkan penurunan yang tajam kadar serum kalium Anda (hipokalemia).
Jika Anda memiliki asma yang parah, Anda harus berhati-hati. Hal ini disebabkan karena terjadi kekurangan oksigen dalam darah dan beberapa pengobatan lain yang bersamaan dengan Innovair, seperti obat-obatan untuk mengobati penyakit jantung atau tekanan darah tinggi, yang dikenal sebagai diuretik atau obat-obatan lain yang digunakan untuk mengobati asma dapat menyebabkan penurunan kadar kalium yang buruk. Untuk alasan ini dokter mungkin akan menganjurkan untuk mengukur kadar kalium dalam darah Anda secara berkala.
Jika Anda menggunakan kortikosteroid dosis tinggi dalam waktu lama, pada kondisi stress Anda mungkin membutuhkan kortikosteroid dengan dosis yang lebih tinggi.
Kondisi tersebut termasuk misalnya dibawa ke rumah sakit setelah kecelakaan, memiliki cedera serius atau sebelum operasi.
Dalam hal ini, dokter yang merawat Anda akan memutuskan apakah Anda mungkin perlu meningkatkan dosis kortikosteroid dan mungkin memberikan beberapa tablet steroid atau injeksi steroid.
Jika Anda perlu pergi ke rumah sakit, ingatlah untuk membawa semua obat-obatan dan inhaler yang ada pada Anda, termasuk Innovair dan obat-obatan atau tablet yang dibeli tanpa resep, dalam kemasan aslinya, jika memungkinkan.

Anak-anak dan remaja :
Innovair tidak boleh digunakan untuk anak dan remaja dibawah 18 tahun, sampai tersedianya data pendukung.

Innovair dan obat-obatan lainnya:
Beritahu dokter, apoteker, atau perawat Anda jika Anda sedang mengkonsumsi atau baru saja mengkonsumsi obat lain.

Jangan gunakan beta blocker secara bersamaan dengan obat ini. Jika Anda perlu menggunakan beta blocker (termasuk tetes mata), efek formoterol dapat berkurang atau mungkin tidak bekerja sama sekali. Di sisi lain, menggunakan obat beta adrenergik lainnya (obat yang bekerja dengan cara yang sama seperti formoterol) dapat meningkatkan efek formoterol.

Menggunakan Innovair bersama-sama dengan:

- Obat-obatan untuk mengobati irama jantung yang abnormal (quinidine, disopiramid, procainamide), obat-obatan yang digunakan untuk mengobati reaksi alergi (antihistamin), obat-obatan untuk mengobati gejala depresi atau gangguan mental seperti inhibitor monoaminoxidase (misalnya phenelzine dan isocarboxazid), trisiklik antidepresan (misalnya amitryptiline dan imipramine), fenotiazin dapat menyebabkan beberapa perubahan pada elektrokardiogram (EKG, rekam jantung). Mereka juga mungkin meningkatkan risiko gangguan irama jantung (aritmia ventrikel).
- Obat-obatan untuk mengobati penyakit Parkinson (L-dopa), untuk mengobati kelenjar tiroid (L-tiroksin) yang kurang aktif, obat-obatan yang mengandung oksitosin (yang menyebabkan kontraksi rahim) dan alkohol dapat menurunkan toleransi jantung Anda terhadap beta-2 agonis, seperti formoterol.
- Monoaminoxidase inhibitor (MAOIs), termasuk obat dengan sifat yang mirip seperti furazolidone dan prokarbazin, digunakan untuk mengobati gangguan mental, dapat menyebabkan kenaikan tekanan darah.
- Obat-obatan untuk mengobati penyakit jantung (digoxin) dapat menyebabkan penurunan kadar kalium darah Anda. Hal ini dapat meningkatkan kemungkinan keabnormalan ritme/irama jantung.
- Obat-obatan lain yang digunakan untuk mengobati asma (teofilin, aminofilin atau steroid) dan diuretik (tablet air) dapat menyebabkan penurunan kadar kalium.
- Beberapa anestesi dapat meningkatkan risiko keabnormalan ritme/irama jantung.

Kehamilan, menyusui dan kesuburan :

Tidak ada data klinis tentang penggunaan Innovair selama kehamilan. Innovair tidak boleh digunakan jika Anda sedang hamil, menduga bahwa Anda mungkin hamil atau berencana untuk hamil, atau jika Anda sedang menyusui, kecuali atas saran dari dokter Anda.

Berkendara dan menggunakan mesin.

Innovair tidak akan mempengaruhi kemampuan Anda untuk mengemudi dan menggunakan mesin.

Innovair mengandung alkohol :

Innovair mengandung sejumlah kecil alkohol. Setiap aktuasi (embusan) dari inhaler Anda mengandung 12% alkohol.

Untuk orang-orang melakukan kegiatan olahraga:

- Penggunaan obat tanpa keperluan terapi merupakan doping dan bagaimanapun dapat menentukan hasil yang positif untuk test antidoping.
- Penggunaan produk obat yang mengandung etil alkohol dapat memberikan hasil positif untuk tes antidoping berdasarkan batas konsentrasi alkohol yang ditetapkan oleh beberapa federasi olahraga.

