Patient Leaflet According to the Pharmacists' Regulations (Preparations) – 1986

This medicine is sold with a doctor's prescription only

Flutiform 50/5
Flutiform 125/5
Flutiform 250/10
Suspension for Inhalation

Active ingredients:

Each **Flutiform 50/5** inhaler actuation contains:
Fluticasone propionate 50 mcg and formoterol fumarate dihydrate 5 mcg.

Each **Flutiform 125/5** inhaler actuation contains:
Fluticasone propionate 125 mcg and formoterol fumarate dihydrate 5 mcg.

Each **Flutiform 250/10** inhaler actuation contains:
Fluticasone propionate 250 mcg and formoterol fumarate dihydrate 10 mcg.

For the list of additional ingredients, see section 6.
See also 'Important information about some of the medicine's ingredients' in section 2.
Read the leaflet carefully in its entirety before using the medicine.
This leaflet contains concise information about the medicine. If you have any further questions, please refer to your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.
The use of Flutiform 50/5 is not intended for children under 5 years of age.
The use of Flutiform 125/5 is not intended for children under 12 years of age.
The use of Flutiform 250/10 is not intended for children and adolescents under 18 years of age.

1. What is the medicine intended for?

The medicine is intended for treatment of asthma patients, in cases suited for combined treatment of corticosteroids and long-acting beta agonists by inhalation.

Fluticasone propionate helps to reduce swelling and inflammation in the lungs.

Formoterol fumarate dihydrate is a long-acting bronchodilator which helps the airways in your lungs stay open, making it easier for you to breathe.

Therapeutic groups:
Fluticasone propionate: corticosteroids.
Formoterol fumarate dihydrate: beta agonist (long-acting).

2. Before using the medicine

Do not use the medicine if:

You are sensitive (allergic) to the active ingredients or to any of the other ingredients the medicine contains (for a list of the other ingredients, see section 6).

Special warnings regarding the use of this medicine:

Tell your doctor before (and during) the treatment with Flutiform if you are suffering or have suffered in the past from:

- Tuberculosis: the symptoms include a persistent cough with blood-streaked phlegm, fever, tiredness, loss of appetite, weight loss, night sweats.
- Tonsil or respiratory tract infection (bacterial, viral, fungal or other).
- Heart problems such as: problems with the blood flow to your heart or narrowing of one of your heart valves (the aortic valve), heart failure (can cause shortness of breath and/or ankle swelling), a condition where the heart muscle is enlarged, an irregular heart beat or if you have been told that your heart trace is abnormal (prolongation of the QTc interval);
- An abnormal bulging of a blood vessel wall (aneurysm).
- Impaired functioning of the adrenal gland (including a condition where it was damaged as a result of steroid treatment) such as: headache, weakness, tiredness, abdominal pain, loss of appetite, weight loss, dizziness, low blood pressure, diarrhea, feeling unwell or a tumor of the adrenal gland.
- Diabetes
- High blood pressure
- An overactive thyroid gland which can cause increased appetite, weight loss, sweating.
- Low blood potassium levels (can cause muscle weakness, twitching or abnormal heart rhythm).
- Liver problems.

Additional warnings:

- If you are going to have **surgery**, or are **extremely stressed**, inform your doctor, as you may need additional steroid treatment in order to control your asthma.
- Flutiform is not intended for treatment of a sudden asthma attack. You must keep at hand an inhaler for immediate relief of asthma attacks.
- Contact your doctor if you experience blurred vision or other visual problems.

Use in Children:

The use of Flutiform 50/5 is not intended for children under 5 years of age.
The use of Flutiform 125/5 is not intended for children under 12 years of age.
The use of Flutiform 250/10 is not intended for children and adolescents under 18 years of age.

Tests and follow-up:

- The doctor will monitor your asthma symptoms and your response to the treatment.
- Diabetic patients may need closer monitoring.
- In certain cases, your doctor may test your blood potassium levels.
- In children over the age of 5 using the medicine for a long period, monitoring of growth is recommended.

Drug interactions:

If you are taking, or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, please tell your doctor or pharmacist. Especially if you are taking:

- Medicines of the beta-blocker class such as: atenolol, propranolol, sotalol or metoprolol (for treatment of blood pressure and heart problems), timolol (for instance in eye drops for treatment of glaucoma).
- Certain medicines used to treat asthma and breathing problems such as: theophylline or aminophylline.

