INNOVAIR® NEXThaler®
Beclometasone dipropionate /
Formoterol fumarate dihydrate

100 micrograms/6 micrograms per dose inhalation powder

1. NAME OF THE MEDICINAL PRODUCT

Innovair Nexthaler 100 micrograms/6 micrograms per inhalation inhalation powder.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each metered dose of 10 mg inhalation powder contains:
100 micrograms of beclometasone dipropionate anhydrous and 6 micrograms of formoterol fumarate dihydrate.
This is equivalent to a delivered dose (the dose leaving the mouthpiece) of 81.9 micrograms of beclometasone dipropionate anhydrous and 5.0 micrograms of formoterol fumarate dihydrate.

Excipients with known effect:
Each inhalation contains 9.9 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Inhalation powder.

The multidose inhaler contains a white or almost white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Asthma

Innovair Nexthaler is indicated in the regular treatment of asthma where use of a combination product (inhaled corticosteroid and long-acting beta$_2$-agonist) is appropriate:
- patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta$_2$-agonist or
- patients already adequately controlled on both inhaled corticosteroids and long-acting beta$_2$-agonists.

Innovair Nexthaler is indicated for adult patients.

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

4.2 Posology and method of administration

INNOVAIR NEXTHALER is for inhalation use.

ASTHMA
INNOVAIR NEXTHALER is not intended for the initial management of asthma. The dosage of Innovair Nexthaler 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 an individual 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.

Because of its extrafine particle size distribution, dose adjustment is required when patients are transferred to Innovair Nexthaler inhalation powder from a formulation with a non-extrafine particle size distribution. When switching patients from previous treatments, it should be considered that the recommended total daily dose of beclometasone dipropionate for Innovair Nexthaler is lower than that for current beclometasone dipropionate-containing non-extrafine products and should be adjusted to the needs of the individual patient. However, patients who are transferred to Innovair Nexthaler inhalation powder from **Innovair Nexthaler** pressurised inhalation solution do not need dose adjustment.

There are two treatment approaches:

A. **Maintenance therapy**: Innovair Nexthaler is taken as regular maintenance treatment with a separate as needed rapid-acting bronchodilator.

B. **Maintenance and reliever therapy**: Innovair Nexthaler is taken as regular maintenance treatment 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 daily.

B. Maintenance and reliever therapy
Patients take their daily maintenance dose of Innovair Nexthaler and in addition take Innovair Nexthaler as needed in response to asthma symptoms. Patients should be advised to always have Innovair Nexthaler available for rescue use.

Innovair Nexthaler 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 Nexthaler as-needed inhalations.

Dose recommendations for adults 18 years and above:
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 Nexthaler in children and adolescents under 18 years of age have not been established. Innovair Nexthaler should not be used in children aged 5-11 years, because of safety concerns. In adolescents aged 12 – 17 years is also not recommended because there is no dose recommendation is available currently.

Patients should be regularly reassessed by a doctor, so that the dosage of Innovair Nexthaler 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-down could include the inhaled corticosteroid alone. Patients should be advised to take Innovair Nexthaler 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 Nexthaler in patients with hepatic or renal impairment (see section 5.2).

Method of administration
Nexthaler is a breath-operated inhaler. Moderate and severe asthmatic patients and COPD patients were shown to be able to produce sufficient inspiratory flow to trigger dose release from Nexthaler(see section 5.1). The delivery of Innovair Nexthaler is flow-independent in the range of inspiratory flow that this patient population can achieve through the inhaler.

Correct use of the Nexthaler inhaler is essential in order for the treatment to be successful. The patient should be advised to read the Patient Information Leaflet carefully and follow the instructions for use as given in the leaflet. For the convenience of the prescriber these instructions are provided in section 6.6.

Whenever possible patients should stand or sit in an upright position when inhaling from their inhaler.

With Nexthaler, a dose is made available for inhalation only when the cover is fully opened. Opening the cover, inhaling and closing the cover in sequence drive the dose counter mechanism. The patient should be instructed to close the cover full, at all times. The number of doses shown in the window on the shell

does not decrease on closing the cover if the patient has not inhaled through the inhaler.

The patient should be instructed to only open the inhaler's cover when needed. In the event that the patient has opened the inhaler but not inhaled, and the cover is closed, the dose is moved back to the powder reservoir within the inhaler; the following dose can be safely inhaled.

Optimal lung delivery is obtained if the patient inhales by breathing in quickly and deeply through the inhaler. A breath holding period of 5-10 seconds (or as long as comfortable for the patient) is suggested before breathing out.
The patient must be made aware that exhaling through the Nexthaler, before or after inhalation of the dose, must be avoided as this would affect its performance.
Patients should rinse their mouth or gargle with water or brush their teeth after inhaling (see section 4.4).

INSTRUCTIONS FOR USE OF NEXTHALER INHALER

A. Contents of the Package

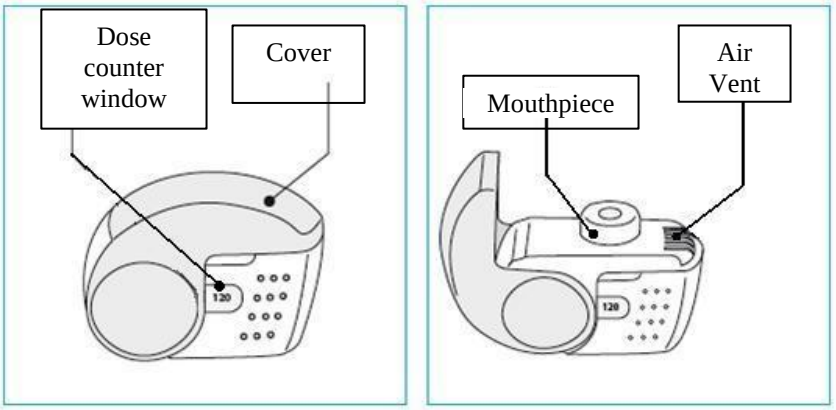
For information on the contents of the pack, see section 6.5.
If the package contents are not the same as described in section 6.5, return your inhaler to the person who supplied it and get a new one.

B. General Warnings & Precautions

- **Do not** remove the inhaler from the pouch if you do not intend to use it immediately.
- Only use your inhaler as indicated.
- Keep the cover closed until you need to take a dose from your inhaler.
- When you are not using your inhaler keep it in a clean and dry place.
- **Do not** attempt to take your Nexthaler inhaler apart for any reason.
- Do not use your Nexthaler inhaler :
    - After its expiry date
    - If it is more than 2 months since you opened the pouch
    - If it is broken
    - If the dose counter window shows "0"
    - If you cannot read the dose counter window

  In this cases, dispose your inhaler, or return it to the person who supplied it, and get a new one. Ask your pharmacist how to dispose of inhalers no longer required.

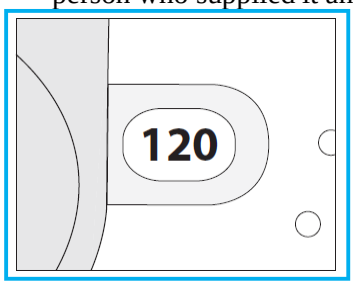
C. Key features of your Nexthaler inhaler



Taking a dose from your Nexthaler inhaler requires just three simple steps: Open, Inhale, Close.

D. Before using a new Nexthaler inhaler

1. **Open the pouch and take out your inhaler.**
   - **Do not** use your inhaler if the pouch is not sealed or it is damaged – return it to the person who supplied it and get a new one.
   - Use the label on the box to write down the date you open the pouch.
2. **Inspect your inhaler.**
   - If your inhaler looks broken or damaged, return it to the person who supplied it and get a new one.
3. **Check the Dose Counter Window. If your inhaler is brand new you will see "120" in the Dose Counter Window.**
   - **Do not** use a new inhaler if the number shown is less than "120" – return it to the person who supplied it and get a new one.



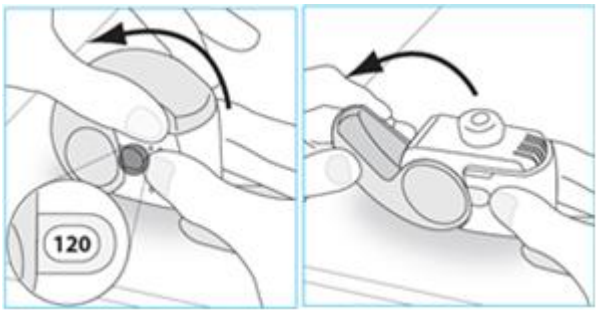
E. How to use your Nexthaler inhaler

- If you are not sure you are receiving your dose correctly contact your pharmacist or doctor.
- If you are not sure the dose counter has gone down by one after inhalation, wait until your next scheduled dose and take this as normal. Do not take an extra dose.

E.1. Open

1. **Hold your inhaler firmly in the upright position.**
2. **Check the number of doses left: any number between "1" and "120" shows that there are doses left.**
   - If the Dose Counter Window shows "0" there are no doses left – dispose of your inhaler and get a new one.

3. **Open the cover fully.**

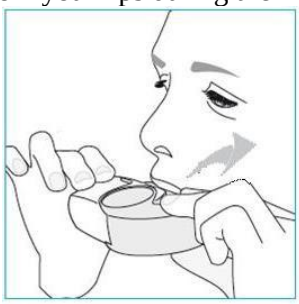


4. **Before inhaling breathe out as far as is comfortable.**
    - **Do not** breathe out through your inhaler.

E.2. Inhale

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

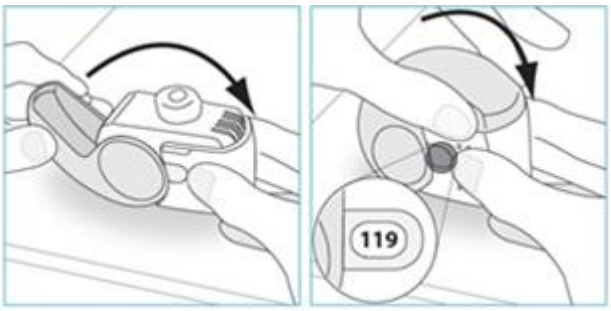
1. **Lift your inhaler up, bring it to your mouth and place your lips around the mouthpiece.**
    - **Do not** cover the air vent when holding your inhaler.
    - **Do not** inhale through the air vent.
2. **Take a quick and deep breath through your mouth.**
    - You may notice a taste when you take your dose.
    - You may hear or feel a click when you take your dose.
    - **Do not** inhale through your nose.
    - **Do not** remove your inhaler from your lips during the inhalation.



