

**PATIENT PACKAGE INSERT IN
ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) - 1986**

The medicine is dispensed with a
doctor's prescription only

Trimbow

Pressurised inhalation solution

Composition

**The active ingredients and their quantities:
Each delivered dose (the dose leaving the
mouthpiece) contains:**

87 micrograms of beclometasone dipropionate,
5 micrograms of formoterol fumarate dihydrate,
9 micrograms of glycopyrronium (as 11
micrograms glycopyrronium bromide).

Inactive ingredients and allergens: see
section 6 in the leaflet "Further information".

**Read this leaflet carefully in its entirety
before using the medicine.** This leaflet contains
concise information about the medicine. If you
have further questions, refer to the doctor or
pharmacist.

This medicine has been prescribed to treat your
ailment. Do not pass it on to others. It may harm
them even if it seems to you that their ailment
is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Trimbow is indicated for maintenance treatment
in adult patients with moderate to severe chronic
obstructive pulmonary disease (COPD) who
are not adequately treated by a combination
of an inhaled corticosteroid and a long-acting
beta2-agonist or a combination of a long-acting
beta2-agonist and a long-acting muscarinic
antagonist.

Trimbow is a medicine to help breathing that
contains the three active substances:

- beclometasone dipropionate,
- formoterol fumarate dihydrate and
- glycopyrronium.

Beclometasone dipropionate belongs to a
group of medicines called corticosteroids which
act to reduce the swelling and irritation in your
lungs.

Formoterol and glycopyrronium are medicines
called long-acting bronchodilators. They act
in different ways to relax the muscles in your
airways, helping to open the airways wider and
allowing you to breathe more easily.

Regular treatment with these three active
substances helps to relieve and prevent
symptoms such as shortness of breath,
wheezing (breathing with a whistling sound)
and cough in adult patients with COPD. Trimbow
can reduce exacerbations (flare-ups) of COPD
symptoms. COPD is a serious long-term
disease in which the airways become blocked
and air sacs inside the lungs become damaged,
leading to difficulty breathing.

Therapeutic group:

Drugs for obstructive airway diseases, adrenergics
in combination with anticholinergics including
triple combinations with corticosteroids.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active
ingredients (beclometasone dipropionate,
formoterol fumarate dihydrate or
glycopyrronium) or to any of the other
ingredients of this medicine (listed in
section 6 "Further information").

Special warnings regarding use of the medicine:

Trimbow is used as a maintenance treatment for
your COPD. Do not use this medicine to treat a
sudden attack of breathlessness or wheezing.

If your breathing gets worse:

If you develop worsening shortness of breath or
wheezing, straight after inhaling your medicine,
stop using Trimbow inhaler and use your quick-
acting "reliever" inhaler straightaway. You should
contact your doctor straightaway. Your doctor
will assess your symptoms and if necessary
may start you on a different treatment.

See also section 4, "Side effects".

If your COPD gets worse:

If your symptoms get worse or are difficult to
control (e.g. if you are using a separate "reliever"
inhaler more frequently) or if your "reliever"
inhaler does not improve your symptoms, see
your doctor immediately. Your COPD may be
getting worse and your doctor may need to
prescribe a different treatment.

Before using the medicine, inform the doctor if:

- you have any heart problems, such as angina
(heart pain, pain in the chest), a recent heart
attack (myocardial infarction), heart failure,
narrowing of the arteries around your heart
(coronary heart disease), disease of your
heart valves or any other abnormalities of
your heart or if you have a condition known
as hypertrophic obstructive cardiomyopathy
(also known as HOCM, a condition where the
heart muscle is abnormal).
- you have disorders of your heart rhythm such
as irregular heart rate, a fast pulse rate or
palpitations or if you have been told that your
heart trace (ECG) is abnormal.
- you have narrowing of the arteries (also
known as arteriosclerosis), if you have high
blood pressure or if you have an aneurysm
(abnormal bulging of the blood vessel wall).
- you have an overactive thyroid gland.
- you have low blood levels of potassium
(hypokalaemia). The combination of
Trimbow with some other COPD medicines
or medicines such as diuretics (medicines
that make the body lose water, to treat heart
disease or high blood pressure), can cause
a sharp fall in your blood level of potassium.
Therefore, your doctor may wish to measure
the potassium levels in your blood from time
to time.
- you have any disease of your liver or kidneys.
- you have diabetes. High doses of formoterol
may increase your blood glucose and
therefore you may need to have extra blood
tests to check your blood sugar when you
start using this medicine, and from time to
time during treatment.
- you have a tumour of the adrenal gland
(known as a pheochromocytoma).
- you are due to have an anaesthetic.
Depending on the type of anaesthetic, it may
be necessary to stop using Trimbow at least
12 hours before the anaesthesia.
- you are being, or have ever been, treated
for tuberculosis (TB) or if you have a chest
infection.
- you have an eye problem called narrow-angle
glaucoma.
- you have difficulty passing urine.
- you have an infection of the mouth or throat.