- Medicines containing adrenaline or related substances including other beta-agonists like salbutamol, atenolol, metoprolol, propranolol, timolol). Additional long-acting beta-agonists should not be used together with this inhaler. If your asthma becomes worse between doses of Flutiform, you should use the inhaler intended for immediate relief of asthma attacks.
- Antihistamines (for allergy treatment). Diuretics (for treating high blood pressure or fluid buildup).
- Medicines for treatment of heart problems such as: digoxin, quinidine, disopyramide, procainamide.
- Medicines to treat mental problems or depression such as: tricyclic antidepressants (for example: amitriptyline, imipramine), monoamine oxidase inhibitors (for example: phenelzine, isocarboxazid). You must inform your doctor if you have taken these medicines in the last two weeks.
- Medicines to treat psychiatric problems (such as phenothiazines, antipsychotics).
- Other medicines containing steroids.
- Antifungals such as: ketoconazole, itraconazole.
- Some medicines may increase the effects of Flutiform and your doctor may wish to monitor your condition if you are taking these medicines concurrently with Flutiform. These medicines include inter alia certain medicines for treatment of AIDS/the HIV virus such as: ritonavir, atazanavir, indinavir, nelfinavir, saquinavir, cobicistat.
- Antibiotics such as: clarithromycin, telithromycin, furazolidone.
- Levodopa (for treatment of Parkinson's disease).
- Levothyroxine (for treatment of an underactive thyroid gland).
- Oxytocin (medicine to induce labor).
- Procarbazine (for treatment of Hodgkin's disease).
- Anesthetics (used in surgery).

Use of the medicine and alcohol consumption: consult your doctor.

Pregnancy and breastfeeding:
If you are pregnant, think you are pregnant, plan to become pregnant or if you are breastfeeding, consult your doctor before using the medicine.

Driving and use of machinery:
This medicine is unlikely to affect your ability to drive or use machines.

Important information about some of the medicine's ingredients:
- Flutiform contains small amounts (1 mg per inhalation actuation) of ethanol (alcohol).
- Flutiform contains a small amount of sodium cromoglicate. If you are using an additional preparation that contains sodium cromoglicate, you can use it as usual.

3. How to use this medicine?

Always use according to the doctor's instructions. You should check with your doctor or pharmacist if you are not sure regarding the dosage and the manner of treatment.
The dosage and the manner of treatment will be determined by the doctor only. Your doctor will prescribe the dose required for treatment of your asthma.

The standard dosage for adults, adolescents and children over 5 years of age is usually: two actuations (puffs) in the morning and two in the evening.

The use of the highest Flutiform dosage (Flutiform 250/10) is intended only for adults. Do not use Flutiform 250/10 in children and adolescents under 18 years of age.
The use of the medium Flutiform dosage (Flutiform 125/5) is intended only for adults and adolescents over 12 years of age. Do not use Flutiform 125/5 in children under 12 years of age.

The use of the lowest Flutiform dosage (Flutiform 50/5) is intended only for children, adolescents and adults over 5 years of age. Do not use Flutiform 50/5 in children under 5 years of age.

Do not exceed the recommended dosage.
Attention! This medicine is intended for inhalation only.

Instructions for use:
The medicine is contained in an aerosol can which sits inside a plastic actuator (the inhaler). The inhaler includes a dosimeter that shows you how many metered inhalation doses still remain in the inhaler, after it has been primed (see Diagram 1). The dosimeter is color-coded: it starts off green; when there are less than 50 metered doses left it changes to yellow; and when there are less than 30 metered doses left it changes to red. The dosimeter counts down from 120 to 60 in intervals of 10, and from 60 to 0 in intervals of 5.* When the dosimeter is near to 0, you must contact your doctor in order to receive a prescription for a new inhaler. Do not use your inhaler when the counter reads zero.

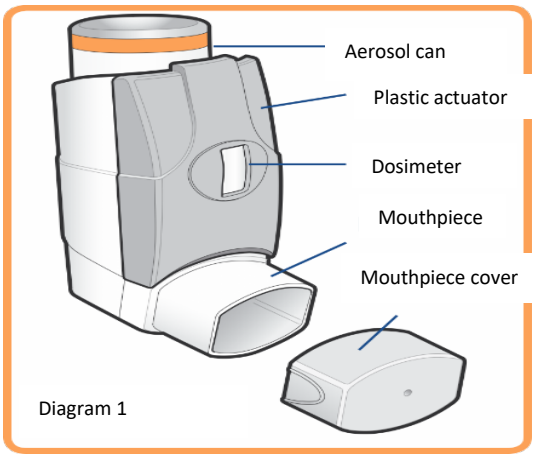


Diagram 1

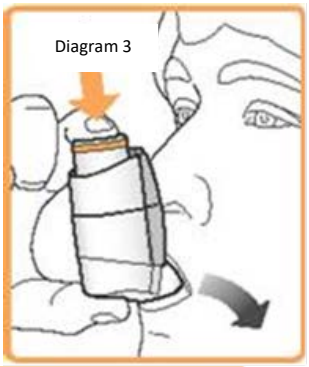
Preparation of the inhaler:
- **Before you use your inhaler for the first time or if it has not been used for more than 3 days**, it must be 'primed' to ensure it works properly and releases the correct dose.
- **If your inhaler has been exposed to freezing temperatures** it must be allowed to warm at room temperature for 30 minutes then it must be 'primed' to ensure it works properly and releases the correct dose.