3. **Remove your inhaler from your mouth.**
4. **Hold your breath for 5 to 10 seconds or as long as is comfortable.**
5. **Breathe out slowly.**
    - **Do not** breathe out through your inhaler.

E.3. Close

1. **Move your inhaler back to the upright position and close the cover fully.**
2. **Check that the dose counter has gone down by one.**



3. **If you need to take another dose, repeat steps E.1 to E.3**

F. Cleaning

- Normally, it is not necessary to clean your inhaler.
- If necessary you may clean your inhaler after use with a dry cloth or tissue.
    - **Do not** clean your inhaler with water or other liquids. Keep it dry.

G. Storage and Disposal

- Do not expose your inhaler to heat or direct sunlight
- For information on storage conditions and disposal instructions, see sections 6.4 and 6.6.

4.3 Contraindications

Hypersensitivity to beclometasone dipropionate, formoterol fumarate dihydrate or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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

The management of asthma should normally follow a stepwise programme and patient response should be monitored clinically and by lung function tests.
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 is potentially life- threatening and the patient should undergo urgent medical assessment. Consideration should be given to the need for increased treatment with corticosteroids, either inhaled or oral therapy, or antibiotic treatment if an infection is suspected.
Patients should not be initiated on Innovair Nexthaler 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 Nexthaler. Patients should be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsenafter initiation on Innovair Nexthaler.
As with other inhalation therapy paradoxical bronchospasm may occur with an immediate increase in wheezing, cough and shortness of breath after dosing. This should be treated immediately with a fast-acting inhaled bronchodilator. Innovair Nexthaler should be discontinued immediately, the patient

assessed and alternative therapy instituted if necessary.

INNOVAIR NEXTHALER is not intended for the initial management of asthma.

For treatment of acute asthma attacks patients should be advised to have their short-acting bronchodilator available at all times, either INNOVAIR NEXTHALER (for patients using INNOVAIR NEXTHALER as maintenance and reliever therapy) or a separate rapid-acting bronchodilator (for patients using INNOVAIR NEXTHALER as maintenance therapy only).

Patients should be reminded to take Innovair Nexthaler daily as prescribed even when asymptomatic. The reliever inhalations of INNOVAIR NEXTHALER 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 Nexthaler. Regular review of patients as treatment is stepped down is important. The lowest effective dose of Innovair Nexthaler should be used (see section 4.2).

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 patients with COPD include current smoking, older age, low body mass index (BMI) and severe COPD.

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, glaucoma, and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). It is important therefore that the dose of inhaled corticosteroid is titrated 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 and adolescents aged less than 16 years 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.

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 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.

Innovair Nexthaler should be administered with caution in patients with active or quiescent pulmonary tuberculosis, fungal and viral infections in the airways.

Innovair Nexthaler should be used with caution (which may include monitoring) in patients with cardiac arrhythmias, especially third degree atrioventricular block and tachyarrhythmias, idiopathic subvalvular aortic stenosis, hypertrophic obstructive cardiomyopathy, ischaemic heart disease, severe heart failure, severe 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 Nexthaler is used by patients with thyrotoxicosis, diabetes mellitus, phaeochromocytoma and untreated hypokalaemia.

Potentially serious hypokalaemia may result from beta$_2$-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 (see section 4.5). 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 Nexthaler is not administered for at least 12 hours before the start of anaesthesia as there is a risk of cardiac arrhythmias.

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 fungal infections and dysphonia.

The medicinal product contains lactose. Lactose contains small amounts of milk proteins, which may cause allergic reactions. Patient with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Visual disturbance

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 opthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serious chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacokinetic interactions

Beclomethasone dipropionate undergoes a very rapid metabolism via esterase enzymes.
Beclomethasone is less dependent on CYP3A metabolism than some other corticosteroids, and in general interactions are unlikely; however the possibility of systemic effects with concomitant use of strong CYP3A inhibitors (e.g ritonavir, cobicistat) cannot be excluded, and therefore caution and appropriate monitoring is advised with the use of such agents.

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.
The use of other beta-adrenergic drugs may have potentially additive effects, therefore caution is required when theophylline or other beta-adrenerigic drugs are prescribed concomitantly with formoterol.
Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, certain antihistamines (e.g. terfenadine), monoamine oxidase inhibitors and tricyclic antidepressants can prolong the QTc-interval and increase the risk of ventricular arrhythmias.

In addition L-dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance towards $beta_2$-sympathomimetics.
Concomitant treatment with monoamine oxidase inhibitors including agents with similar properties such as furazolidone and procarbazine may precipitate hypertensive reactions.
There is an elevated risk of arrhythmias in patients receiving concomitant anaesthesia with halogenated hydrocarbons.
Concomitant treatment with xanthine derivatives, steroids, or diuretics may potentiate a possible hypokalaemic effect of $beta_2$-agonists (see section 4.4). Hypokalaemia may increase the disposition towards arrhythmias in patients who are treated with digitalis glycosides.

4.6 Fertility, pregnancy and lactation

Fertility

There are no data in humans. In animal studies in rats, the presence of beclometasone dipropionate at high doses in the combination was associated with reduced female fertility and embryotoxicity (see section 5.3).

Pregnancy

There are no relevant clinical data on the use of Innovair Nexthaler in pregnant women. Animal studies using beclometasone dipropionate and formoterol combination showed evidence of toxicity to reproduction and to the fetuses after high systemic exposure (see section 5.3). High doses of corticosteroids administered to pregnant animals are known to cause abnormalities of fetal development including cleft palate and intra-uterine growth retardation. Because of the tocolytic actions of beta$_2$-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 or during labour unless there is no other (safer) established alternative.

Administration of Innovair Nexthaler during pregnancy should only be considered if the expected benefits outweigh the potential risks.

Lactation

There are no relevant clinical data on the use of Innovair Nexthaler during 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 Nexthaler to women who are breast-feeding should be considered if the expected benefits outweigh the potential risks. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Innovair Nexthaler therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Innovair Nexthaler has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The most common adverse reaction is tremor. In a 12-week clinical trial with Innovair Nexthaler, tremor was seen only with the highest dose regimen (2 inhalations bid), appeared most frequently atthe beginning of treatment and was mild in intensity. No patient was withdrawn from the trial as a result of tremor.

Clinical Trials Experience in asthma patients

The safety of Innovair Nexthaler was assessed in active- and placebo-controlled clinical trials in which 719 patients aged 12 and older with asthma of varying severity were exposed to the drug. The incidence of adverse reactions in the table below relates to asthmatic patients aged 12 years and older and is based upon the safety findings of two pivotal clinical trials where Innovair Nexthaler was administered at the doses recommended in this SmPC for a period of 8-12 weeks. No psychiatric disorders were observed in the clinical trials with Innovair Nexthaler but they are included in the table as a potential class-effect of inhaled corticosteroids.

Undesirable effects which have been associated with beclometasone dipropionate and formoterol administered as a fixed combination (Innovair Nexthaler) are given below, listed by system organ class. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1,000 to <1/100), rare (≥ 1/10,000 to < 1/1,000) and very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	**Adverse Reaction**	**Frequency**
Infections and infestations	Nasopharyngitis	Uncommon
	Oral candidiasis	Uncommon
	Pneumonia (in COPD patients)	Common
Metabolism and nutrition disorders	Hypertriglyceridaemia	Uncommon
Psychiatric disorders	Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children)	Frequency not known
Eye disorders	Vision, blurred (see section 4.4)	Frequency not known
Nervous system disorders	Tremor	Common
	Headache	Uncommon
Cardiac disorders	Tachycardia	Uncommon
	Sinus bradycardia	Uncommon
	Angina pectoris	Uncommon
	Myocardial ischaemia	Uncommon
Respiratory, thoracic and mediastinal disorders	Throat irritation, exacerbation of asthma	Uncommon
	Dyspnoea	Uncommon
	Oropharyngeal pain	Uncommon
	Dysphonia	Uncommon

	Cough	Uncommon
Gastrointestinal disorders	Nausea	Uncommon
General disorders and administration site conditions	Fatigue	Uncommon
	Irritability	Uncommon
Investigations	Electrocardiogram QT prolonged	Uncommon
	Cortisol free urine decreased	Uncommon
	Blood cortisol decreased	Uncommon
	Blood potassium increased	Uncommon
	Blood glucose increased	Uncommon
	Electrocardiogram poor r-wave progression	Uncommon

Among the observed adverse reactions those typically associated with formoterol are: tremor, headache, tachycardia, sinus bradycardia, angina pectoris, myocardial ischaemia, QT prolongation.

Among the observed adverse reactions those typically associated with beclometasone dipropionate are: nasopharyngitis, oral candidiasis, dysphonia, throat irritation, irritability, cortisol free urine decreased, blood cortisol decreased, blood glucose increased.

Additional adverse reactions not observed in the clinical experience with Innovair Nexthaler but typically associated with the inhaled administration of beclometasone dipropionate are other oral fungal infections and pneumonia. Taste disturbances have occasionally been reported during inhaled corticosteroid therapy.

See section 4.4 for measures to minimize the occurrence of oral fungal infections, oral candidiasis and dysphonia.

Systemic effects of inhaled corticosteroids (e.g. beclometasone dipropionate) may occur particularly when administered at high doses prescribed for prolonged periods, these may include Cushing's Syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, growth retardation in children and adolescents, cataract and glaucoma (see also section 4.4).

Additional adverse reactions not observed in the clinical experience with therapeutic doses of Innovair Nexthaler but typically associated with the administration of beta$_2$-agonist such as formoterol are palpitations, atrial fibrillation, ventricular extrasystoles, tachyarrhythmia, potentially serious hypokalaemia and increase/decrease of blood pressure. Insomnia, dizziness, restlessness, and anxiety

have occasionally been reported during inhaled formoterol therapy. Formoterol may also inducemuscle cramps, myalgia.

Hypersensitivity reactions including rashes, urticaria, pruritus and erythema and oedema of the eye, face, lips and throat (angioedema) have been reported.

As with other inhalation therapy paradoxical bronchospasm may occur with an immediate increase in wheezing, cough and shortness of breath after dosing (see also section 4.4).

Paediatric population
Available pharmacokinetic data do not support the safety of INNOVAIR NEXTHALER in children aged 5-11 years. There is limited clinical information in adolescents 12 – 17 years of age (see sections 4.2, 5.1 and 5.2). In a 12 weeks randomised clinical trial in adults and adolescents, 162 adolescents aged 12 – 17 years with moderate to severe asthma received Innovair Nexthaler or the corresponding pressurised inhalation solution formulation, 1 or 2 inhalations bid; the frequency, type and severity of adverse drug reactions were not different in adolescents compared to adults.