3. Cara menggunakan Innovair

Innovair digunakan untuk inhalasi.
Selalu gunakan obat ini seperti yang telah diinformasikan oleh dokter atau apoteker Anda. Anda harus mengecek dengan dokter atau apoteker Anda jika Anda tidak yakin.

Asthma
Dokter Anda akan memastikan pemeriksaan rutin untuk memastikan Anda memakai dosis optimal dan Innovair. Dokter Anda akan menyesuaikan pengobatan dengan dosis terendah yang dapat mengontrol gejala Anda dengan baik.

Innovair dapat diresepkan oleh dokter Anda dengan dua cara berbeda :

a) Innovair digunakan setiap hari untuk mengobati asma bersamaan dengan pelega (Inhaler) yang terpisah untuk mengobati gejala asma yang memburuk, seperti kesulitan bernafas, mengi dan batuk
b) Innovair digunakan setiap hari untuk mengobati asma dan juga digunakan untuk mengobati gejala asma yang memburuk seperti, kesulitan bernafas, mengi dan batuk.

a) Menggunakan Innovair berbarengan dengan menggunakan Inhaler
Orang dewasa dan orang tua:
Dosis yang direkomendasikan dari obat ini adalah satu atau dua puff dua kali sehari.
Dosis maksimum adalah 4 puff

Ingat : Anda harus selalu membawa Inhaler Anda setiap saat, untuk mengobati memburuknya gejala asma atau bila tiba-tiba terkena serangan asma.

b) Penggunaan Innovair menggunakan inhaler Anda sendiri
Orang dewasa dan Orang tua:
Dosis yang di rekomendasikan adalah satu embusan pada pagi hari dan satu embusan pada malam hari. Anda harus mengunakan Innovair sebagai pelega (Inhaler) untuk mengobati gejala asma yang mendadak. Apabila Anda terkena gejala asma, ambil satu embusan dan tunggu beberapa menit.
Jika Anda tidak merasa baikan, ambil lagi satu embusan.
Jangan menggunakan 6 kali embusan dalam satu hari

<u>Dosis maksimum untuk Innovair adalah 8 embusan</u>
Jika Anda merasa membutuhkan lebih dari 8 embusan perhari untuk mengontrol gejala asma Anda, hubungi dokter Anda untuk melihat saran dokter. Dokter Anda mungkin membutuhkan perubahan pada pengobatan Anda.

Dokter Anda akan memberikan pemeriksaan rutin untuk memastikan Anda memakai dosis optimal dari Innovair. Dokter akan menyesuaikan pengobatan Anda dengan dosis terendah yang dapat mengontrol gejala Anda dengan baik. Tidak dianjurkan untuk mengubah dosis tanpa komunikasi dengan dokter Anda.

Penggunaan untuk anak dan remaja umur dibawah 18 tahun :
Anak-anak dan remaja kurang dari 18 tahun tidak dianjurkan mengkonsumsi obat ini.

Penyakit Paru Obstruktif Kronik (PPOK)

Dewasa dan orang tua:
Dosis yang direkomendasikan adalah 2 embusan pada pagi hari dan 2 embusan pada malam hari.

Pada pasien yang berisiko:
Pada usia lanjut tidak perlu dilakukan penyesuaian dosis. Tidak ada informasi yang tersedia mengenai penggunaan Innovair pada pasien dengan masalah hati atau ginjal. Innovair efektif untuk pengobatan asma dengan dosis beklometason dipropionat yang mungkin lebih rendah dibandingkan dengan beberapa inhaler yang mengandung beklometason dipropionat. Jika Anda telah menggunakan inhaler yang berbeda yang mengandung beklometason dipropionat sebelumnya, dokter akan menyarankan untuk menggunakan dosis Innovair yang tepat untuk asma Anda.

Jangan meningkatkan dosis.
Jika Anda merasa bahwa obat ini tidak terlalu efektif, selalu komunikasikan dengan dokter Anda sebelum meningkatkan dosis.

Jika Anda menggunakan Innovair melebihi dosis yang seharusnya:

- Menggunakan formoterol secara berlebihan memiliki efek sebagai berikut: merasa sakit, sakit denyut jantung cepat, jantung berdebar, gangguan irama jantung, perubahan tertentu pada elektrokardiogram (rekam jantung), sakit kepala, gemetar, merasa mengantuk, juga banyak asam dalam darah, kadar kalium darah yang rendah, tingginya tingkat glukosa dalam darah. Dokter Anda akan menyarankan untuk melakukan beberapa tes darah untuk memeriksa kalium darah dan kadar glukosa darah Anda.
- Menggunakan terlalu banyak beklometason dipropionat dapat menyebabkan masalah jangka pendek dengan kelenjar adrenal Anda. Meskipun dapat membaik dalam beberapa hari, dokter Anda mungkin perlu memeriksa kadar kortisol serum Anda.

Informasikan kepada dokter jika Anda memiliki gejala-gejala tersebut.

Jika Anda lupa untuk menggunakan Innovair:

Gunakan segera mungkin setelah Anda ingat. Jika waktu untuk penggunaan berikutnya hampir dekat, abaikan dosis yang telah terlewatkan, dianjurkan untuk mengambil dosis berikutnya pada waktu yang tepat. Jangan menggandakan dosisnya.