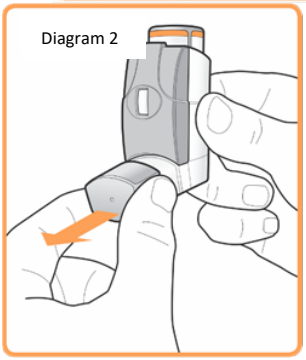
To prime the inhaler:
- Remove the mouthpiece cover and shake the inhaler well.
- Point the mouthpiece away from you and release four puffs into the air. To release each puff (actuation) press down on the aerosol can.

Using your inhaler:
If you feel shortness of breath, wheezing or breathing difficulties while using the inhaler, you should continue to use Flutiform but go to your doctor as soon as possible, as you may need additional treatment.

Perform the following steps, making sure to perform steps 2 to 5 slowly:
1. Remove the mouthpiece cover (see Diagram 2) and check that your inhaler is clean and free from dust.
2. Shake the inhaler immediately before release of every puff (actuation), to ensure that the contents of the inhaler are uniform,
3. Sit upright or stand. Breathe out as slowly and as deeply as possible.

4. Hold the inhaler upright with your thumb on the base of the inhaler under the mouthpiece and your forefinger on the top of the inhaler. Place the mouthpiece inside your mouth tightening your lips around it. Do not bite the mouthpiece (see Diagram 3).
5. Breathe in slowly and deeply through your mouth and, at the same time, press down on the aerosol can to release one puff (actuation). Continue to breathe in deeply (ideally for about 4-5 seconds).
6. While holding your breath, remove the inhaler from your mouth. Continue to hold your breath for as long as you can (ideally about 10 seconds). And breathe out slowly. Do not breathe out into the inhaler.
7. For release of the metered amount for the second inhalation, hold the inhaler upright for about 30 seconds and then repeat stages 2 to 6.
8. Replace the mouthpiece cover.





You can practice in front of a mirror.
If you see a 'mist' from the top of the inhaler or around your mouth when you use your inhaler then you may not have inhaled your medicine properly. Take another dose by repeating from Step 2 onwards.

- After using the inhaler, rinse your mouth out, gargle with water or brush your teeth. These actions can help reduce the risk of developing a fungal infection, a sore mouth and throat or a hoarse voice.
- If you have weak hands it may be easier to hold the inhaler in both hands placing both index fingers on the aerosol can and both thumbs on the base of the inhaler.
- If necessary, and in consultation with your doctor or pharmacist, you can use a spacer device (AeroChamber Plus).

Cleaning the inhaler:
Clean your inhaler once weekly and carefully follow the cleaning instructions:
- Remove the mouthpiece cover. Do not remove the aerosol can from the plastic actuator.

- Clean the inside and outside of the mouthpiece and the plastic actuator with a clean dry cloth or tissue.
- Replace the mouthpiece cover.
- The metal canister must not come into contact with water.

If you accidentally took a higher dosage contact your doctor for advice.

If serious overdose symptoms appear or a child used the medicine or swallowed it, proceed immediately to a doctor or hospital emergency room to receive medical assistance. Bring the medicine package with you. Overdose symptoms include: severe chest pain, high or low blood pressure, headache, muscle cramps, difficulty in sleeping, nervousness, dry mouth, loss of appetite, seizures, convulsions, tremor, dizziness, fainting, tiredness feeling sick or generally unwell. There may also be changes in the rate of your heart beat, low blood potassium levels, an increase or decrease in the amount of sugar in your blood, abdominal pain, nausea, vomiting, weight loss, decreased level of consciousness (which could make you feel confused and drowsy).

If you have taken more than the prescribed dose for a long period of time, you should talk to your doctor because large doses may reduce the amount of steroid hormones produced normally in your body (see 'Side Effects' section).

If you forgot to use the inhaler at the set time, take the dose as soon as you remember. If it is time for the next dose, skip the forgotten dose. Do not take a double dose to compensate for the forgotten dose.