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 :
Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat,
Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR.

4.9 Overdose

The highest recommended dose of Innovair Nexthaler in a single administration is 2 inhalations. Four cumulative inhalations of Innovair Nexthaler (total beclometasone dipropionate 400 micrograms, formoterol 24 micrograms given as a single dose) have been studied in asthmatic patients. The cumulative treatment did not cause abnormal, clinically relevant effect on vital signs and neither serious nor severe adverse reactions were observed (see also section 4.8).

For the pressurised inhalation solution formulation, inhaled doses of 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 hospitalised. 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

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 (see section 4.4.). Monitoring of adrenal reserve may be necessary. Treatment should be continued at a dose sufficient to control asthma.

Single supra-therapeutic doses up to 800 micrograms of beclometasone dipropionate, 48 micrograms of formoterol, administered via Innovair Nexthaler are generally safe and well tolerated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Adrenergics, inhalants: formoterol and other drugs for obstructive airway diseases.
ATC-code: R03AK08.

Mechanisms of action and pharmacodynamic effects

Innovair Nexthaler contains beclometasone dipropionate and formoterol in a dry powder formulation resulting in an extrafine aerosol with an average mass median aerodynamic diameter (MMAD) of 1.4-1.5 micrometers and co-deposition of the two components. The aerosol particles of Innovair Nexthaler are on average much smaller than the particles delivered in non-extrafine formulations.

A radio-labelled drug deposition study in asthmatic adults has demonstrated that a high proportion of the drug (estimated 42% of the nominal dose) is deposited in the lung, with a homogenous deposition through the airways. These delivery characteristics support the use of a low corticosteroid dose with enhanced local pharmacodynamic effects, which were shown to be equivalent to the corresponding pressurised inhalation solution (see *Clinical experience*).

The two actives of Innovair Nexthaler have different modes of action. In common with other inhaled corticosteroids and beta$_2$-agonist combinations, additive effects are seen in respect of reduction in 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 dose administration.

Clinical experience

The efficacy of the two components of Innovair Nexthaler inhalation powder has been assessed in three separate studies in comparison with the 100 micrograms/6 micrograms pressurised inhalation solution formulation in moderate to severe patients with persistent asthma. Overall, the efficacy of the two inhalers is expected to be equivalent in clinical practice at both 1 and 2 inhalations bid.

In one study the primary objective was the efficacy evaluation of the inhaled corticosteroid component measured on bronchodilation (pre-dose FEV_1). A clinically significant improvement in pre-dose FEV_1 was seen in 696 patients with moderate to severe symptomatic asthma at the end of a 3 months

treatment period in comparison with baseline values, with 1 inhalation bid and 2 inhalations bid of both formulations. A mean increase of at least 250 mL was observed. There was no clinically relevant difference in pre-dose FEV_1 between Innovair Nexthaler inhalation powder and the pressurised inhalation solution at either dosage. A significant dose-response was observed for morning PEF. Statistical significance for the dose-response in pre-dose FEV_1 was not reached. Measurements of control of asthma such as morning and evening asthma symptoms scores and percentage of days without symptoms improved significantly from baseline through to the end of the treatment period, particularly for the two high doses of both formulations.

In the second study the primary aim was the efficacy evaluation on the long-acting $beta_2$-agonist component of Innovair Nexthaler. In this study bronchodilation at the onset and up to 12 hrs after single doses administration was measured by serial spirometric evaluations of FEV_1 (FEV_1 AUC over at least 80% of formoterol duration of action). Compared with placebo, Innovair Nexthaler, one inhalation and four inhalations of both actives significantly improved the FEV_1 AUC_{0-12}. Both doses of Innovair Nexthaler inhalation powder were non-inferior to the corresponding dose of the pressurised inhalation solution formulation. A statistically significant dose-response was found with both formulations between the low and high dose.

In the third study, after a 4-week run-in period with beclometasone dipropionate/formoterol pressurised inhalation solution fixed combination, 1 inhalation bid, 755 controlled asthmatic patients were randomised to 8 weeks of treatment with the same inhaler, with Innovair Nexthaler inhalation powder or with beclometasone dipropionate 100 micrograms per dose inhalation powder, all given at 1inhalation bid. The primary objective was the change from baseline over the entire treatment period in mean morning expiratory flow (PEF). After 8 weeks of treatment there was no difference in the primary endpoint between the two combination inhalers, both being significantly better than beclometasone dipropionate monotherapy. No differences were found between the two combination inhalers in measures of symptoms such as the asthma control questionnaire score and the number of rescue-free days.

An open-label placebo study was conducted to verify that the inspiratory flow which could begenerated through the Nexthaler inhaler is not influenced by patient's age, disease and disease severity, and therefore the activation and drug delivery from the device could be achieved in all patients. The primary endpoint was the percentage of patients in each age and disease group able to activate the inhaler. Eighty-nine patients, in the age range 5-84 years, including moderate and severe asthmatics (FEV_1 > 60% and ≤ 60% predicted, respectively), and moderate and severe COPD patients (FEV_1 ≥ 50% and < 50% predicted, respectively) participated in the trial. All patients, irrespective of age, disease and disease severity, were able to generate sufficient inspiratory flow to activate the Nexthaler inhaler.

In an additional open label placebo study it was demonstrated by assessing the inspiration profile through the Innovair Nexthaler that mild to severe COPD patients, regardless of their functional limitation, were able to effectively activate and use the device.

Paediatric population

There are very limited clinical data available on the use of INNOVAIR NEXTHALER in children aged 5-11 years. Compared with an equivalent dose of licensed free combination products containing beclometasone dipropionate anhydrous (BDP) and formoterol (FF), administration of a single dose of an experimental fixed dose formulation containing the same extrafine active ingredients as INNOVAIR NEXTHALER, but using a lower dose strength (50µg BDP and 6µg FF), resulted in markedly higher systemic bioavailability for both components (see section 5.2).

This higher systemic availability was associated with a statistically significant decrease in plasma potassium (point estimate 0.94, 95%CI [0.92; 0.96]) and increase in time-averaged heart rate (point estimate 1.06, 95%CI [1.01; 1.10]). Moreover, a trend towards cortisol suppression and increase in urinary glucose values was observed in children of the test group as compared to the reference treatment. In adolescents only limited information was obtained.

In a 3 months randomised clinical trial 162 subjects aged 12 – 17 years with a diagnosis of moderate to severe asthma received either Innovair Nexthaler or the corresponding pressurised inhalation solution formulation, 1 or 2 inhalations bid. The change in pre-dose FEV_1 at the end of treatment was greater in the adolescents than in adults.
See also sections 4.2, 4.8 and 5.2 for information on paediatric use.

5.2 Pharmacokinetic properties

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 the active metabolite arises from lung 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 part 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 from a pressurised metered dose inhaler 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 120 L/h respectively), with a small volume of distribution at steady state for beclometasone dipropionate (20L) and larger tissue distribution for its active metabolite (424L). Metabolic disposition of beclometasone dipropionate mainly (82%) results in its active metabolite beclometasone-17-monopropionate.
Plasma protein binding is moderately high (87%).

Excretion
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
The pharmacokinetics of beclometasone dipropionate in patients with **renal or hepatic impairment** has not been studied; however, as beclometasone dipropionate undergoes a very rapid metabolism via esterase enzymes present in intestinal fluid, serum, lungs and liver, to originate the more polarproducts beclometasone-21-monopropionate, beclometasone-17-monopropionate and beclometasone, hepatic impairment is not expected to modify the pharmacokinetics and safety profile of beclometasone dipropionate.
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 a metered dose inhaler

(MDI) may range 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.

Metabolism

Formoterol is widely metabolised 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.

Excretion

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.

Paediatric population

In single dose pharmacokinetic studies in asthmatic children aged 5-11 years, two experimental paediatric fixed-dose formulations containing the same extrafine active ingredients as INNOVAIR NEXTHALER, but using lower dose strengths (A: 50µg BDP and 6µg FF = 50/6; B: 35µg BDP and 4µg FF = 35/4), were compared with equivalent doses of licensed free combination products containing BDP and FF. Due to the absence of charcoal block, only systemic exposure as a measure of safety was determined. Compared with the free combination, BDP/FF 50/6 resulted in greater systemic exposure ($AUC0_t$) and peak concentrations (C_{max}) of all three analytes, parent compound BDP, the active metabolite beclometasone-17-monopropionate (B17MP) and formoterol. Subsequent reduction of the dose strength by about 30% to BDP/FF 35/4 still resulted in markedly higher $AUC0_t$ of B17MP (point estimator 152.5, 90%CI [141.1 164.8]) as well as the parent compound BDP (point estimator 188.6, 90%CI [163.8 217.1]). AUC_0 of formoterol was within and C_{max} slightly exceeded the bioequivalence range of 80-125%.

Clinical experience

The systemic exposure to beclometasone dipropionate and formoterol in the combination has been compared to the single components. There was no evidence of pharmacokinetic or pharmacodynamic (systemic) interactions between beclometasone dipropionate and formoterol.

The pharmacokinetics of Innovair Nexthaler inhalation powder has been compared with that of the corresponding pressurised inhalation solution formulation. The analysis of the steroid component focused on beclometasone-17-monopropionate, the main active metabolite of beclometasone

dipropionate.
Systemic absorption and metabolism of beclometasone dipropionate was rapid and C_{max} was reached 5 min postdose for both treatments but was higher (+ 68 %) with Innovair Nexthaler inhalation powder. AUCt was about 3 times higher after inhalation of Innovair Nexthaler through the Nexthaler inhaler compared with the pressurised inhalation solution. C_{max} for beclometasone-17-monopropionate, the main active metabolite, representing about 82% of the total blood level, was reached on average after 30 min and 15 min with the Nexthaler and with the pressurised inhalation solution, respectively. Plasma concentration of beclometasone-17-monopropionate was lower (C_{max} -49% and AUC_t - 29%), after inhalation of the inhalation powder than via the pressurised inhalation solution. After inhalation of Innovair Nexthaler with the Nexthaler inhaler, the peak concentration (C_{max}) of formoterol was reached within 5 minutes and was higher (+ 47 %) for the inhalation powder, whereas the overall exposure (AUC_t) was comparable in the two treatments.
In one study the relative lung delivery was investigated by using a charcoal blockade to exclude drug absorption from the gastrointestinal tract, and adopting an approved spacer, the AeroChamber Plus® for the reference product (the pressurised inhalation solution). In this setting, the Nexthaler and the pressurised inhalation solution were shown to be equivalent for the AUC_t of both beclometasone-17-monopropionate and formoterol (the ratio inhalation powder/pressurised inhalation solution and the 90% confidence intervals were within 80-125%); however, C_{max} of beclometasone-17-monopropionate was lower (-38%) following inhalation from the Nexthaler.