If any of the above applies to you, tell your
doctor before you use Trimbow.

If you have or have had any medical problems
or any allergies or if you are not sure if you can
use Trimbow, talk to your doctor or pharmacist
before using the inhaler.

If you are already using Trimbow

If you are using Trimbow or high doses of other
inhaled corticosteroids over long periods and
you come into a situation of stress (e.g. being
taken to hospital after an accident, having a
serious injury or before an operation) you may
need more of this medicine. In such a situation,
your doctor may need to increase your dose of
corticosteroids to cope with the stress and may
prescribe them as tablets or injections.

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

Children and adolescents

The medicine is not intended for use in children and adolescents under 18 years of age.

Tests and monitoring

Trimbow does not contain a high-dose inhaled corticosteroid, but your doctor may wish to measure the cortisol levels in your blood from time to time.

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines, and nutritional supplements, inform the doctor or pharmacist. Particularly if you are taking:

- medicines similar to Trimbow used for your lung disease.
- Some medicines may increase the effects of Trimbow and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat).
- **Do not use this medicine with a beta-blocker medicine** (used for treating certain heart problems such as angina or for reducing blood pressure) unless your doctor has chosen a beta-blocker that does not affect your breathing. Beta-blockers (including beta-blocker eye-drops) may reduce the effects of formoterol or make it not work at all. On the other hand, using other beta2-agonist medicines (which work in the same way as formoterol) may increase the effects of formoterol.

Using Trimbow together with:

- medicines for treating
 - abnormal heart rhythms (quinidine, disopyramide, procainamide),
 - allergic reactions (antihistamines),
 - symptoms of depression or mental disorders such as monoamine oxidase inhibitors (for example phenelzine and isocarboxazid), tricyclic antidepressants (for example amitriptyline and imipramine), phenothiazinescan cause some changes in the electrocardiogram (ECG, heart trace). They may also increase the risk of disturbances of heart rhythm (ventricular arrhythmias).
- medicines for treating Parkinson's disease (levodopa), to treat an underactive thyroid gland (levothyroxine), medicines containing oxytocin (which causes uterine contraction) and alcohol can increase the chances of formoterol side effects on the heart.
- monoamine oxidase inhibitors (MAOIs), including medicines with similar properties like furazolidone and procarbazine, used to treat mental disorders, can cause a rise in blood pressure.
- medicines for treating heart disease (digoxin) can cause a fall in your blood potassium level. This may increase the likelihood of abnormal heart rhythms.
- other medicines used to treat COPD (theophylline, aminophylline or corticosteroids) and diuretics may also cause a fall in your potassium level.
- some anaesthetics can increase the risk of abnormal heart rhythms.
- Disulfiram, a medicine used in the treatment of people with alcoholism (drinking problems) or metronidazole, an antibiotic to treat infection in your body can cause side effects (e.g. feeling sick, being sick, stomach pain) due to the small amount of alcohol in Trimbow.

Pregnancy, breast-feeding and fertility

There are no experience or safety data from the use of Trimbow in pregnant or breast-feeding women.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

You should only use Trimbow during pregnancy if you are advised to do so by your doctor. It is preferable to avoid the use of Trimbow during labour due to the inhibitory effects of formoterol on uterine contractions.

You should not use Trimbow during breast-feeding. You and your doctor must make a decision whether to discontinue breast-feeding or to discontinue/abstain from Trimbow therapy taking into account the benefit of breast-feeding for your child and the benefit of therapy for you.

Driving and using machines

It is unlikely that this medicine will affect your ability to drive and use machines.

Important information about some of the ingredients of the medicine

Trimbow contains a small amount of alcohol (ethanol). Every actuation (puff) from your inhaler contains 8.9 mg of ethanol.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions.

Check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen of the medicine. **The dosage and treatment regimen will be determined by the doctor only.**

Adults

The usual dose is two puffs in the morning and two puffs in the evening.

If you feel that the medicine is not very effective, talk to your doctor.

If you have been using a different inhaler containing beclometasone dipropionate previously, ask your doctor for advice, as the effective dose of beclometasone dipropionate in Trimbow for the treatment of COPD may be lower than that of some other inhalers.

Do not exceed the recommended dose.

Route of administration

Trimbow is for inhalation use.

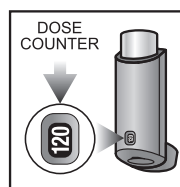
You should inhale the medicine through your mouth and this takes the medicine directly into your lungs.