Adhere to the treatment as recommended by your doctor.
Even if your state of health improves, do not stop the treatment with this medicine without consulting your doctor or pharmacist.
If you stop taking the medicine: you must make sure to use the inhaler every day as directed by your doctor, in order to control your asthma, even if you feel well. If you want to stop using your inhaler, talk to your doctor. Your doctor will decide on how to do this, usually by decreasing the dose gradually so as not to trigger an asthma attack.

Do not take or use any medicines in the dark! Carefully check the label and dose each time you take the medicine. Wear glasses if you need them.
If you have further questions concerning the use of the medicine, consult your doctor or pharmacist.

4. Side effects

As for any medicine, the use of Flutiform may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them. Your doctor will prescribe the lowest dose necessary to control your asthma which may reduce the possibility of side effects occurring.

Contact a doctor immediately if the following side effects appear:

- Allergic reaction. A severe allergic reaction is rare. Symptoms of an allergic reaction include: sudden swelling of the eyelids, face, throat, tongue or lips, rash or itching (especially those covering the whole body), dizziness, light-headedness, fainting, sudden change in your breathing pattern (such as increased wheezing or shortness of breath).

- Blurred vision or other problems with vision.

Stop using the inhaler and contact your doctor, if immediately after use of Flutiform you notice an increase in wheezing and shortness of breath. In this case use the inhaler you have for cases in which you need immediate relief and contact your doctor at once.

Additional side effects:

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

- Worsening of asthma.
- Headache, shaking, irregular or strong heartbeats (palpitations); dizziness; difficulty in sleeping; insomnia; alteration of voice, hoarse voice; dry mouth, sore or irritated throat; rash.

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

- Increase in blood sugar level. If you are diabetic you may need to check your blood sugar more often and adjust your diabetic treatment. The doctor may carry out monitoring more frequently.
- Fungal infection in the mouth and throat; inflammation of the sinuses (sinusitis); rapid heartbeat; chest pain associated with heart disease; muscle cramps; coughing or shortness of breath; diarrhea; indigestion; changes in sense of taste; feeling of spinning (vertigo); abnormal dreams; agitation; itchy skin; high blood pressure; a feeling of unusual weakness; swelling of hands, feet or ankles (edema).

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- Blurred vision, sleeping problems, feeling worried or depressed, aggression, anxiety, restlessness, nervousness, over-excitement, irritability (these side effects are more frequent in children).

- The following side effects are associated with use of formoterol fumarate: low blood potassium levels (can cause muscle weakness, twitching, abnormal heart rhythm), QTc interval prolongation in heart trace, high level of lactic acid in the blood, nausea, muscle pain.
- The use of inhaled steroids can affect the normal production of steroid hormones in your body, particularly if you use high doses for a long time. The effects includes: changes in bone mineral density (thinning of the bones); cataract, glaucoma (increased pressure in the eye), bruising or thinning of the skin; increased risk of catching an infection, slowing of the rate of growth of children and adolescents, round (moon shaped) face, an effect on the adrenal gland (a small gland next to the kidney) which means you may have symptoms such as weakness, tiredness, difficulty in coping with stress, abdominal pain, loss of appetite, weight loss, headache, dizziness, very low blood pressure, diarrhea, nausea, vomiting, seizures.

These effects are less likely to happen with inhaled steroids than with steroid tablets.

If a side effect appears, if any of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult your doctor.

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. How to store the medicine?

Avoid poisoning! This medicine, and any other medicine, must be stored in a closed place out of the reach and sight of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: store below 25°C. Do not refrigerate or freeze.
- If your inhaler has been exposed to freezing temperatures it must be allowed to warm at room temperature for 30 minutes then it must be ‘primed’ before use (see section 3 'How to use this medicine').

- Do not use the inhaler for more than 3 months after it has been removed from the foil pouch or if the dosimeter reads "0" (zero).
- Do not expose to temperatures higher than 50°C. The aerosol can contains a pressurized liquid so do not puncture, break or burn the can even when apparently empty.

6. Additional information

- **In addition to the active ingredient, the preparation also contains the following ingredients:**
  Sodium cromoglicate, ethanol, hydrofluoroalkane (HFA 227)

- **What does the medicine look like and what does the package contain?**
  The inhaler includes the aerosol can which contains a white suspension, in a white and gray plastic actuator. The mouthpiece cover is light gray.
  Each inhaler contains 120 puffs (actuators).
  There is one inhaler in a pack.

Registration holder: Rafa Laboratories Ltd., PO Box 405, Jerusalem 9100301.
Manufacturer: Recipharm HC Ltd., Cheshire, England

Medicine registration number in the National Medicines Registry of the Ministry of Health:

Flutiform 50/5: 150 62 33812
Flutiform 125/5: 150 63 33813
Flutiform 250/10: 150 64 33814

Approved in March 2021