5.3 Preclinical safety data

Non-clinical data of the individual components of Innovair Nexthaler reveal no special hazard for humans based on conventional studies of safety pharmacology and repeated dose toxicity. The toxicity profile of the combination reflected that of single components with no increase in toxicity or unexpected findings.

Reproduction studies in rats showed dose-dependent effects. The presence of beclometasone dipropionate at high doses was associated with reduced female fertility, decrease in the number of implantations 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-monopropionate (more than 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 Nexthaler.

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (which contains small amounts of milk proteins)
magnesium stearate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

After first opening the pouch, the medicinal product should be used within 2 months.

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.
Only remove the inhaler from its foil package immediately before first use.

Before first opening the pouch:
This medicinal product does not require any special temperature storage conditions.

After first opening the pouch:
Do not store above 30°C.

6.5 Nature and contents of container

Each carton contains 1 Nexthaler inhaler which contain 1.50 g inhalation powder and provide 120 inhalations. The inhaler is contained in a heat sealed protective pouch (foil package) made of PET/Al/ PE (Polyethylene Terephtalate/Aluminium/ Polyethylene) or PA/Al/PE (Polyamide/Aluminium/ Polyethylene).

Innovair Nexthaler is a multi-dose inhalation device. The device consists of a casework comprising a lower shell with window to display number of doses left and an integral cover. When opened, the cover, which also drives the dose counter mechanism, reveals a mouthpiece through which the drug is inhaled. The lower shell and mouthpiece are made from acrylonitrile butadiene styrene and the cover is made from polypropylene.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.
Instruction for use of the Nexthaler inhaler are provided below for the benefit of health professionals.

HARUS DENGAN RESEP DOKTER

Reg. No. DKI2060600667A1

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® NEXThaler®
Beclometasone dipropionate / Formoterol fumarate dihydrate

100 micrograms/6 micrograms per dose inhalation powder

For use in adults

Beclometasone dipropionate anhydrous/Formoterol fumarate dihydrate

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, nurse or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Innovair Nexthaler is and what it is used for

Innovair Nexthaler is a powder that is inhaled through your mouth and delivered deeply into your lungs. It contains two active ingredients: beclometasone dipropionate anhydrous 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 in your lungs.

- Formoterol fumarate dihydrate belongs to a group of medicines called long-acting bronchodilators. These relax the muscles in your airways, widening the airways so that it is easier for you to breathe air in and out of your lungs.

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

Asthma
Innovair Nexthaler is used to treat asthma in adults.
If you are prescribed Innovair Nexthaler it is likely that either:

- Your asthma is not adequately controlled by using inhaled corticosteroids and “as needed” short-acting bronchodilators

or

- Your asthma is responding well to both corticosteroids and long-acting bronchodilators.

COPD

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

2. What you need to know before you use Innovair Nexthaler

Do not use Innovair Nexthaler

if you are allergic to beclometasone dipropionate anhydrous or formoterol fumarate dihydrate or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor before using Innovair Nexthaler if you have any of the following:

- Heart problems, these include any known disorder of your heart and/or heart function
- Disorders of the 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
- High blood pressure
- Narrowing of the arteries (also known as arteriosclerosis), or if you know that you have an aneurysm (an abnormal bulging of the blood vessel wall)
- An overactive thyroid gland
- Low blood levels of potassium
- Any disease of your liver or kidneys
- 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.
- Tumour of the adrenal gland (known as a phaeochromocytoma)
- You are due to have an anaesthetic. Depending on the type of anaesthetic, it may be necessary to stop taking innovair nexthaler at least 12 hours before the anaesthesia.
- 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 any of the above applies to you, always inform your doctor before you use Innovair Nexthaler.

If you are not sure whether you can use Innovair Nexthaler talk to your doctor, asthma nurse or pharmacist before using the inhaler.

Your doctor may wish to measure the potassium levels in your blood from time to time especially if your asthma is severe. Like many bronchodilators Innovair Nexthaler can cause a sharp fall in your serum potassium level (hypokalaemia). This is because a lack of oxygen

in the blood combined with some other treatments you may be taking together with Innovair Nexthaler can make the fall in potassium level worse.

If you are using an inhaler to take high doses of corticosteroids over a long period of time, 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 Nexthaler and any medicines or tablets bought without a prescription, in their original package, if possible.

Contact your doctor if you experience blurred vision or other visual disturbances.

Children and adolescents
Do not give this medicine to children and adolescents aged less than 18 years.

Other medicines and Innovair Nexthaler
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Innovair Nexthaler may affect the way some other medicines work. Also, some medicines can affect the way Innovair Nexthaler works.

In particular, tell your doctor or pharmacist if you are using any of the following medicines:

- Some medicines may increase the effects of [product name] and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat).
- Beta-blocker medicines. Beta blockers are medicines used to treat many conditions including heart problems, high blood pressure or glaucoma (increased pressure in the eyes). If you need to use beta blockers (including eye-drops), the effect of formoterol may be reduced or formoterol may not work at all.
- Beta adrenergic drugs (drugs which work in the same way as formoterol) may increase the effects of formoterol.
- Medicines for treating abnormal heart rhythms (quinidine, disopyramide, procainamide)
- Medicines to treat allergic reactions (antihistamines such as terfenadine)
- Medicines to treat symptoms of depression or mental disorders such as monoaminoxidase inhibitors (for example phenelzine and isocarboxazid) or tricyclic antidepressants (for example amitryptiline and imipramine) or phenothiazines
- Medicines to treat Parkinson's Disease (L-dopa)
- Medicines to treat an underactive thyroid gland (L-thyroxine)
- Medicines containing oxytocin (which causes uterine contraction)
- Medicines to treat mental disorders such as monoaminoxidase inhibitors (MAOIs), including drugs with similar properties like furazolidone and procarbazine
- Medicines to treat heart disease (digoxin)
- Other medicines used to treat asthma (theophylline, aminophylline or steroids)
- Diuretics (water tablets)

Also tell your doctor or pharmacist if you are going to have a general anaesthetic for an operation or for dental work.

Innovair Nexthaler with alcohol
You should avoid drinking alcohol unless you have talked to your doctor first. Alcohol can lower your heart's tolerance to one of the active ingredients of Innovair Nexthaler, formoterol.

Pregnancy and breast feeding
There is no clinical data on the use of Innovair Nexthaler during pregnancy.
If you think you are pregnant or are planning to become pregnant please consult your doctor. You should only use Innovair Nexthaler during pregnancy if you are advised to do so by your doctor. Your doctor will decide whether you must stop taking Innovair Nexthaler during breastfeeding or you should take Innovair Nexthaler but refrain from breastfeeding. Always follow the advice of your doctor strictly.

Driving and using machines
Innovair Nexthaler is unlikely to affect your ability to drive and use machines. However if you experience side effects such as dizziness and/or trembling, your ability to drive or operate machinery may be affected.

Innovair Nexthaler contains lactose.

Lactose contains small amounts of milk proteins, which may cause reactions in allergic patients. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to use Innovair Nexthaler

Always use Innovair Nexthaler exactly as your doctor has told you. You should check with your doctor, nurse or pharmacist if you are not sure.

Innovair Nexthaler delivers an extrafine aerosol which results in more of each dose being delivered to your lungs. Your doctor may, therefore, prescribe a lower dose of this inhaler than your previous inhalers.

Asthma
Your doctor will give you a regular check-up to make sure you are taking the correct dose of Innovair Nexthaler. Once your asthma is well controlled your doctor may consider it appropriate to gradually reduce the dose of Innovair Nexthaler. **Under no circumstances** should you change the dose without first speaking to your doctor.

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

a) **use Innovair Nexthaler 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 Nexthaler every day to treat your asthma and also use Innovair Nexthaler to treat sudden worsening of your asthma symptoms, such as shortness of breath, wheezing and cough

a) Using Innovair Nexthaler together with a separate "reliever":
Adults and the elderly:
The recommended dose of this medicine is 1 or 2 inhalations twice daily.
The maximum daily dose is 4 inhalations.

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 Nexthaler as your only asthma inhaler:

Adults and the elderly:
The usual maintenance dose is one inhalation in the morning and one inhalation in the evening.

You should also use INNOVAIR NEXTHALER as a "reliever" inhaler to treat sudden asthma symptoms.

If you get asthma symptoms, take one inhalation and wait a few minutes.
If you do not feel better, take another inhalation.

The maximum daily dose of INNOVAIR NEXTHALER is 8 inhalations, which includes 2 maintenance doses (one inhalation in the morning and one inhalation in the evening) and additional 6 reliever inhalation per day.

If you feel you need more inhalations each day to control your asthma symptoms, contact your doctor to seek his advice. He may need to change your treatment.

Do not increase the dose.
If you feel that the medicine is not effective, always talk to your doctor before increasing the dose.

Chronic obstructive pulmonary disease (COPD)

Adults and the elderly:
The recommended dose is 2 inhalations in the morning and 2 inhalations in the evening.

How to use Innovair Nexthaler:

Innovair Nexthaler is for inhalation use.

If you have used more Innovair Nexthaler than you should:

- contact your doctor or nearest hospital casualty department immediately for advice. Take your medicine with you so that the people can see what you have taken;
- side effects may occur. Tell your doctor if you have any unusual symptoms as he/she may wish to carry out further tests or decide about any measures that may be necessary.

If you forget to use Innovair Nexthaler:
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 Nexthaler:
Even if you are feeling better, do not stop using Innovair Nexthaler or lower the dose. If you want to do this, talk to your doctor. It is very important for you to use Innovair Nexthaler every day as prescribed by your doctor even though you may have no symptoms.

<u>If your breathing does not change:</u>
If your symptoms do not improve after inhaling Innovair Nexthaler, you may be using it incorrectly. Therefore check the instructions below for correct use and/or contact your doctor or nurse to be trained properly again.

<u>If your asthma gets worse:</u>
If your symptoms get worse or are difficult to control (e.g. if you are using your "reliever" inhaler more frequently) or if your "reliever" inhaler does not improve your symptoms, you should continue to use Innovair Nexthaler but go to see your doctor as soon as possible. Your doctor may need to change your dose of Innovair Nexthaler or prescribe an additional or alternative treatment.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

INSTRUCTIONS FOR USE OF NEXTHALER INHALER

A. Contents of the Package

This package contains :

- 1 instruction leaflet
- 1 Innovair Nexthaler in a sealed protective pouch.