Jika Anda berhenti menggunakan Innovair :

Jangan menurunkan dosis atau menghentikan penggunaan obat.

Bahkan jika Anda merasa lebih baik, jangan berhenti menggunakan Innovair atau menurunkan dosis. Jika Anda ingin melakukan hal ini, komunikasikan dengan dokter Anda. Sangatlah penting bagi Anda untuk menggunakan Innovair secara teratur bahkan meskipun Anda sudah tidak merasakan gejala.

Jika pernapasan Anda semakin memburuk:

Jika sesak nafas Anda makin memburuk atau mengi, segera setelah menghirup obat Anda, hentikan menggunakan Innovair segera dan segeralah menggunakan inhaler yang dapat meredakan dengan cepat. Anda harus menghubungi langsung dokter Anda. Dokter akan memeriksa gejala Anda dan jika diperlukan dokter mungkin mulai mencoba dengan pengobatan yang berbeda. Lihat juga bagian 4. Kemungkinan efek samping.

Jika asma Anda semakin parah:

Jika gejala menjadi lebih buruk atau sulit untuk dikontrol (misalnya jika Anda menggunakan obat pelega atau innovair sebagai inhaler obat pelega lebih sering) atau jika obat pelega (inhaler)atau innovair tidak memperbaiki gejala Anda, periksakan ke dokter dengan segera. Asma Anda mungkin semakin parah dan dokter mungkin perlu mengubah dosis Innovair Anda atau meresepkan pengobatan alternatif.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan produk ini, tanyakan kepada dokter atau apoteker Anda.

Cara Penggunaan

Obat ini berada dalam canister bertekanan dalam wadah plastik dengan mouthpiece. terdapat penghitung (dose counter) di bagian belakang inhaler, yang akan memberikan informasi berapa banyak dosis yang tersisa. Setiap kali Anda menekan canister, obat tersemprot keluar dan penghitung akanberkurang 1 dosis / angka . Berhati-hatilah untuk tidak menjatuhkan inhaler karena dapat menyebabkan counter mengitung mundur.

Cek inhaler Anda

Sebelum menggunakan inhaler untuk pertama kali atau jika Anda belum menggunakan inhaler selama 14 hari atau lebih, Anda harus mengecek inhaler Anda untuk memastikannya berfungsi dengan baik.

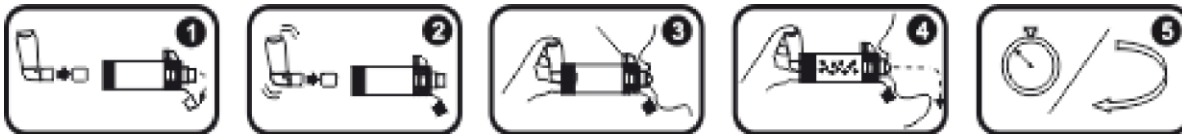
1. Lepaskan tutup pelindung dari *mouthpiece*
2. Pegang inhaler tegak lurus dengan *mouthpiece* di bagian bawah
3. Jauhkan *mouthpiece* dari Anda dan tekan *canister* dengan kuat untuk melepaskan satu dosis

4. Periksa penghitung dosis. Jika penggunaan pertama, penghitung dosis tertera 120.

Bagaimana cara menggunakan inhaler
Bila memungkinkan, berdiri atau duduk dalam posisi tegak pada saat menghirup

Gunakan Innovair dengan spacer

1. Lepaskan tutup pelindung dari Innovair dengan spacer.
2. Masukkan puffer ke bagian belakang perangkat spacer.
3. Letakkan bibir Anda di sekitar *mouthpiece*.
4. Setelah Anda siap, perlahan hembuskan napas. Mulai menghirup dan tekan canister sehingga obat tersemprot masuk ke dalam spacer bersamaan,
5. Tunggu beberapa saat sebelum menghirup dosis berikutnya. Sesuaikan dengan dosis yang dianjurkan dokter Anda dan berapa lama jeda diperlukan.



Penting: Jangan lakukan langkah 2 sampai 5 terlalu cepat.

Setelah digunakan, tutup dengan tutup pelindung dan periksa penghitung dosis.
persiapkan inhaler pengganti saat penghitung menunjukkan angka 20. Hentikan penggunaan inhaler saat penghitung menunjukkan 0 karena isapan yang tersisa di perangkat mungkin tidak cukup untuk memberi Anda dosis penuh

Jika Anda memiliki tangan yang lemah, lebih mudah untuk memegang inhaler dengan kedua tangan: Pegang bagian atas inhaler dengan kedua jari telunjuk dan bagian bawahnya dengan kedua ibu jari.
Untuk menurunkan risiko infeksi jamur di mulut dan tenggorokan, bilas mulut Anda atau berkumur dengan air atau sikat gigi Anda setiap kali Anda menggunakan inhaler.
Jika Anda merasa efek Innovair berlebihan atau tidak cukup, beritahu dokter atau apoteker Anda.
Penting bagi Anda untuk membaca brosur yang disertakan pada perangkat spacer dan mengikuti petunjuk penggunaan perangkat spacer serta cara membersihkannya dengan hati-hati.

