ATIMOS 12 mcg
pressurised inhalation solution

Formoterol fumarate

COMPOSITION

Each actuation contains:
Active ingredient: Formoterol Fumarate Dihydrate 12 mcg
Excipients: anhydrous ethanol, 1N hydrochloric acid, HFA 134a (norfluran)

PHARMACEUTICAL FORM AND CONTENT

Pressurised solution for inhalation.
Pressurised container with standard actuator, sufficient for 100 inhalations.
The product does not contain any substances that might be harmful for stratospheric ozone.

THERAPEUTIC CLASS: selective agonist of beta$_2$-adrenergic receptors

THERAPEUTIC INDICATIONS

1. Prophylaxis and treatment of bronchoconstriction in patients with asthma as an add-on to inhaled glucocorticosteroid treatment.

2. Prophylaxis of bronchospasm induced by inhaled allergens, cold air, or exercise.

CONTRAINDICATIONS

Hypersensitivity to the active ingredient, or to any of the excipients, or any other chemically related substances. Tachyarrhythmiae, 3rd grade atrioventricular block, idiopathic hypertrophic subaortal stenosis, hypertrophic obstructive cardiomyopathy, idiopathic or drug-induced long-QT syndrome (QTc > 0.44 seconds), severe hyperthyroidism.
Generally contraindicated during pregnancy and lactation (see also "Special Warnings").

PRECAUTIONS FOR USE

Antiinflammatory therapy

In general, if a regular therapy with beta$_2$-agonists is required, asthmatic patients should receive a regular antiinflammatory therapy. Therefore, if treatment with ATIMOS is recommended, the additional necessity to prescribe an antiinflammatory therapy should also be evaluated.
When patients are already undergoing this therapy (inhaled or oral corticosteroids), this should be continued without any change, even when an improvement of symptoms occurs.
Should symptoms persist, or should a dose increase of ATIMOS become necessary, the possibility of worsening of the base disease and the need to revise the therapy should be considered.

Concomitant Diseases

Particular caution should be paid, in particular as far as the dose of ATIMOS is concerned, in patients concomitantly showing the following pathological conditions: ischemic cardiopathy, myocardial infarction, severe hypertension, cardiac arrhythmia, heart failure, coronary heart disease, occlusive vascular diseases, especially arteriosclerosis, diabetes mellitus, prostatic hypertrophy, glaucoma. Due to the hyperglycemic effect of beta$_2$-stimulants, in diabetic patients additional controls of glycemia should be prescribed.

Hypokalemia
Therapy with beta$_2$-agonists can potentially cause a serious hypokalemia. A particular caution should be paid in patients suffering from severe asthma, as this effect might be strengthened by hypoxia and by concomitant treatments.
It is recommended to monitor potassium plasma levels in patients with low basic potassium values or peculiar risks for decrease blood potassium level.

Paradoxical bronchospasm
As for other inhaling therapies, the possibility of paradoxical bronchospasm onset should be taken into consideration. In these cases, therapy should be immediately discontinued and another suitable therapy instituted.

It is recommended to strictly follow the recommended dosage instructions in order to avoid the onset of serious side effects, above all of cardiovascular type.

This medicinal product contains a small quantity of ethanol, lower than 100mg per dose.

DRUG INTERACTIONS
ATIMOS contains a small quantity of ethanol. The theoretical possibility of an interaction with disulfiram or metronidazole, in particularly sensitive subjects treated with these drugs.
Drugs such as quinidine, disopyramide, procainamide, phenothiazines, antihistaminics and tricyclic antidepressants can prolonge the QT interval and increase the risk of ventricular arrhythmiae (see also “Contraindications”).
Concomitant administration of other adrenergic drugs is not recommended, due to possible enhancement of the cardiovascular side effects.
The concomitant administration of ATIMOS to patients treated with MAO inhibitors or tricyclic antidepressants should be performed with caution, as the action of beta$_2$-agonists on the cardiovascular system can be increased.
Concomitant treatment with xanthines derivatives, steroids or diuretics may enhance the potassium lowering effect of beta$_2$ stimulants. Hypokalemia induced by beta$_2$ stimulants may increase the possibility of heart arrhytmiae occurrence in patients treated with digitalis (See also "Precautions of use").
Beta-blockers may decrease or antagonise the effects of ATIMOS. The drug should therefore not be concomitantly administered with beta-blockers (including eye drops), unless compelling reasons apply.

SPECIAL WARNINGS
For sportsmen: the use of the drug without therapeutic need is considered as doping: it can produce doping effects and positivity to anti-doping tests even at therapeutic doses.
The inhalatory administration is only allowed to prevent and/or treat asthma and asthma due to physical exercise.
Unwanted effects, such as tremor or agitation, when present, may affect the capacity to drive or operate machinery.
Pregnancy and lactation: safety of use of ATIMOS during pregnancy and lactation has not been established yet. Avoid its use as much as possible during pregnancy.
Like other beta$_2$ stimulants, formoterol can inhibit labour due to the relaxing effect on the smooth uterine muscles.
It is not known if formoterol passes into maternal milk. The substance was, however, found in the milk of treated rats. Mothers who are taking ATIMOS should not breast feed.

DOSAGE, METHOD AND FREQUENCY OF ADMINISTRATION

The dosage depends on the type and severity of disease.
Treatment is reserved for adults. Use of Atimos in children and adolescent is not recommended.

