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

The medicine is dispensed with a doctor's prescription only

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

Active ingredients:

Each inhaler puff of **Flutiform 50/5** contains:
50 mcg fluticasone propionate and 5 mcg formoterol fumarate dihydrate.

Each inhaler puff of **Flutiform 125/5** contains:
125 mcg fluticasone propionate and 5 mcg formoterol fumarate dihydrate.

Each inhaler puff of **Flutiform 250/10** contains:
250 mcg fluticasone propionate and 10 mcg formoterol fumarate dihydrate.

For the list of other ingredients, see section 6.
See also 'Important information about some of the medicine's ingredients' in section 2.
Read this entire leaflet carefully 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 for the treatment of 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 with 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 the lungs to stay open, making it easier 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 often with blood-streaked phlegm, fever, tiredness, loss of appetite, weight loss, night sweats.
- An infection of the lungs or airways (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 heartbeat 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 (an aneurysm).
- Diabetes
- High blood pressure
- An overactive thyroid gland which can cause increased appetite, weight loss or sweating.
- Low blood levels of potassium that can cause muscle weakness, twitching or abnormal heart rhythm.
- Poor adrenal gland function (if your adrenal gland is not working properly, you may have symptoms such as: headaches, weakness, tiredness, abdominal pain, loss of appetite, weight loss, dizziness, very low blood pressure, diarrhoea, feeling or being sick or fits) or a tumor of the adrenal gland (phaeochromocytoma).
- Liver problems.

Additional warnings:

- If you are going to have surgery, or are extremely stressed, tell your doctor, as you may need additional steroid treatment to control your asthma.
- Flutiform is not intended for treatment of a sudden asthma attack. You must keep with you 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, tell the doctor or pharmacist. Especially if you are taking:

- Medicines known as beta-blockers such as: atenolol, propranolol, sotalol or metoprolol (to treat blood pressure and heart problems), timolol (for instance in eye drops to treat glaucoma).
- Certain other 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 or beta-antagonists including atenolol, metoprolol, propranolol, timolol). Additional long-acting $beta_2$ agonists should not be used together with this inhaler. If your asthma becomes worse between doses of Flutiform, you should use your quick acting 'reliever' inhaler intended for immediate relief of asthma attacks.
- Antihistamines (for allergy treatment).
- Diuretics (to treat high blood pressure or fluid buildup).
- Medicines used to treat heart failure, such as: digoxin.
- Medicines to treat heart rhythm problems, such as: quinidine, disopyramide, procainamide.
- Medicines to treat symptoms of depression or mental disorders, such as: monoamine oxidase inhibitors (for example: phenelzine, isocarboxazid), tricyclic antidepressants (for example: amitriptyline, imipramine). You must also tell the doctor if you have taken any of these types of medicines in the last two weeks.
- Medicines to treat psychiatric or mental disorders (such as phenothiazines or antipsychotics).
- Other medicines containing steroids.
- Antifungal medicines such as: ketoconazole, itraconazole.
- Some medicines may increase the effects of Flutiform and your doctor may wish to monitor your condition carefully if you are taking these medicines concurrently with Flutiform. These medicines include among others certain medicines for the treatment of HIV, such as: ritonavir, atazanavir, indinavir, nelfinavir, saquinavir, cobicistat.
- Antibiotics such as: clarithromycin, telithromycin, furazolidone.
- Levodopa (to treat Parkinson's disease).
- Levothyroxine (to treat an underactive thyroid gland).
- Oxytocin (medicine to induce labor).
- Procarbazine (to treat Hodgkin's disease).
- Anaesthetics (used in surgery). If you are going to have an operation under a general anaesthesia, please tell the doctor at the hospital that you are using this medicine.

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 2 mg of ethanol (alcohol) in each treatment dose (2 inhalations). The amount in each dose is equivalent to less than 1 ml of beer or 1 ml of wine. The small amount of alcohol in this preparation will not have any noticeable effect.
- Flutiform contains a small amount of sodium cromoglicate. If you are using an additional preparation that contains cromoglicate (used to treat asthma, allergic rhinitis and allergic conjunctivitis), you should continue as normal.