Cara Membersihkan
bersihkan inhaler Anda seminggu sekali. Saat membersihkan, jangan lepaskan *canister* dari aktuator dan jangan gunakan air atau cairan lain untuk membersihkan inhaler .
Untuk membersihkan inhaler Anda:
1. Lepaskan tutup pelindung dari *mouthpiece* dengan menariknya dari inhaler Anda.
2. Lap bagian dalam dan luar *mouthpiece* dan aktuator dengan kain atau tisu kering yang bersih.
3. Pasang kembali penutup *mouthpiece*

4. Kemungkinan efek samping

Seperti semua obat-obatan, Innovair dapat menyebabkan efek samping, meskipun tidak semua orang terkena efek samping tersebut.
Seperti pengobatan inhaler lainnya, setelah menggunakan innovair terdapat resiko dalam memeperburuk pernafasan dan mengi yang biasa disebut “paradoksial bronkospasmae”. Jika ini terjadi, Anda harus menghentikan penggunaan Innovair dan segera menggunakan inhaler pelega yang memiliki aksi cepat untuk mengobati gejala tersebut. Dan Anda harus segera menghubungi dokter Anda.
Beritahukan pada dokter Anda segera jika mengalami reaksi sensitivitas seperti alergi kulit, gatal pada kulit, ruam kulit, kemerahan pada kulit, pembengkakan pada kulit atau membrane mukosaterutama pada mata, wajah, bibir dan tenggorokan.
Kemungkinan efek samping tercantum di bawah ini sesuai dengan frekuensi kejadiannya

Umum (mempengaruhi kurang dari 1 dari 10 orang):
Infeksi jamur (pada mulut dan tenggorokan)
Sakit kepala, suara serak, sakit tenggorokan.
Pneumonia pada pasien dengan penyakit PPOK : Beritahukan pada dokter Anda jika Anda memperlihatkan gejala seperti : peningkatan produksi sputum, perubahan warna sputum, deman, batuk dan kesulitan bernafas.

Tidak umum (mempengaruhi kurang dari 1 dalam 100 orang);
Palpitasi, detak jantung cepat tidak biasa dan gangguan irama jantung, beberapa perubahan dalam Elektrokardiogram (EKG), gejala flu, infeksi jamur vagina, peradangan sinus, rhinitis, peradangan telinga, iritasi tenggorokan, batuk dan batuk berdahak, serangan asma.
Mual, rasa tidak normal atau gangguan rasa, bibir terasa terbakar, mulut kering, kesulitan menelan, gangguan pencernaan, sakit perut, diare.
Nyeri pada otot dan otot kram, kemerahan pada wajah, peningkatan aliran darah ke beberapa jaringan dalam tubuh, keringat berlebihan, gemetar, gelisah, pusing, *nettle rash* atau gatal-gatal.

Perubahan dari beberapa konstituen darah: penurunan jumlah sel darah putih, peningkatan jumlah trombosit darah, penurunan kadar kalium dalam darah, peningkatan kadar gula darah, peningkatan kadar insulin, asam lemak bebas dan keton.
Efek samping di bawah ini juga dilaporkan sebagai efek yang tidak umum terjadi pada pasien dengan penyakit PPOK:

- Pengurangan jumlah kortisol pada darah; hal ini disebebkan oleh efek dari kontikosteroin pada kelenjar anrenal Anda.
- Detak jantung yang tidak biasa
- Ruam yang gatal

Jarang terjadi (mempengaruhi kurang dari 1 dalam 1.000 orang).
Merasa sesak dada, detak jantung lemah (yang disebabkan oleh kontraksi terlalu awal ventrikel jantung), peningkatan atau penurunan tekanan darah, peradangan ginjal, pembengkakan kulit dan selaput lendir yang bertahan selama beberapa hari, ruam yang gatal.

Sangat jarang (mempengaruhi kurang dari 1 dalam 10.000 orang).
Sesak napas, memburuknya asma, penurunan jumlah trombosit darah, pembengkakan tangan dan kaki.
Menggunakan inhalasi kortikosteroid dosis tinggi selama waktu yang lama dapat menyebabkan kasus efek sistemik yang sangat jarang: termasuk permasalahan bagaimana kelenjar adrenal Anda bekerja (adrenosuppression), penurunan kepadatan mineral tulang (penipisan tulang), gangguan perkembangan pada anak-anak dan remaja, peningkatan tekanan dalam mata Anda (glaukoma), katarak, gangguan tidur, depresi atau merasa cemas,kurangnya istirahat, gelisah, terlalu bersemangat atau mudah marah.

Pelaporan efek samping
Jika terjadi efek samping segera beritahukan pada dokter, apoteker atau perawat Anda. Ini termasuk segala efek samping yang tidak disebutkan di leaflet.
Anda juga boleh melaporkan langsung adanya efek samping kepada sistem pelaporan nasional.
Dengan melaporkan efek samping Anda telah membantu menyediakan informasi mengenai keamanan produk ini.