If the package contents are not the same as this, return your inhaler to the person who supplied it and get a new one.

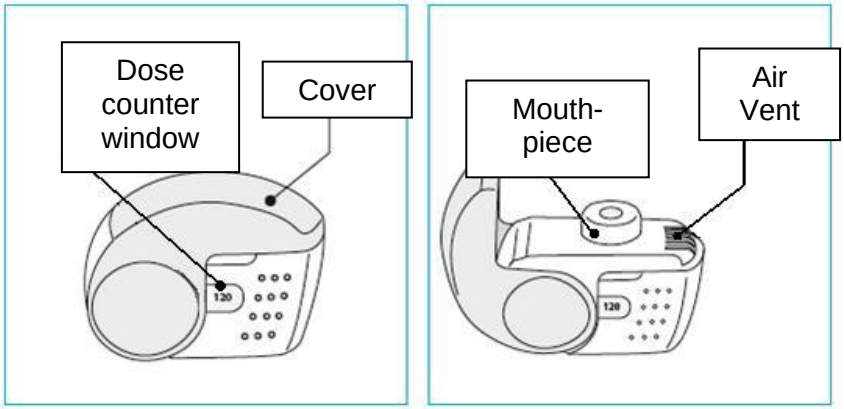
B. General Warnings & Precautions

- **Do not** remove the inhaler from the pouch if you do not intend to use it immediately.
- Only use your inhaler as indicated.
- Keep the cover closed until you need to take a dose from your inhaler.
- When you are not using your inhaler keep it in a clean and dry place.

- **Do not** attempt to take your Nexthaler inhaler apart for any reason.
- **Do not use your Nexthaler inhaler :**
    - After its expiry date
    - If it is more than 2 months since you opened the pouch
    - If it is broken
    - If the dose counter windows shows “0”
    - If you cannot read the dose counter window

If these case, dispose your inhaler, or return it to the person who supplied it, and get a new one. Ask your paharmacist how to dispose of inhaler no longer required.

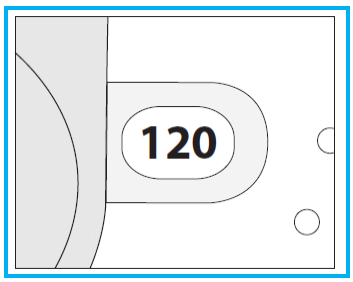
C. Key features of your Nexthaler inhaler



Taking a dose from your Nexthaler inhaler requires just three simple steps: Open, Inhale, Close.

D. Before using a new Nexthaler inhaler

1. **Open the pouch and take out your inhaler.**
    - **Do not** use your inhaler if the pouch is not sealed or it is damaged – return it to the person who supplied it and get a new one.
    - Use the label on the box to write down the date you open the pouch.
2. **Inspect your inhaler.**
    - If your inhaler looks broken or damaged, return it to the person who supplied it and get a new one.
3. **Check the Dose Counter Window. If your inhaler is brand new you will see “120” in the Dose Counter Window.**
    - **Do not** use a new inhaler if the number shown is less than “120” – return it to the person who supplied it and get a new one.

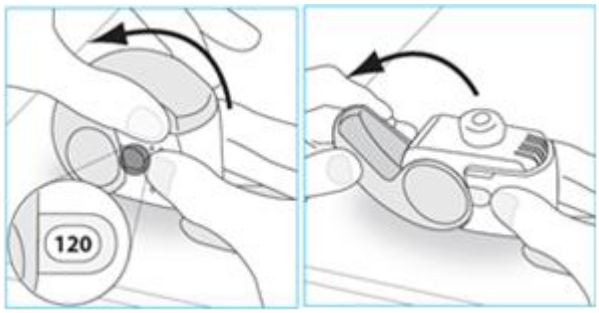


E. How to use your Nexthaler inhaler

- If you are not sure you are receiving your dose correctly contact your pharmacist or doctor.
- If you are not sure the dose counter has gone down by one after inhalation, wait until your next scheduled dose and take this as normal. Do not take an extra dose.

E.1. Open

1. **Hold your inhaler firmly in the upright position.**
2. **Check the number of doses left: any number between "1" and "120" shows that there are doses left.**
   - If the Dose Counter Window shows "0" there are no doses left – dispose of your inhaler and get a new one.
3. **Open the cover fully.**



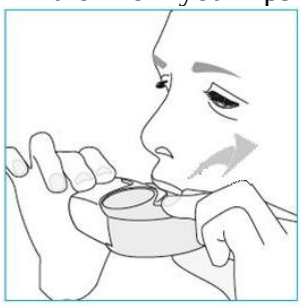
4. **Before inhaling breathe out as far as is comfortable.**
   - **Do not** breathe out through your inhaler.

E.2. Inhale

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

1. **Lift your inhaler up, bring it to your mouth and place your lips around the mouthpiece.**
   - **Do not** cover the air vent when holding your inhaler.
   - **Do not** inhale through the air vent.
2. **Take a forceful and deep breath through your mouth.**
   - You may notice a taste when you take your dose.

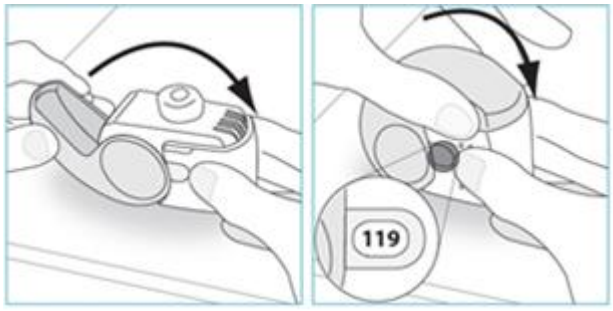
- You may hear or feel a click when you take your dose.
- **Do not** inhale through your nose.
- **Do not** remove your inhaler from your lips during the inhalation.



3. **Remove your inhaler from your mouth.**
4. **Hold your breath for 5 to 10 seconds or as long as is comfortable.**
5. **Breathe out slowly.**
   - **Do not** breathe out through your inhaler.

E.3. Close

1. **Move your inhaler back to the upright position and close the cover fully.**
2. **Check that the dose counter has gone down by one.**



3. **If you need to take another dose, repeat steps E.1 to E.3.**

F. Cleaning

- Normally, it is not necessary to clean your inhaler.
- If necessary you may clean your inhaler after use with a dry cloth or tissue.
- **Do not** clean your inhaler with water or other liquids. Keep it dry.

G. Storage and Disposal

- Do not expose your inhaler to heat or direct sunligt
- For information on storage conditions and disposal instructions, see section 5.

4. Possible side effects

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

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

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

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

You should contact your doctor or pharmacist immediately:
- If you experience any of the side effects below and they cause you distress, are severe or last for several days

If you are worried in any way or if there is anything you do not understand.

Common (may affect up to 1 in 10 people):
- Trembling.
- Pneumonia (infection of the lung) in copd patients

Tell your doctor if you have any of the following while taking Innovair Nexthaler they could be symptoms of a lung infection:
• Fever or chills
• Increased mucus production, change in mucus colour
• Increased cough or increased breathing difficulties

Uncommon (may affect up to 1 in 100 people):
- Cold-like symptoms, sore throat
- Fungal infections (of the mouth and throat). Rinsing your mouth or gargling with water and brushing your teeth immediately after inhalation may help to prevent these side effects.
- Worsening of your asthma symptoms, difficulty breathing
- Hoarseness
- Cough
- Unusually fast heart beat
- Unusually slow heart beat
- Crushing chest pain
- Headache
- Feeling sick
- Feeling tired or nervous
- Changes in the electrocardiogram (ecg)
- Low level of cortisol in your urine or in your blood
- High level of potassium in your blood
- High level of glucose in your blood
- High level of fats in your blood.

Not known (frequency cannot be estimated from the available data):

- blurred vision.

Side effects which have been observed with similar medicines for inhalation containing beclometasone dipropionate and/or formoterol are:
- Palpitations
- Uneven heart beat
- Abnormal or impaired sense of taste
- Muscle pain and muscle cramps
- Restlessness, dizziness
- Feeling anxious
- Sleep disorders
- A fall in the level of potassium in the blood
- Increase/decrease of blood pressure.

Using high-dose inhaled corticosteroids over a long time can cause systemic effects these include:
- Problems with how your adrenal glands work (adrenosuppression)
- Thinning of the bones
- Growth retardation in children and adolescents
- Increased pressure in your eyes (called glaucoma), cataracts
- Rapid weight gain, particularly of the face and torso
- Sleeping problems, depression or feeling worried, restless, nervous, over-excited or irritable. These effects are more likely to occur in children.
- Abnormal behaviour.

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 to Indonesia.localPV@ZambonGroup.com. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Innovair Nexthaler

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton, pouch and label after Exp. The expiry date refers to the last day of that month.

Store in the original package in order to protect from moisture. Only remove the inhaler from its pouch immediately before first use.

Before first opening the pouch:
This medicinal product does not require any special temperature storage conditions.

After first opening the pouch:
Do not store above 30°C.

After first opening the pouch, the medicinal product should be used within 2 months.
Use the label on the box to write down the date you open the pouch.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Innovair Nexthaler contains
The active substances are: beclometasone dipropionate anhydrous and formoterol fumarate dihydrate.

Each metered dose contains 100 micrograms of beclometasone dipropionate anhydrous and 6 micrograms of formoterol fumarate dihydrate. This corresponds to a delivered dose from the mouthpiece of 81.9 micrograms of beclometasone dipropionate anhydrous and 5 micrograms of formoterol fumarate dihydrate.

The other ingredients are: lactose monohydrate (which contains small amounts of milk proteins) and magnesium stearate.

What Innovair Nexthaler looks like and contents of the pack
This medicinal product is presented as a white to almost white inhalation powder contained in a plastic inhaler called Nexthaler.
Each pack contains one inhaler which provides 120 inhalations.
The inhaler comes in a sealed protective pouch (aluminium foil package).

HARUS DENGAN RESEP DOKTER

Reg. No. DKI2060600667A1

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® NEXThaler®
Beclometasone dipropionate /
Formoterol fumarate dihydrate

100 micrograms/6 micrograms per dose inhalation powder

PENGGUNAAN PADA PASIEN DEWASA

Beclomethasone dipropionate anhydrous / Formoterol fumarate dihydrate

Bacalah leaflet ini dengan seksama sebelum Anda mulai menggunakan obat ini, karena berisi informasi penting untuk anda

- Simpan leaflet ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, perawat atau apoteker Anda.
- Obat ini hanya diresepkan untuk Anda. Jangan berikan obat ini kepada orang lain, karena dapat membahayakan mereka, bahkan jika tanda-tanda penyakit mereka sama dengan penyakit Anda.
- Jika Anda mengalami efek samping, bicarakan dengan dokter, perawat atau apoteker Anda.
- Termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini.