Asthma

Adults

***Maintenance therapy*:** one or two puffs of 12 mcg (12-24 mcg) twice a day. The maximum recommended maintenance dose is 48mcg per day.

If necessary, one or two additional puffs can be administered during the day to give relief from symptoms, provided the recommended daily maximum dose of 48mcg per day is not exceeded. However, if the need to take additional puffs becomes more frequent (for example more than two days a week) then a medical opinion should be sought to re-evaluate the therapy, because it could signify that the base illness is worsening.

Atimos should not be used to relieve the acute symptoms of an asthma attack. In the event of an attack, short acting β_2- agonist should be used.

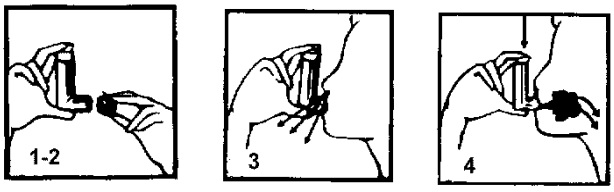
Prophylaxis of bronchospasm induced by inhaled allergens, cold air, or exercise

Adults

One 12 mcg puff should be inhaled approximately 15 minutes prior to exercise or exposure. Patients with severe asthma may need two 12 mcg puffs.

Instructions for use

Clinical efficacy and safety of Atimos inhaler in use with a spacer is not known, monitoring of condition is advised when product is use together with a spacer.
The successful result of the treatment depends on a correct use of the inhaler.
Inhaler test: to test the inhaler prior to using it for the first time (or if it has not been used for three days or more), remove the mouthpiece cover by carefully pressing the sides and then release one puff into the air to make sure that it works.
The following instructions should be carefully followed:



1)-2) Hold the inhaler between the thumb and forefinger, with the mouthpiece facing downwards, as shown in the figure. Remove the mouthpiece cover.
3) breathe out completely, then place the mouthpiece in your mouth and close your lips around it;
4) while breathing in through your mouth, press once with the forefinger.

Once the inspiration is complete, hold your breath for as long as possible.

When finished, replace the mouthpiece cover. The mouthpiece should be kept clean by washing with warm water, after having removed the pressurised canister.

OVERDOSE

Symptoms

An overdose of ATIMOS provokes typical symptoms of beta$_2$-stimulants such as nausea, vomiting, headache, tremors, drowsiness, palpitations, tachycardia, ventricular arrythmia, hypotension/hypertension, metabolic acidosis, hypokalemia, hyperglycemia.

Treatment

Symptomatic therapy or aspecific support. Hospitalization in severest cases. The use of cardioselective beta-blockers can be considered, however extreme caution should be taken when adopting such a treatment, as therapy with beta-blockers may provoke an acute asthma attack.

POSSIBLE SIDE EFFECTS

The frequency of Adverse Reactions has been classified as follows:
Common (> 1/100 < 1/10)
Uncommon (> 1/1,000 < 1/100)
Rare (> 1/10,000 < 1/1,000)
Very rare (< 1/10,000) including isolated reports

Blood and lymphatic system disorders
Very rare including isolated reports: thrombopenia

Cardiac disorders
Common: palpitations
Uncommon: tachycardia, tachyarrhythmia
Rare: ventricular extrasystoles, angina pectoris
Very rare including isolated reports: atrial fibrillation

Gastrointestinal disorders
Uncommon: nausea, dysgeusia

General disorders and administration site conditions
Very rare including isolated reports: peripheral oedema

Immune system disorders
Rare: angioneurotic oedema

Investigations
Uncommon: blood insulin increased, free fatty acids increased, blood ketone body increased
Rare: blood pressure increased, blood pressure decreased

Metabolism and nutrition disorders
Uncommon: hypokalaemia, hyperglycaemia

Musculoskeletal and connective tissue disorders
Uncommon: muscle cramps, myalgia

Nervous system disorders
Common: tremor, headache
Uncommon: restlessness, dizziness

Very rare including isolated reports: CNS stimulating effects have been sporadically reported following inhalation of β_2-sympathomimetics, manifesting as hyperexcitability. These effects were mainly observed in children up to 12 years of age.

Psychiatric disorders
Very rare including isolated reports: abnormal behaviour, sleep disorders, hallucinations

Renal and urinary disorders
Rare: nephritis

Respiratory, thoracic and mediastinal disorders
Common: cough
Uncommon: throat irritation
Rare: paradoxical bronchospasm
Very rare including isolated reports: dyspnoea, exacerbation of asthma

Skin and subcutaneous tissue disorders
Uncommon: pruritus, exanthema, hyperhidrosis
Rare: urticaria

Tremor, nausea, dysgeusia, throat irritation, hyperhidrosis, restlessness, headache, dizziness and muscle cramps may resolve spontaneously within one to two weeks of continued treatment.

SHELF-LIFE AND STORAGE

The shelf life is reported on the box. The validity period refers unopened product correctly stored in refrigerator at 2 – 8^{o}C. Do not use the medicine after the expiry date reported on the box.

For pharmacies: to ensure that there is a period of at least 3 month between the date of dispensing and the expiry date printed on the box.

Once in use, ATIMOS can be stored at room temperature of below 30 ^{o}C and must be used within a maximum of 3 months.

The pressurised canister must not be pierced. It must not be put, even when empty, near sources of heat. It must not be frozen or placed in direct sunlight.

Keep out of the reach and sight of children

Manufactured by:

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