5. Bagaimana menyimpan Innovair.

Jauhkan obat dari pengelihatan dan jangkauan anak-anak.
Jangan gunakan Innovair lebih dari 2 bulan dari tanggal Anda mendapatkan inhaler tersebut dari apoteker dan jangan pernah menggunakan inhaler yang telah melewati tanggal kadaluwarsa yang tertera pada dus dan label.
Jangan menyimpan inhaler di atas suhu 30° C.
Jika inhaler terpapar suhu yang sangat dingin , ambil canister dari corong dan hangatkan dengan tangan Anda selama beberapa menit sebelum digunakan. Jangan hangatkan denganalat.

Peringatan: *Canister* berisi cairan bertekanan. Jangan meletakkan *canister* pada suhu yang lebih tinggi dari 50° C. Jangan menusuk *canister* tersebut.
Obat tidak boleh dibuang melalui air limbah atau limbah rumah tangga. Tanyakan kepada apoteker Anda bagaimana membuang obat-obatan yang tidak diperlukan lagi. Langkah-langkah ini akan membantu untuk menjaga lingkungan.

6. Isi kemasan dan informasi lainnya.

Apa isi dari Innovair ?
Zat aktif: beklometason dipropionat, formoterol fumarat dihidrat.
Setiap aktuasi dari inhaler mengandung 100 mikrogram beklometason dipropionat dan 6 mikrogram formoterol fumarat dihidrat. Dosis yang dihantarkan dari corong sebesar 84.6 mikrogram beklometason dipropionat dan 5.0 mikrogram formoterol fumarat dihidrat.
Bahan lainnya adalah: etanol anhidrat, asam klorida, propelan: norflurane (HFA 134-a).

7. Waktu Simpan.
17 bulan.
Mengandung 12% alkohol.
HARUS DENGAN RESEP DOKTER.
Kemasan:
Dus, 1 canister with dose counter 120 actuations
No. Reg. DKI1460600568A1

Diproduksi oleh :
Chiesi Farmaceutici S.p.A.
Via san Leonardo 96
43122 Parma – Italy

Diimpor oleh :
PT. Tunggal Idaman Abdi
Jakarta – Indonesia

Dipasarkan oleh:
PT. Zambon Indonesia
Jakarta - Indonesia

INNOVAIR®
Beclometasone dipropionate 100 mcg
Formoterol fumarate dihydrate 6 mcg
Metered dose inhaler (HFA)
100/6 micrograms per actuation pressurised inhalation solution

Innovair 100/6 micrograms per actuation pressurised inhalation solution

beclometasone dipropionate/ formoterol fumarate dehydrate.

For use in adults.
Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist or nurse
- This medicine has been prescribed for you only. Do not pass it on others. It may harm them, even if their signs of illness symptoms are the same as yours.
- If any of the side effects talk to your doctor, or pharmacist or nurse. This include any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Innovair is and what it is used for

Innovair is a pressurised inhalation solution containing two active substances which are inhaled through your mouth and delivered directly into your lungs.
The two active substances are beclometasone dipropionate and formoterol fumarate dihydrate. Beclometasone dipropionate belongs to a group of medicines called corticosteroids which have an anti-inflammatory action reducing the swelling and irritation for your lungs.
Formoterol fumarate dihydrate belongs to a group of medicines called long-acting bronchodilators which relax the muscles in your airways and by doing this widen the airways which makes it easier for you to breathe air in and out of your lungs.

Together these two active substances make breathing easier, by providing relief from symptoms such as shortness of breath, wheezing and cough in patients with asthma or COPD and also help to prevent the symptoms of asthma.

Asthma
Innovair is indicated the regular treatment of asthma in adult with asthma in whom:

- Asthma is not adequately controlled by using inhaled corticosteroids and "as needed" short-acting bronchodilators or
- Asthma is responding well to treatment with both corticosteroids and long-acting bronchodilators.

COPD
Innovair can also be used to treat the symptoms of severe chronic obstructive pulmonary dis-ease (COPD) in adult patients.
COPD is a long-term disease of the airways in the lungs which is primarily caused by cigarette smoking.

2. Before you use Innovair

Do not use Innovair
if you are allergic or think you are allergic to one or other of the active ingredients of Innovair or if you are allergic to other medicines or inhalers used to treat asthma or to any of the other ingredients of Innovair (listed in section 6:Content of the pack and other information), contact your doctor for advice.

Warnings and precautions
Talk to your doctor or pharmacist or nurse before using Innovair:

- If you have any heart problems, such as angina (heart pain, pain in the chest), a recent heart attack (myocardial infarction), heart failure, narrowing of the arteries around your heart (coronary heart disease) valvular heart disease or any other known abnormalities of your heart or if you have a condition known as hypertrophic obstructive cardiomyopathy (also known as HOCM, a condition where the heart muscle is abnormal).
- If you have narrowing of the arteries (also known as arteriosclerosis), if you have high blood pressure or if you know that you have an aneurysm (an abnormal bulging of the blood vessel wall)).
- If you have disorders of your heart rhythm such as increased or irregular heart rate, a fast pulse rate or palpitations or if you have been told that your heart trace is abnormal.
- If you have an overactive thyroid gland.
- If you have low blood levels of potassium.
- If you have any disease of your liver or kidneys.