Informasi dalam leaflet ini.

1. Apa Innovair Nexthaler dan kegunaanya

Innovair Nexthaler adalah serbuk obat yang dihirup melalui mulut dan masuk ke dalam paru-paru. Obat ini mengandung dua bahan aktif: Beclometasone dipropionate anhydrous dan Formoterol fumarate dihydrate.

- Beclometasone dipropionate merupakan obat golongan steroid (disebut kortikosteroid). Dimana memiliki aksi mengurangi peradangan, pembengkakan dan iritasi hingga saluran napas kecil pada paru-paru .

- Formoterol fumarate dihydrate merupakan golongan bronkodilator masa kerja lama. Bahan aktif ini dapat merelaksasi otot-otot di saluran pernapasan, memperlebar saluran pernapasan sehingga lebih mudah bagi Anda untuk menghirup udara masuk dan keluar dari paru-paru.

Kombinasi dua zat aktif ini dapat melegakan gejala sesak napas, mengi dan batuk pada penderita Asma atau PPOK sehingga memudahkan Anda bernapas. Dan juga bermanfaat mencegah gejala Asma.

Asma
Innovair Nexthaler digunakan untuk pengobatan Asma pada orang dewasa
Anda mungkin diresepkan Innovair Nexthaler, pada kondisi sebagai berikut :
- Asma Anda tidak terkontrol dengan baik oleh pengobatan kortikosteroid inhalasi dan bronkodilator kerja pendek jika dibutuhkan.

atau
- Asma Anda dapat terobati dengan baik oleh pengobatan kortikosteroid maupun bronkodilator masa kerja panjang

PPOK
Innovair Nexthaler juga dapat digunakan untuk mengobati gejala Penyakit Paru Obstruktif Kronik berat (PPOK) pada pasien dewasa. PPOK merupakan penyakit kronis pada saluran napas di paru-paru yang terutamanya disebabkan oleh merokok.

2. **Apa yang perlu Anda ketahui sebelum menggunakan Innovair Nexthaler?**

Jangan gunakan Innovair Nexthaler:

Jika Anda alergi terhadap Beclometasone diproprionate anhydrous atau Formoterol fumarate dihydrate atau bahan lain dari obat ini (tercantum di bagian 6).

Peringatan dan Perhatian

Sebelum menggunakan Innovair Nexthaler sampaikan pada dokter Anda jika Anda memiliki hal-hal berikut:
- Masalah jantung, termasuk gangguan jantung dan/atau fungsi jantung yang diketahui
- Kelainan pada irama jantung seperti denyut jantung yang meningkat atau tidak beraturan, denyut nadi cepat atau palpitasi, atau jika Anda telah diberitahu bahwa detak jantung Anda tidak normal
- Tekanan darah tinggi
- Penyempitan arteri (juga dikenal sebagai arteriosclerosis), atau jika Anda tahu bahwa Anda memiliki aneurisma (kondisi abnormal dinding pembuluh darah yang melebar)
- Kelenjar tiroid yang terlalu aktif
- Kadar kalium dalam darah rendah
- Penyakit pada hati atau ginjal
- Diabetes. Jika Anda menghirup dosis tinggi Formoterol maka glukosa darah Anda dapat meningkat sehingga Anda mungkin perlu melakukan beberapa tes darah tambahan untuk memeriksa gula darah saat Anda mulai menggunakan inhaler ini dan dari waktu ke waktu selama perawatan

- Tumor kelenjar adrenal (dikenal sebagai phaeochromocytoma)
- Anda akan melakukan anestesi. Bergantung pada jenis anestesi, mungkin konsumsi Innovair Nexthaler perlu dihentikan minimal 12 jam sebelum anestesi.
- Anda sedang atau pernah diobati untuk tuberkulosis (TB) atau jika Anda terinfeksi virus atau jamur.

Jika hal-hal di atas terjadi kepada Anda, selalu beritahu dokter Anda sebelum Anda menggunakan Innovair Nexthaler.
Jika Anda tidak yakin apakah Anda dapat menggunakan Innovair Nexthaler, sampaikan ke dokter, perawat atau apoteker Anda sebelum menggunakannya.

Dokter akan mengukur kadar kalium dalam darah dari waktu ke waktu terutama pada pasien Asma berat. Seperti banyak bronchodilator lainnya, Innovair Nexthaler dapat menyebabkan penurunan kadar potasium yang signifikan (hipokalemia). Ini karena kurangnya oksigen dalam darah yang dikombinasikan dengan beberapa perawatan lain yang mungkin Anda konsumsi bersama dengan Innovair sehingga dapat memperburuk penurunan kadar kalium.

Jika Anda menggunakan inhaler kortikosteroid dosis tinggi dalam jangka waktu yang lama, pada kondisi stres anda mungkin membutuhkan kortikosteroid dengan dosis yang lebih tinggi. Situasi stress mungkin terjadi karena kecelakaan, cedera serius, atau sebelum operasi. Dalam kasus ini dokter yang merawat anda akan memutuskan apakah dosis kortikosteroid perlu ditingkatkan 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 anda miliki, termasuk Innovair Nexthaler dan obat-obatan atau tablet yang dibeli tanpa resep, dalam kemasan aslinya jika memungkinkan.
Hubungi dokter apabila mengalami penglihatan kabur atau gangguan penglihatan lainnya

Anak-anak dan remaja
Jangan berikan obat ini kepada anak-anak dan remaja berusia di bawah 18 tahun.

Obat lain dan Innovair Nexthaler
Beritahu dokter atau apoteker Anda jika menggunakan obat lainnya, termasuk jenis inhaler lain atau obat tanpa resep dokter. Hal ini karena Innovair Nexthaler dapat mempengaruhi cara kerja obat lain. Selain itu, beberapa obat-obatan dapat mempengaruhi cara kerja Innovair Nexthaler.

Beritahu dokter atau apoteker jika Anda menggunakan obat dibawah ini :

- Beberapa obat yang mungkin dapat meningkatkan efek Innovair Nexthaler dan memerlukan pengawasan dokter jika Anda menggunakan obat-obatan tersebut (termasuk beberapa obat HIV: ritonavir, cobicistat)
- Obat obatan golongan Beta Bloker. yaitu golongan obat yang digunakan untuk menangani banyak kondisi termasuk masalah jantung, tekanan darah tinggi, ataupun glaukoma (peningkatan tekanan di mata). Jika Anda perlu menggunakan obat Beta Bloker (termasuk obat tetes mata), efek Formoterol akan berkurang atau Formoterol tidak mempunyai efek sama sekali.

- Obat lain yang bekerja dengan mekanisme yang sama dengan Formoterol (yaitu obat beta adrenergik, biasa digunakan untuk mengobati Asma). Dapat meningkatkan efek dari Formoterol
- Obat untuk mengobati irama jantung abnormal (Quinidine, disopyramide, procainamide)
- Obat untuk mengobati reaksi alergi (beberapa antihistamin misalnya terfenadine)
- Obat untuk mengobati depresi atau gangguan mental seperti penghambat monoaminoksidase (seperti phenelzine dan isocarboxazid) atau trisiklik anti depresan (seperti amitriptilin dan imipramine,) atau fenotiazine
- Obat untuk mengobati penyakit Parkinson (L-dopa)
- Obat untuk mengobati kelenjar tiroid yang kurang aktif (L-tiroksin)
- Obat-obatan yang mengandung oksitosin (yang menyebabkan kontraksi uterus)
- Obat untuk mengobati gangguan jiwa seperti penghambat monoaminoksidase (MAOI) , termasuk obat-obatan dengan sifat serupa seperti furazolidone dan procarbazine
- Obat untuk mengobati penyakit jantung (digoxin)
- Obat lain untuk mengobati Asma (teofilin, aminofilin atau steroid)
- Diuretik

Informasikan juga kepada dokter jika Anda akan mendapat anestesi umum untuk operasi atau untuk pengobatan gigi

Innovair Nexthaler dengan alkohol
Anda harus menghindari minum alkohol kecuali jika Anda telah berbicara dengan dokter terlebih dahulu. Alkohol bisa menurunkan toleransi jantung Anda ke salah satu bahan aktif Innovair Nexthaler, Formoterol.

Kehamilan dan menyusui
Belum ada data klinis tentang penggunaan Innovair Nexthaler selama kehamilan. Jika Anda sedang hamil atau berencana untuk hamil, konsultasikan dengan dokter Anda. Penggunaan Innovair Nexthaler selama kehamilan hanya diperbolehkan atas saran dari dokter. Dokter akan memutuskan apakah harus berhenti mengkonsumsi Innovair Nexthaler selama menyusui atau harus mengkonsumsi Innovair Nexthaler dan berhenti menyusui. Selalu ikuti saran dokter Anda secara ketat.

Mengemudi dan menggunakan mesin
Innovair Nexthaler tidak mempengaruhi kemampuan Anda untuk mengemudikan dan menggunakan mesin. Namun jika Anda mengalami efek samping seperti pusing dan atau gemetaran, kemampuan mengemudi atau mengoperasikan mesin mungkin akan terpengaruh.

Innovair Nexthaler mengandung Laktosa.
Laktosa mengandung sejumlah kecil protein susu, yang dapat menyebabkan reaksi pada pasien yang alergi terhadap susu. Jika Anda pernah diberitahu oleh dokter bahwa Anda memiliki intoleransi terhadap beberapa gula, hubungi dokter Anda sebelum menggunakan obat ini.

3. **Cara menggunakan Innovair Nexthaler**

Selalu gunakan Innovair Nexthaler sesuai arahan dokter Anda. Tanyakan pada dokter, perawat atau apoteker jika Anda tidak yakin.

Innovair Nexthaler merupakan aerosol *ekstrafine* dapat meningkatkan deposisi obat pada paru-paru Anda. Oleh karena itu, dokter mungkin akan meresepkan dosis yang lebih rendah dibanding inhaler sebelumnya.

Asma

Dokter Anda akan melakukan pemeriksaan rutin untuk memastikan Anda menggunakan dosis yang benar terhadap Innovair Nexthaler. Saat Asma Anda terkontrol dengan baik, dokter mungkin mempertimbangkan secara bertahap untuk mengurangi dosis Innovair Nexthaler. Dalam keadaan apapun selalu diskusikan dengan dokter apabila akan mengubah dosis.