3. How to use the medicine?

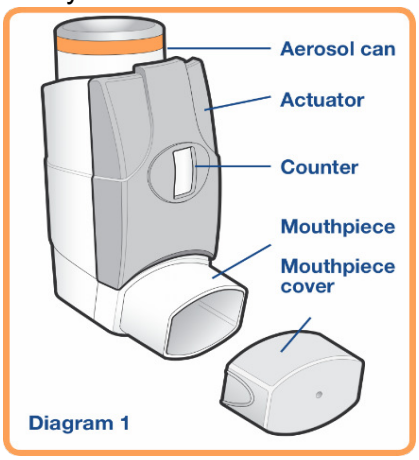
Always use the medicine according to the doctor's instructions. You should check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen.
The dosage and treatment regimen will be determined by the doctor only. Your doctor will prescribe the dose required for the treatment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

The standard dosage for adults, adolescents, and children over 5 years of age is usually: two puffs (actuations) 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 counter, which shows you how many puffs (actuations) are left in the inhaler after it has been primed (see Diagram 1). The counter is color-coded: it starts off green; when there are less than 50 puffs (actuations) left it changes to yellow; and when there are less than 30 puffs (actuations) left it changes to red. The counter counts down from 120 to 60 in intervals of 10, and from 60 to 0 in intervals of 5. When the counter is near to zero, you should contact your doctor in order to receive a prescription for a new inhaler. Do not use your inhaler when the counter reads zero.



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.

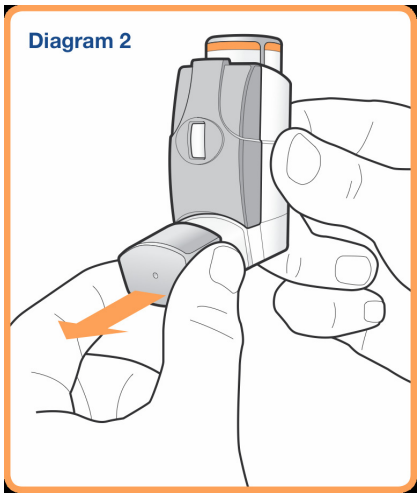
To prime the inhaler:
- Remove the mouthpiece cover and shake the inhaler well.
- Point the mouthpiece away from you and release one puff (actuation) into the air, by pressing down on the aerosol can. This step should be performed 4 times.

The inhaler should always be shaken immediately before use.

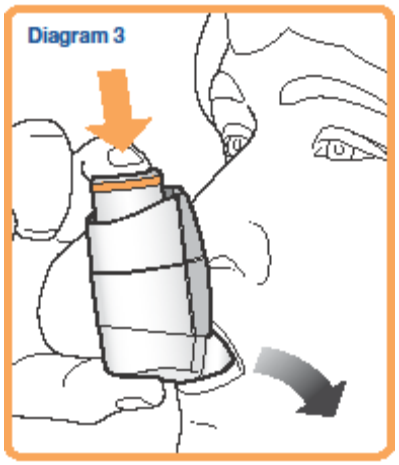
Using the inhaler:
If you feel shortness of breath, wheezing or breathing difficulties while using the inhaler, you should continue to use Flutiform but go to see your doctor as soon as possible, as you may need additional treatment.

Perform the following steps, making sure to perform steps 2 to 5 slowly:

1. Remove the mouthpiece cover (see Diagram 2) and check that the inhaler is clean and free from any dust.



2. The inhaler should be shaken immediately before releasing each puff (actuation), to ensure that the contents of the inhaler are evenly mixed.
3. Sit upright or stand. Breathe out as far as is comfortable and as slowly and as deeply as possible.
4. Hold the inhaler upright (as shown in Diagram 3) and put the mouthpiece in your mouth with your lips around it. Hold the inhaler with your thumb on the base of the mouthpiece and forefinger/index finger on the top of the inhaler. Do not bite the mouthpiece.
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 steadily and deeply (ideally for about 2-3 seconds in children and 4-5 seconds in adults).