- If you have diabetes (if you inhale high doses of formoterol your blood glucose may increase and therefore you may need to have some additional blood tests to check your blood sugar when you start using this inhaler and from time to time during treatment).
- If you have a tumour of the adrenal gland (known as a phaeochromocytoma).
- If you are due to have an anaesthetic. Depending on the type of anaesthetic, it may be necessary to stop taking Innovair at least 12 hours before the anaesthesia.
- If you are being, or have ever been, treated for tuberculosis (TB) or if you have a known viral or fungal infection of your chest.
- If you must avoid alcohol for any reason

If any of the above apply to you, always inform your doctor before you use Innovair.
If you have or had any medical problems or any allergies or if you are not sure as to whether you can use Innovair talk to your doctor, asthma nurse or pharmacist before using the inhaler.
Treatment with beta-2-agonist like the formoterol contained in Innovair can cause a sharp fall in your serum potassium level (hypokalaemia). **If you have severe asthma, you should take special care**. This is because a lack of oxygen in the blood and some other treatments you may be taking together with Innovair, such as medicines for treating heart disease or high blood pressure, known as diuretics or "water tablets" or other medicines used to treat asthma can make the fall in potassium level worse. For this reason your doctor may wish to measure the potassium levels in your blood from time to time.

If you take higher doses of inhaled corticosteroids over long periods, you may have more of a need for corticosteroids in situations of stress. Stressful situations might include being taken to hospital after an accident, having a serious injury or before an operation. In this case, the doctor treating you will decide whether you may need to increase your dose of corticosteroids and may prescribe some steroid tablets or a steroid injection.
Should you need to go to the hospital, remember to take all of your medicines and inhalers with you, including Innovair and any medicines or tablets bought without a prescription, in their original package, if possible.

Children and adolescents
Innovair should not be used in children and adolescent less than 18 years old, until further data become available.

Other medicines and Innovair:
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines.
Do not use beta blockers with this medicine. If you need to use beta blockers (including eye-drops), the effect of formoterol may be reduced or formoterol may not work at all. On the other hand, using other beta adrenergic drugs (drugs which work in the same way as formoterol) may increase the effects of formoterol.

Using Innovair together with:

- Medicines for treating abnormal heart rhythms (quinidine, disopyramide, procainamide), medicines used to treat allergic reactions (antihistamines), medicines for treating symptoms of depression or mental disorders such as monoaminoxidase inhibitors (for example phenelzine and isocarboxazid), tricyclic antidepressants (for example amitryptiline and imipramine), phenothiazines can cause some changes in the electrocardiogram (ECG, heart trace). They may also increase the risk of disturbances of heart rhythm (ventricular arrhythmias).
- Medicines for treating Parkinson's Disease (L-dopa), to treat an underactive thyroid gland (L-thyroxine), medicines containing oxytocin (which causes uterine contraction) and alcohol can lower your heart's tolerance to beta-2 agonists, such as formoterol.
- Monoaminoxidase inhibitors (MAOIs), including drugs with similar properties like furazolidone and procarbazine, used to treat mental disorders, can cause a rise in blood pressure.
- Medicines for treating heart disease (digoxin) can cause a fall in your blood potassium level. This may increase the likelihood of abnormal heart rhythms.
- Other medicines used to treat asthma (theophylline, aminophylline or steroids) and diuretics (water tablets) may cause a fall in your potassium level.
- Some anaesthetics can increase the risk of abnormal heart rhythms.

Pregnancy, breast feeding and fertility

There are no clinical data on the use of Innovair during pregnancy.

Innovair should not be used if you are pregnant, think that you might be pregnant or are planning to become pregnant, or if you are breast-feeding, unless you are advised to do so by your doctor

Driving and using machines

Innovair is unlikely to affect your ability to drive and use machines.

Innovair contains alcohol

Innovair contains a small amount of alcohol. Every actuation (puff) from your inhaler contains 12% of alkohol.

For people carrying out sport activities:

- The use of the medicinal product without therapeutic need constitutes doping and can however determine positivity to antidoping tests
- The use of medicinal products containing ethyl alcohol can give positivity to antidoping tests concerning alcohol concentration limits indicated by some sport federations

3. How to use Innovair

Innovair is for inhalation use.

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Asthma
Your doctor will give you a regular check-up to make sure you are taking the optimal dose of Innovair. Your doctor will adjust your treatment to the lowest dose that best controls your symptoms.

Innovair can be prescribed by your doctor in two different ways:

a) Use Innovair every day to treat your asthma together with a separate "reliever" inhaler to treat sudden worsening of asthma symptoms, such as shortness of breath, wheezing and cough
b) Use Innovair every day to treat your asthma and also use Innovair to treat sudden worsening of your asthma symptoms, such as shortness of breath, wheezing and cough

a) Using Innovair together with a separate "reliever":

Adults and the elderly:
The recommended dose of this medicine is one or two puffs twice daily.
The maximum daily dose is 4 puffs.

Remember: You should always have your quick-acting "reliever" inhaler with you at all times to treat worsening symptoms of asthma or a sudden asthma attack.

b) Using Innovair as your only asthma inhaler:

Adults and the elderly:
The recommended dose is one puff in the morning and one puff in the evening.
You should also use Innovair as a "reliever" inhaler to treat sudden asthma symptoms.
If you get asthma symptoms, take one puff and wait a few minutes.
If you do not feel better, take another puff.
Do not take more than 6 reliever puffs per day.