Innovair Nexthaler dapat diresepkan oleh Dokter anda melalui dua cara yaitu:

a) Innovair Nexthaler digunakan setiap hari untuk mengobati asma, bersama dengan inhaler lain seperti inhaler “pelega” (Reliever) untuk mengobati gejala asma yang memburuk seperti sesak napas, mengi dan batuk
b) Innovair Nexthaler dapat digunakan setiap hari untuk mengobati asma, dan juga bisa digunakan ketika gejala asma memburuk seperti sesak napas, mengi dan batuk.

a) Penggunaan Innovair Nexthaler bersamaan dengan inhaler “pelega” (reliever) terpisah:
Dewasa dan lanjut usia :

Dosis yang dianjurkan untuk obat ini adalah 1 atau 2 kali inhalasi dua kali sehari. Dosis maksimum harian adalah 4 kali inhalasi.

Ingat: Bawalah selalu inhaler “pelega” (reliever) kerja cepat bersama Anda setiap saat untuk mengobati gejala asma yang memburuk atau jika terkena serangan asma mendadak.

b) Penggunaan Innovair Nexthaler sebagai satu-satunya inhaler asma

Dewasa dan lanjut usia

Dosis pemeliharaan biasa adalah 1 inhalasi pada pagi hari dan 1 inhalasi pada malam hari.

Anda juga dapat menggunakan Innovair Nexthaler sebagai Inhaler “pelega” (reliever) untuk mengobati gejala asma yang mendadak.

Jika Anda mengalami gejala asma, gunakan 1 inhalasi dan tunggu beberapa saat.

Jika gejala belum membaik, hirup 1 inhalasi kembali

Dosis maksimal harian sebanyak 8 kali Inhalasi, termasuk 2 dosis pemeliharaan (1 inhalasi di pagi hari dan 1 inhalasi di sore hari) dan penambahan 6 inhalasi pelega (reliever) per hari.

Jika Anda membutuhkan dosis yang lebih untuk mengatur gejala asma, hubungi Dokter Anda. Dokter mungkin akan mengubah pengobatan Anda.

Jangan menaikkan dosisnya. Jika Anda merasa obat tidak efektif, selalu diskusikan dengan dokter sebelum menambah dosis.

PPOK
Dewasa dan lansia:
Dosis yang dianjurkan adalah dua inhalasi di pagi hari dan dua inhalasi di malam hari.

Bagaimana cara menggunakan Innovair Nexthaler?

Innovair Nexthaler adalah untuk penggunaan inhalasi.

Jika Anda menggunakan Innovair Nexthaler lebih dari yang seharusnya:
- Segera hubungi dokter atau segera ke rumah sakit terdekat. Bawa obat Anda sehingga dapat dipastikan berapa banyak yang telah Anda gunakan.
- Efek samping bisa terjadi. Beritahu dokter jika Anda mengalami gejala yang tidak biasa, dokter mungkin akan melakukan tes lebih lanjut atau perlu melakukan tindakan lebih lanjut.

Jika Anda lupa menggunakan Innovair Nexthaler:
Gunakan sesegera mungkin saat Anda teringat. Jika sudah dekat waktu untuk dosis berikutnya, lewati dosis yang terlupa, inhalasi dosis berikutnya pada waktu yang terjadwalkan.
Jangan menggandakan dosis.

Jika Anda berhenti menggunakan Innovair Nexthaler:
Bahkan jika Anda merasa lebih baik, jangan berhenti menggunakan Innovair Nexthaler atau menurunkan dosisnya. Jika Anda ingin menurunkan dosis, komunikasikan dengan dokter. Sangatlah penting bagi Anda untuk menggunakan Innovair Nexthaler secara teratur meskipun Anda sudah tidak merasakan gejala.
Jika pernapasan Anda tidak membaik:
Jika gejala Anda tidak membaik setelah meng-inhalasi Innovair Nexthaler, Anda mungkin menggunakannya dengan tidak tepat. Oleh karena itu, periksa petunjuk penggunaan pada leaflet ini dengan seksama dan / atau hubungi dokter atau perawat Anda untuk mendapatkan petunjuk cara penggunaan yang tepat.

Jika Asma Anda memburuk:
Jika gejala Anda memburuk atau sulit dikontrol (misalnya jika Anda menggunakan "pelega" inhaler lebih sering) atau jika inhaler "pelega" Anda tidak memperbaiki gejala Anda, Anda harus terus menggunakan Innovair Nexthaler dan ke dokter sesegera mungkin.
Dokter Anda mungkin perlu mengubah dosis Innovair Nexthaler Anda atau memberi resep tambahan atau alternatif pengobatan lainnya

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

INSTRUKSI PENGGUNAAN INNOVAIR NEXTHALER

Bacalah semua instruksi berikut sebelum mulai menggunakan inhaler ini.
Jika Anda mengalami masalah menggunakan inhaler ini, silakan hubungi dokter, perawat atau apoteker Anda.

A. Isi Kemasan

Paket ini berisi:

- 1 brosur instruksi
- 1 Innovair Nexthaler di dalam kantong pelindung yang tertutup rapat.

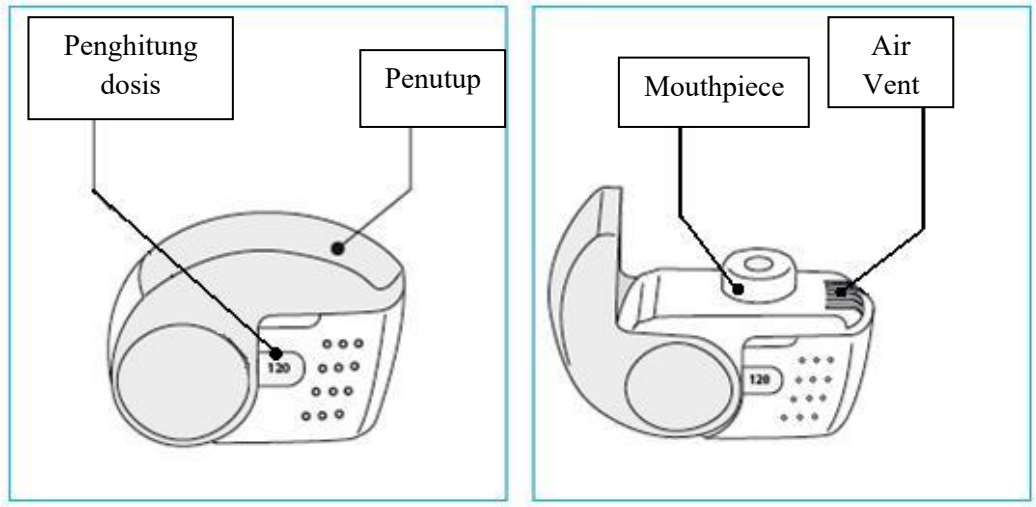
Jika isi paket tidak sesuai, kembalikan inhaler Anda ke orang yang menyediakannya (misalnya apoteker atau dokter) dan mintalah yang baru

B. Peringatan Umum & Tindakan Pencegahan

- **Jangan** keluarkan inhaler dari kemasannya jika Anda tidak berniat menggunakannya segera.
- Hanya gunakan inhaler sesuai indikasi.
- Simpan dalam keadaan tertutup hingga penggunaan dosis berikutnya.
- Saat tidak digunakan, simpanlah inhaler Anda di tempat yang bersih dan kering.
- **Jangan** bongkar rangkaian Innovair Nexthaler 100/6 dengan alasan apa pun.
    - Jangan gunakan Nexthaler:
    - Setelah tanggal kedaluwarsa
    - Jika lebih dari 2 bulan sejak Anda membuka kantong
    - Jika rusak
    - Jika penghitung dosis menunjukkan “0”
    - Jika Anda tidak dapat membaca jendela penghitung dosis.

Apabila hal diatas terjadi terhadap anda, buang inhaler Anda, atau kembalikan ke orang yang menyediakannya, dan dapatkan yang baru. Tanyakan kepada apoteker Anda bagaimana cara membuang inhaler yang tidak diperlukan lagi

C. Fitur utama dari Innovair Nexthaler Anda



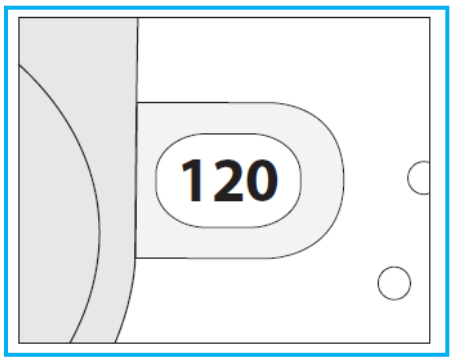
Menghirup dosis Innovair Nexthaler 100/6 hanya membutuhkan tiga langkah sederhana yaitu: **Buka, Hirup, Tutup.**

D. Sebelum menggunakan inhaler Nexthaler baru

1. **Buka kemasan dan ambil inhaler Anda.**
   - **Jangan** gunakan inhaler jika kemasan telah terbuka atau rusak - kembalikan dan mintalah yang baru.
   - Gunakan label di box untuk menulis tanggal saat Anda membuka kemasan.

2. **Periksa inhaler Anda.**
   Jika inhaler Anda terlihat rusak atau sudah rusak, kembalikan dan mintalah yang baru.

3. **Periksa Penghitung Dosis**. Jika inhaler Anda baru, Anda akan melihat "120" di penghitung dosis.
   Jangan gunakan inhaler baru jika angka yang ditampilkan kurang dari "120" - kembalikan dan mintalah yang baru.



E. Cara menggunakan Innovair Nexthaler 100/6

- Jika Anda tidak yakin dapat menggunakan dosis dengan benar, hubungi dokter atau apoteker
- Jika Anda tidak yakin penghitung dosis berkurang setelah dihirup, tunggulah sampai dosis terjadwal Anda berikutnya dan gunakan seperti biasa. Jangan menghirup dosis ekstra.