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

Testing your inhaler

Before using the inhaler for the first time, you should test your inhaler to make sure that it is working properly, as follows:

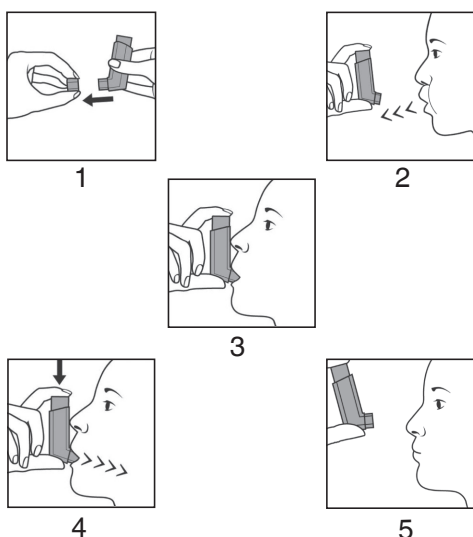
1. Check that the dose counter reads 121
2. Remove the protective cap from the mouthpiece
3. Hold your inhaler upright with the mouthpiece at the bottom
4. Direct the mouthpiece away from yourself and firmly press the pressurised container to release one puff
5. Check the dose counter. If you are testing your inhaler for the first time, the counter should read 120:



How to use your inhaler

Stand or sit up when inhaling.

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



1. Remove the protective cap from the mouthpiece and check that the mouthpiece is clean and free from dust and dirt.
2. Breathe out as slowly and deeply as possible, in order to empty your lungs.
3. Hold the inhaler upright with the mouthpiece at the bottom and place the mouthpiece between your teeth without biting it. Then place your lips around the mouthpiece, with the tongue flat under it.
4. Breathe in slowly and deeply through your mouth to fill your lungs with air (this should take about 4–5 seconds). Just after starting to breathe in, press down firmly on the top of the pressurised container to release one puff.
5. Hold your breath for as long as possible and, finally, remove the inhaler from your mouth and breathe out slowly. Do not breathe out into the inhaler.
6. Check that the dose counter (120 puffs) has moved down by one.

For the second puff, keep the inhaler in the upright position for about half a minute, then repeat steps 2 to 5.

If you see 'mist' coming from the top of the inhaler or the sides of your mouth, this means that Trimbow will not be getting into your lungs as it should. Take another puff, following the instructions starting again from step 2.

After use, replace the protective cap.

To prevent a fungal infection in the mouth and throat, rinse your mouth or gargle with water without swallowing it or brush your teeth after each use of your inhaler.

When to get a new inhaler

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

If you have a weak grip, it may be easier to hold the inhaler with both hands: hold the upper part of the inhaler with both index fingers and its lower part with both thumbs.

If you find it difficult to use the inhaler while starting to breathe in, you may use the AeroChamber Plus spacer device. Ask your doctor or pharmacist about this device.

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

Cleaning of the Trimbow inhaler

You should clean your inhaler once a week.

1. Do not remove the pressurised container from the inhaler and do not use water or other liquids to clean your inhaler.
2. Remove the protective cap from the mouthpiece by pulling it away from your inhaler.
3. Wipe inside and outside of the mouthpiece and the inhaler with a clean, dry cloth or tissue.
4. Replace the mouthpiece cap.

If you use more Trimbow than you should

It is important that you take your dose as advised by your doctor. Do not exceed your prescribed dose without talking to your doctor.

If you use more Trimbow than you should, side effects, as described in section 4, may occur.

Tell your doctor if you have used more Trimbow than you should and if you experience any of these symptoms. Your doctor may wish to carry out some blood tests.

If you took an overdose, or if a child accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the medicine package with you.

If you forget to use Trimbow

Use it as soon as you remember. If it is almost time for your next dose, do not take the dose you have missed, but just take the next dose at the correct time. Do not double the dose.

If you stop using Trimbow

It is important to use Trimbow every day. Do not stop using Trimbow or lower the dose, even if you are feeling better or you have no symptoms. Adhere to the treatment regimen recommended by your doctor.

Even if you are feeling better, do not stop taking the medicine or lower the dose. If you want to do this, talk to your doctor.

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have further questions regarding the use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of Trimbow may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

There is a risk of worsening shortness of breath and wheezing immediately after using Trimbow and this is known as paradoxical bronchospasm (may affect up to 1 in 1,000 patients). If this occurs you should stop using Trimbow and use your quick-acting "reliever" inhaler straightaway to treat the shortness of breath and wheezing. You should contact your doctor straightaway.

Tell your doctor immediately

- if you experience any allergic reactions like skin allergies, hives, skin itching, skin rash (may affect up to 1 in 100 users), reddening of the skin, swelling of the skin or mucous membranes especially of the eyes, face, lips and throat (may affect up to 1 in 1,000 users).
- if you experience eye pain or discomfort, temporary blurring of vision, visual halos or coloured images in association with red eyes. These may be signs of an acute attack of narrow-angle glaucoma (may affect up to 1 in 10,000 users).