The maximum daily dose of Innovair is 8 puffs.
If you feel you need more puffs each day to control your asthma symptoms, contact your doctor to seek his advice. He may need to change your treatment.

Use in children and adolescents aged under 18 years:
Children and adolescents aged less than 18 years must NOT take this medicine.

Chronic obstructive pulmonary disease (COPD)

Adults and the elderly:
The recommended dose is two puffs in the morning and two puffs in the evening.

At-risk patients:
Older people do not need to have their dose adjusted. No information is available regarding the use of Innovair in people with liver or kidney problems.
Innovair is effective for the treatment of asthma in a dose of beclometasone dipropionate which may be lower than that of some other inhalers containing beclometasone dipropionate. If you have been using a different inhaler containing beclometasone dipropionate previously, your doctor will advise you on the exact dose of Innovair you should take for your asthma.

Do not increase the dose
If you feel that the medicine is not very effective, always talk to your doctor before increasing the dose.
If you use more Innovair than you should:

- Taking more formoterol than you should can have the following effects: feeling sick , being sick, heart racing, palpitations, disturbances of heart rhythm, certain changes in the electrocardiogram (heart trace), headache, trembling, feeling sleepy , too much acid in the blood, low blood potassium levels, high levels of glucose in the blood. Your doctor may wish to carry out some blood tests to check your blood potassium and blood glucose levels.
- Taking too much beclometasone dipropionate can lead short-term problems with your adrenal glands. This will get better within a few days however, your doctor may need to check your serum cortisol levels.

Tell your doctor if you have any of these symptoms.
If you forget to use Innovair:
Take it as soon as you remember. If it is almost time for your next dose, do not take the dose you have missed, just take the next dose at the correct time. **Do not double the dose.**

If you stop using Innovair:
Do not lower the dose or stop using the medication.
Even if you are feeling better, do not stop taking Innovair or lower the dose. If you want to do this, talk to your doctor. It is very important for you to use Innovair regularly even though you may have no symptoms.

If your breathing gets worse:
If you develop worsening shortness of breath or wheezing (breathing with an audible whistling sound), straight after inhaling your medicine, stop using Innovair inhaler immediately and use your quick-acting "reliever" inhaler straightaway. You should contact your doctor straightaway. Your doctor will assess your symptoms and if necessary may start you on a different course of treatment. See also section 4. Possible side effects.

If your asthma gets worse:
If your symptoms get worse or are difficult to control (e.g. if you are using a separate "reliever" or Innovair as reliever inhaler more frequently) or if your "reliever" inhaler or innovair does not improve

your symptoms, see your doctor immediately. Your asthma may be getting worse and your doctor may need to change your dose of Innovair or prescribe alternative treatment.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

Method of administration:
This medicine is contained in a pressurised canister in a plastic casing with a mouthpiece. There is a counter on the back of the inhaler, which tells you how many doses are left. Each time you press the canister, a puff of medicine is released and the counter will count down by one. Take care not to drop the inhaler as this may cause the counter to count down.

Testing your inhaler

Before using the inhaler for the first time or if you have not used the inhaler for 14 days or more, you should test your inhaler to make sure that it is working properly.

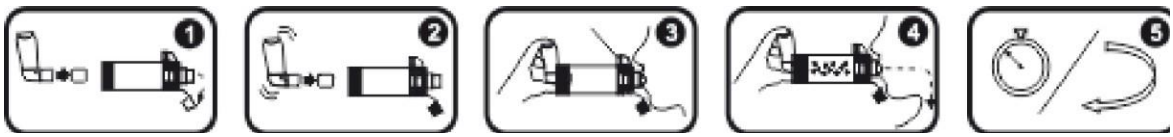
1. Remove the protective cap from the mouthpiece
2. Hold your inhaler upright with the mouthpiece at the bottom
3. Direct the mouthpiece away from yourself and firmly depress the canister to release one puff
4. Check the dose counter. If you are testing your inhaler for the first time, the counter should read 120.

How to use your inhaler

Whenever possible, stand or sit in an upright position when inhaling.

Use Innovair with spacer device

1. Remove the protective cap off both your puffer and the spacer device.
2. Insert the puffer into the Back piece of the spacer device.
3. Put your lips around the mouthpiece.
4. When you are ready, gently exhale. Start to inhale and press your puffer so that your medicine is sprayed into the spacer. Only press one puff at a time.
5. You will have to wait to take another puff of medicine. Check how many puffs your doctor wants you to take and how long to wait between puffs.



Important: Do not perform steps 2 to 5 too quickly.

After use, close with the protective cap and check the dose counter.

You should get a replacement when the counter shows the number 20. Stop using the inhaler when the counter shows 0 as any puffs left in the device may not be enough to give you a full dose.

If you have weak hands, it may be easier to hold the inhaler with both hands: hold the upper part of the inhaler with both index fingers and its lower part with both thumbs.
To lower the risk of a fungal infection in the mouth and throat, rinse your mouth or gargle with water or brush your teeth each time you use your inhaler.
If you think the effect of Innovair is too much or not enough, tell your doctor or pharmacist.