6. While holding your breath, remove the inhaler from your mouth. Continue to hold your breath for as long as you can and breathe out slowly. Do not breathe out into the inhaler.

7. For the second puff (actuation), keep the inhaler upright in a vertical position then repeat steps 2 to 6.
8. After use, 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 the inhaler then you may not have inhaled your medicine properly. Take another dose by repeating Step 2 onwards.

- After using the inhaler, rinse your mouth, gargle with water or brush your teeth and spit out the residue. These actions can help reduce the risk of developing a fungal infection, a sore mouth and throat or a hoarse voice.
- If your hands are weak 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). The spacer device will come with instructions for use and with care and cleaning instructions which you must read carefully.

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.
- Wipe 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 if a child has accidently used the medicine or swallowed it, **refer immediately** to a doctor or proceed to a hospital emergency room to receive medical assistance. Bring the package of the medicine with you. Overdose symptoms include: severe chest pain (angina), high or low blood pressure, a headache, muscle cramps, difficulty sleeping, nervousness, a dry mouth, a loss of appetite, seizures, fits or convulsions, tremor, dizziness, fainting, tiredness, feeling sick and generally unwell. There may also be changes in the rate of your heartbeat, 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 drowsy or confused).

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 the doctor.
Even if there is an improvement in your health, do not stop the treatment with this medicine without consulting the doctor or the pharmacist.
If you stop taking the medicine: It is very important that you takethe inhaler every day as directed by your doctor to control your asthma, even if you feel well. If you want to stop using

your inhaler talk to your doctor first. 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 medicines in the dark! Check the label and the dose <u>each time</u> you take the medicine. Wear glasses if you need them.
If you have further questions concerning the use of the medicine, consult the doctor or pharmacist.

4. Side effects

As with 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:

- An 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 the use of Flutiform you notice an increase in wheezing and shortness of breath. In this case, use the quick acting inhaler you have for instances you need an immediate relief and contact your doctor immediately. Your doctor will assess you and may start you on a different course of treatment. You should carry your quick acting 'reliever' inhaler with you at all times.

<u>Additional side effects:</u>

Uncommon side effects (appear in 1-10 users out of 1,000):
- Worsening of asthma.
- Headache, tremor, irregular heartbeats or strong heartbeats (palpitations), dizziness, difficulty 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):
- An 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 need to monitor you 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; diarrhoea; indigestion; changes in taste; a feeling of dizinness or 'spinning' (vertigo); abnormal dreams; agitation; itchy skin; high blood pressure; a feeling of unusual weakness; swelling of hands, ankles or feet (oedema).

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. The frequency of these side effects is higher among children.

- The following side effects are associated with the use of formoterol fumarate: low blood levels of potassium (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 include: changes in bone mineral density (thinning of the bones), cataract, glaucoma (increased pressure in the eye), bruising or thinning of the skin, an increased risk of contracting infections, slowing of the rate of growth of children and adolescents, a round (moon shaped) face, an effect on the adrenal gland (a small gland next to the kidney) which can be manifested in: weakness, tiredness, difficulty in coping with stress, abdominal pain, loss of appetite, weight loss, headache, dizziness, very low blood pressure, diarrhoea, feeling or being sick or fits.

  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 worsen, 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 the medicine?').
- Do not use the inhaler for more than 3 months after it has been removed from the foil pouch or if the counter 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 grey plastic actuator. The mouthpiece cover is light grey.
  Each inhaler contains 120 puffs (actuations).
  There is one inhaler in a pack.

Registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301, Israel.
Manufacturer: Recipharm HC Ltd., Cheshire, United Kingdom.

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

The leaflet was revised in February 2024 according to MOH's guidelines.