Tell your doctor if you have any of the following while using Trimbow as they could be symptoms of a lung infection (may affect up to 1 in 10 users):

- fever or chills
- increased mucus production, change in mucus colour
- increased cough or increased breathing difficulties.

Possible side effects are listed below according to their frequency.

Common side effects (appear in 1-10 users out of 100):

- sore throat
- runny or stuffy nose and sneezing
- fungal infections of the mouth. Rinsing your mouth or gargling with water and brushing your teeth immediately after inhalation may help to prevent these side effects
- hoarseness
- headache
- urinary tract infection

Uncommon side effects (appear in 1-10 users out of 1,000):

- flu
- inflammation of the sinuses
- itchy, runny or blocked nose
- fungal infections of the throat or of the food pipe (oesophagus)
- fungal infections of the vagina
- restlessness
- trembling
- dizziness
- abnormal or reduced sense of taste
- numbness
- inflammation of the ear
- irregular heart beat
- changes in the electrocardiogram (heart trace)
- unusually fast heart beat and disorders of the heart rhythm
- palpitations (feeling of abnormal beating of the heart)
- reddening of the face
- increased blood flow to some tissues in the body
- cough and productive cough
- irritation of the throat
- nose bleeds
- dry mouth
- diarrhoea
- swallowing difficulties
- feeling sick
- upset stomach
- stomach discomfort after meals
- burning sensation of the lips
- tooth decay
- skin rash, hives, skin itching
- inflammation of the mucous membrane of the mouth with or without ulcers
- increased sweating
- muscle cramps and pain in muscles
- pain in arms or legs
- pain in muscles, bones or joints of the chest
- tiredness
- increase of blood pressure
- fall in the level of some constituents of your blood: of certain white blood cells called granulocytes, of potassium or of cortisol
- increase in the level of some constituents of your blood: glucose, C-reactive protein, number of platelets, insulin, free fatty acid or ketones.

Rare side effects (appear in 1-10 users out of 10,000):

- fungal infections of the chest
- decreased appetite
- sleep disorders (sleeping too little or too long)
- crushing chest pain
- sensation of a missed heart beat, unusually slow heart beat
- leakage of blood from a vessel into the tissues surrounding it
- decrease of blood pressure
- weakness
- pain in the back of the mouth and throat
- inflammation and redness of the pharynx
- dry throat
- painful and frequent urination
- difficulty and pain when passing urine
- inflammation of the kidneys.

Very rare side effects (appear in less than one user out of 10,000):

- low level in the number of certain blood cells called platelets
- feeling breathless or short of breath
- swelling of the hands and feet
- growth retardation in children and adolescents.

Side effects with unknown frequency (frequency cannot be estimated from the available data):

- blurred vision.

Using high-dose inhaled corticosteroids over a long time can cause in very rare cases effects on the body:

- problems with how your adrenal glands work (adrenal suppression)
- decrease in bone mineral density (thinning of the bones)
- clouding of the lens of your eyes (cataract).

The following side effects can also occur with high-dose inhaled corticosteroids used over a long time, but the frequency is not known (frequency cannot be estimated from the available data) at present:

- depression
- feeling worried, nervous, over-excited or irritable.

These events are more likely to occur in children.

If one of the side effects appears or worsens, or if you suffer from side effects that were not mentioned in the leaflet, consult your doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health through link "reporting side effects due to drug treatment" located in the home page of the Ministry of Health website (www.health.gov.it) which refers to an online form, or by entering the following link:

<https://sideeffects.health.gov.it>

Additionally, you may also report to Kamada Ltd by email:

pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.

Do not use after the expiry date (Exp. date) which is stated on the carton and label. The expiry date refers to the last day of that month. Prior to dispensing to the patient (information for the pharmacist):

Store in a refrigerator (2°C-8°C).

Do not freeze.

After dispensing to the patient (information for the patient):

The inhaler may be stored for a maximum of 4 months at a temperature up to 25°C.

Do not expose to temperatures higher than 50°C.

Do not pierce the pressurised container.

The medicine should not be disposed via waste water or household waste. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredients, this medicine also contains:

Norflurane (HFA 134a), Ethanol anhydrous, Hydrochloric acid 1M

What does the medicine look like and the contents of the pack

Trimbow is a pressurised inhalation, solution.

Trimbow comes in a pressurised container (coated aluminium), with a metering valve. The pressurised container is inserted in a plastic inhaler. This incorporates a mouthpiece provided with a plastic protective cap, and a dose counter.

Each pack contains one canister which provides 120 actuations (puffs).

Manufacturer

Chiesi Farmaceutici S.p.A., Parma, Italy.

License holder

Kamada Ltd.,

Beit Kama

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Registration number of the medicine in the National Drug Registry of the Ministry of Health: 164-94-36103