It is important that you read the package leaflet which is supplied with your spacer device and that you follow the instructions on how to use the spacer device and how to clean it, carefully.

Cleaning
You should clean your inhaler once a week. When cleaning, do not remove the canister from the actuator and do not use water or other liquids to clean your inhaler.
To clean your inhaler:
1. Remove the protective cap from the mouthpiece by pulling it away from your inhaler.
2. Wipe inside and outside of the mouthpiece and the actuator with a clean, dry cloth or tissue.
3. Replace the mouthpiece cover

4. Possible side effects

Like all medicines, Innovair can cause side effects, although not everybody gets them.

As with other inhaler treatments, there is a risk of worsening shortness of breath and wheezing immediately after using Innovair and this is known as paradoxical bronchospasm. If this occurs, you should STOP using Innovair immediately and use your quick-acting “reliever” inhaler straightaway to treat the symptoms of shortness of breath and wheezing. You should contact your doctor straightaway.

Tell your doctor immediately if you experience any hypersensitivity reactions like skin allergies, skin itching, skin rash, reddening of the skin, swelling of the skin or mucous membranes especially of the eyes, face, lips and throat.

Other possible side effects are listed below according to their frequency.

Common (affecting less than 1 in 10 people):
Fungal infections (of the mouth and throat), headache, hoarseness, sore throat.
Pneumonia; tell your doctor if you notice any of the following symptoms: increase in sputum production, increase in sputum colour, fever, increasing cough, increased breathing problems.

Uncommon (affecting less than 1 in 100 people);
Palpitations, unusual fast heart beat and disorders of heart rhythm, some changes in the electrocardiogram (ECG), flu symptoms, fungal infections of the vagina, inflammation of the sinuses, rhinitis, inflammation of the ear, throat irritation, cough and productive cough, asthma attack.
Nausea, abnormal or impaired sense of taste, burning of the lips, dry mouth, swallowing difficulties, indigestion, upset stomach, diarrhoea.
Pain in muscle and muscle cramps, reddening of the face, increased blood flow to some tissues in the body, excessive sweating, trembling, restlessness, dizziness, nettle rash or hives.
Alterations of some constituents of the blood: fall in the number of white blood cells, increase in the number of blood platelets, a fall in the level of potassium in the blood, increase in blood sugar level, increase in the blood level of insulin, free fatty acid and ketones.

The following side effects have also been reported as "uncommon" in patients with Chronic Obstructive pulmonary disease":

- Reduction of the amount of cortisol in the blood; this is caused by the effect of cortico-steroids on your adrenal gland.
- Irregular heartbeat.

Rare (affecting less than 1 in 1,000 people)
Feeling chest tightness, missed heartbeat (caused by too early contraction of the ventricles of the heart), increased or decrease in blood pressure, inflammation of the kidney, swelling of skin and mucous membrane persisting for several days, nettle rash or hives.

Very rare (affecting less than 1 in 10,000 people)
Shortness of breath, worsening of asthma, a fall in the number of blood platelets, swelling of the hands and feet.

Using high-dose inhaled corticosteroids over a long time can cause in very rare cases systemic effects: these include problems with how your adrenal glands work (adrenosuppression), decrease in bone mineral density (thinning of the bones), growth retardation in children and adolescents, increased pressure in your eyes (glaucoma), cataracts. Sleeping problems, depression or feeling worried, restless, nervous, over-excited or irritable.

Reporting of side effects
If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the national reporting system.
By reporting side affects you can help provide more information on the safety of this product.

5. How to store Innovair

Keep this medicine out of the sight and reach of children.
Do not use Innovair beyond 2 months from the date you get the inhaler from your pharmacist and never

use after the expiry date which is stated on the carton and label.
Do not store the inhaler above 30 °C.
If the inhaler has been exposed to severe cold, warm it with your hands for a few minutes before using. Never warm it by artificial means.
Warning: The canister contains a pressurised liquid. Do not expose the canister to temperatures higher than 50 °C. Do not pierce the canister.
Medicines should not be disposed via waste water or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Content of the pack and other information

What Innovair contains:
The active substances are: beclometasone dipropionate, formoterol fumarate dihydrate.
Each actuation from the inhaler contains 100 micrograms of beclometasone dipropionate and 6 micrograms of formoterol fumarate dihydrate. This corresponds to a delivered dose from the mouthpiece of 84.6 micrograms of beclometasone dipropionate and 5.0 micrograms of formoterol fumarate dihydrate.
The other ingredients are: ethanol anhydrous, hydrochloric acid, propellant: norflurane (HFA 134-a).

7. Shelf Life

17 months

Mengandung 12% alkohol

HARUS DENGAN RESEP DOKTER

Packing:
Dus, 1 Canister With Dose Counter @ 120 Actuations
Reg. No. DKI1460600568A1

Manufactured by:
Chiesi Farmaceutici S.p.A.
Via San Leonardo 96
43122 Parma – Italy

Imported by:
PT. Tunggal Idaman Abdi
Jakarta – Indonesia

Marketed by:
PT. Zambon Indonesia
Jakarta - Indonesia