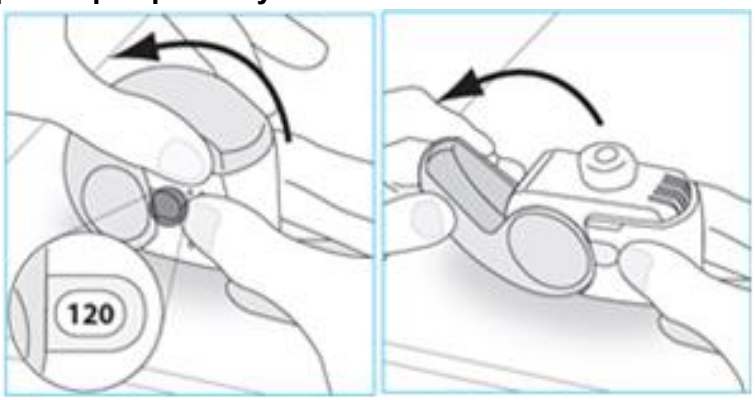
E.1. **Buka**

1. **Pegang inhaler Anda dengan kuat dalam posisi tegak.**

2. Periksa jumlah dosis yang tersisa : angka antara "1" dan "120" menunjukkan berapa dosis yang tersisa.

Jika penghitung dosis menunjukkan "0" maka tidak ada dosis yang tersisa - ganti Innovair Nexthaler 100/6 Anda dengan yang baru.

3. Buka penutup sepenuhnya.



.

4. Sebelum menggunakannya, tarik dan hembuskan napas senyaman mungkin.

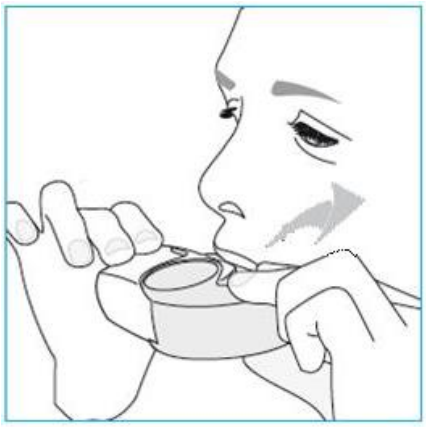
Jangan menghembuskan napas pada inhaler

E.2. Menghirup

Bila memungkinkan, berdirilah atau duduklah dalam posisi tegak saat menghirup.

1. **Angkat inhaler, dekatkan ke mulut dan letakkan bibir di sekitar mouthpiece**.
   - **Jangan** menutupi air vent saat memegang inhaler Anda.
   - **Jangan** menghirup udara melalui air vent.

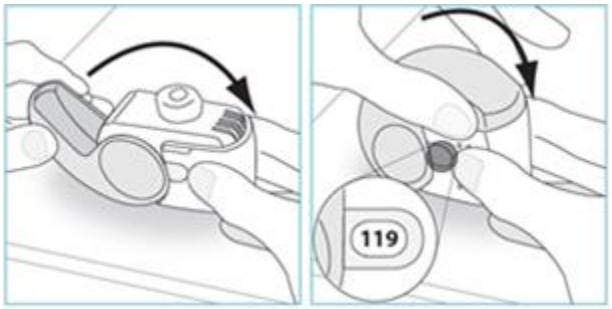
2. **Hirup napas dengan kuat dan dalam lewat mulut Anda.**
   - Anda mungkin merasakan rasa manis saat menghirup Innovair Nexthaler 100/6 .
   - Anda mungkin merasakan atau mendengar bunyi **KLIK** ketika menghirup Innovair Nexthaler 100/6 .
   - **Jangan** menghirup melalui hidung.
   - **Jangan** lepas inhaler dari bibir Anda selama menghirup.



3. **Lepaskan inhaler dari mulut Anda.**
4. **Tahan napas selama 5 sampai 10 detik atau selama Anda merasa nyaman.**
5. **Hembuskan dengan perlahan.**
    - **Jangan** hembuskan napas melalui inhaler.

E.3. Tutup

1. **Kembalikan inhaler ke posisi tegak dan tutup cover sepenuhnya.**
2. **Pastikan penghitung dosis sudah berkurang satu nilai.**



3. **Jika perlu menghirup dosis lain, ulangi langkah E.1 hingga E.3.**

F. Membersihkan

- Umumnya, inhaler tidak perlu dibersihkan.
- Jika diperlukan Anda dapat membersihkan inhaler setelah digunakan dengan lap kering atau tisu.
- Jangan bersihkan inhaler Anda dengan air atau cairan lain. Jaga Inhaler Anda tetap kering.

G. Penyimpanan dan Pemusnahan

- Jauhkan inhaler anda dari panas cahaya matahari langsung
- Untuk informasi penyimpanan dan pembuangan lihat bagian 5.

4. **Kemungkinan efek samping**

Seperti semua obat-obatan, obat ini bisa menimbulkan efek samping, meski tidak semua orang akan mengalaminya.

Seperti inhaler lainnya terdapat risiko memburuknya sesak napas, batuk dan mengi segera setelah menggunakan Innovair Nexthaler, hal ini disebut *paradox bronkospasme*. Jika Anda mengalami hal ini **hentikan penggunaan Innovair Nexthaler dan segera gunakan inhaler "pelega"** Anda untuk mengobati gejala. dan segera hubungi dokter Anda.

Beritahu dokter segera jika Anda mengalami reaksi alergi yang meliputi alergi kulit, kulit gatal, ruam kulit, kemerahan pada kulit, pembengkakan kulit atau selaput lendir terutama pada mata, wajah, bibir dan tenggorokan.

Kemungkinan efek samping lain dari Innovair Nexthaler tercantum di bawah ini sesuai frekuensi kejadian.

Anda harus segera menghubungi dokter atau apoteker Anda:
Jika Anda mengalami salah satu efek samping di bawah ini dan jika efek samping tersebut menyulitkan anda, parah atau berlangsung selama beberapa hari
jika Anda khawatir atau apakah ada sesuatu yang tidak Anda mengerti.

Umum (dapat mempengaruhi hingga 1 dari 10 orang):
- Gemetar
- Pneumonia (infeksi paru) pada pasien PPOK

Beritahu dokter jika Anda mengalami hal-hal berikut saat menggunakan Innovair Nexthaler. kemungkinan terjadi gejala infeksi paru-paru seperti:
- Demam atau menggigil
- Peningkatan produksi lendir, perubahan warna lendir
- Meningkatnya batuk atau meningkatnya kesulitan bernapas.

Jarang (dapat mempengaruhi hingga 1 dari 100 orang):
- Gejala seperti salesma, sakit tenggorokan
- Infeksi jamur (dari mulut dan tenggorokan). Bilas mulut atau berkumur dengan air segera mungkin atau menggosok gigi setelah inhalasi dapat membantu mencegah efek samping.
- Memburuknya gejala Asma, sulit bernapas
- Suara serak
- Batuk
- Denyut jantung yang sangat cepat
- Denyut jantung yang sangat lambat
- Nyeri dada
- Sakit kepala
- Merasa sakit
- Merasa lelah atau gugup

- Perubahan elektrokardiogram (EKG)
- Kortisol rendah dalam urin atau darah
- Kadar kalium tinggi dalam darah
- Kadar glukosa tinggi dalam darah
- Kadar lemak tinggi dalam darah

Tidak diketahui (frekuensi tidak dapat diperkirakan dari data yang tersedia)
- Penglihatan kabur

Efek samping yang telah diamati dengan obat serupa untuk inhalasi yang mengandung Beclometasone dipropionate anhydrous dan / atau Formoterol fumarate dihydrate adalah:
- Palpitasi
- Denyut jantung tidak teratur
- Tidak normal atau terganggunya indra perasa
- Nyeri otot dan kram otot
- Gelisah, pusing
- Merasa cemas
- Gangguan tidur
- Turunnya kadar kalium dalam darah
- Kenaikan / penurunan tekanan darah.

Menggunakan kortikosteroid inhalasi dosis tinggi dalam waktu lama dapat menyebabkan efek sistemik antara lain:
- Masalah fungsi kelenjar adrenal (adrenosupresi)
- Penipisan tulang
- Keterlambatan pertumbuhan pada anak-anak dan remaja
- Peningkatan tekanan pada mata (disebut glaukoma), katarak
- Penambahan berat badan yang cepat, terutama pada wajah dan torso
- Gangguan tidur, depresi atau merasa khawatir, resah, gugup, terlalu bersemangat atau cepat marah. Efek tersebut lebih cenderung terjadi pada anak-anak
- Perilaku abnormal

Pelaporan efek samping
Apabila ada keluhan efek samping atau kondisi tidak nyaman selama dan setelah penggunaan obat, konsultasikan ke dokter, apoteker, atau perawat. Anda dapat juga melaporkan keluhan efek samping atau konsisi tidak nyaman tersebut secara langsung ke Industri Farmasi melalui kontak berikut Indonesia.localPV@ZambonGroup.com Dengan melaporkan efek samping, Anda dapat membantu memberikan informasi lebih lanjut mengenai keamanan obat ini

5. Cara menyimpan Innovair Nexthaler

Jauhkan obat ini dari penglihatan dan jangkauan anak-anak.

Jangan gunakan obat ini setelah tanggal kedaluwarsa yang tercantum pada karton, kemasan dan label.
Tanggal kedaluwarsa mengacu pada hari terakhir bulan yang tercantum.

Simpan dalam kemasan aslinya untuk melindungi dari kelembaban. Hanya keluarkan inhaler dari kemasan sebelum digunakan pertama kali.

Sebelum pertama kali membuka kemasan :
Produk obat ini tidak memerlukan kondisi penyimpanan suhu khusus.

Setelah kemasan dibuka:
Simpan dibawah suhu 30^0C

Setelah kemasan dibuka, produk obat harus digunakan dalam waktu 2 bulan.
Gunakan label pada kotak untuk menuliskan tanggal Anda membuka kemasan.

Jangan membuang obat apapun melalui saluran pembuangan atau limbah rumah tangga.
Tanyakan apoteker Anda bagaimana cara membuang obat yang tidak Anda gunakan lagi. Langkah-langkah ini akan membantu melindungi lingkungan.

6. Isi kemasan dan informasi lainnya

Isi dari Innovair Nexthaler
Zat aktif: Beclometasone dipropionate anhydrous dan Formoterol fumarate dihydrate

Setiap dosis mengandung 100 mikrogram Beclometasone dipropionate anhydrous dan 6 mikrogram Formoterol fumarate dihydrate. Dosis yang dikeluarkan melalui mouthpiece adalah dari 81,9 mikrogram Beclometasone dipropionate anhydrous dan 5 mikrogram dari Formoterol fumarate dihydrate.

Bahan lainnya: Laktosa monohidrat (yang mengandung sejumlah kecil susu protein) dan magnesium stearat.

Seperti apa Innovair Nexthaler dan isinya
Produk obat ini dikemas berupa serbuk berwarna putih di dalam "plastik inhaler" yang disebut Nexthaler.
Dalam satu kemasan terdapat 1 Inhaler yang mengandung 120 inhalasi.

HARUS DENGAN RESEP DOKTER

Reg. No. DKI2060600667A1

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