Bexitrol® F MAXHALER®

Salmeterol and Fluticasone Propionate
Inhalation Powder, Pre-dispensed

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.

Description

Bexitrol® F Maxhaler® is a combination of Salmeterol Xinafoate BP and Fluticasone Propionate BP. Salmeterol Xinafoate is a selective, long acting β_2 agonist used in the treatment of asthma and other forms of diffuse airways obstruction. Fluticasone Propionate is a corticosteroid with mainly glucocorticoid activity. Fluticasone Propionate is stated to exert a topical effect on the lungs without systemic effects at usual dose. Maxhaler® is a moulded plastic device containing a foil strip with 60 regularly placed blisters containing pre-dispensed inhalation powder.

Indications

Asthma

Bexitrol® F is indicated in the regular treatment of asthma where use of a combination product (long- acting β_2 agonist and inhaled corticosteroid) is appropriate:

- Patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting β_2 agonist, or
- Patients already adequately controlled on both inhaled corticosteroid and long-acting β_2 agonist

Bexitrol® F 50/100 μg is not appropriate in adults and children with severe asthma.

Chronic Obstructive Pulmonary Disease (COPD)

Bexitrol® F is indicated for the symptomatic treatment of patients with COPD, with a FEV1 <60% predicted normal (pre-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy.

Dosage and Administration

Patients should be made aware that Bexitrol® F Maxhaler® must be used daily for optimum benefit, even when asymptomatic.

Asthma

Adults and Adolescents (12 years and older)

Bexitrol® F 50/100 Maxhaler®: One Inhalation twice daily
Bexitrol® F 50/250 Maxhaler®: One Inhalation twice daily
Bexitrol® F 50/500 Maxhaler®: One Inhalation twice daily

Children (4 years and older)

Bexitrol® F 50/100 Maxhaler®: One Inhalation twice daily
The maximum licensed dose of fluticasone propionate delivered by Bexitrol® F Maxhaler® in children is 100 μg twice daily.
There are no data available for use of Bexitrol® F in children aged under 4 years.

COPD

Adults

Bexitrol® F 50/500 Maxhaler®: One Inhalation twice daily

Special patient groups: There is no need to adjust the dose in elderly patients or in those with renal impairment. There are no data available for use of Bexitrol® F in patients with hepatic impairment.

Using the Maxhaler®: This is a patient friendly, ready to use and easy to grip device. Use as per instructions for use.

Contraindication

Bexitrol® F is contraindicated in patients with a history of hypersensitivity to any of the ingredients.

Special Warnings and Special Precautions

Deterioration of disease

Bexitrol® F Maxhaler® should not be used to treat acute asthma symptoms for which a fast- and short-acting bronchodilator is required. Patients should be advised to have their inhaler to be used for relief in an acute asthma attack available at all times.

Patients should not be initiated on Bexitrol® F Maxhaler® 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 Bexitrol® F. Patients should be asked to continue treatment but to seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation on Bexitrol® F.

For patients with COPD experiencing exacerbations, treatment with systemic corticosteroids is typically indicated, therefore patients should be instructed to seek medical attention if symptoms deteriorate with Bexitrol® F. Treatment with Bexitrol® F should not be stopped abruptly in patients with asthma due to risk of exacerbation. Therapy should be down-titrated under physician supervision.

As with all inhaled medication containing corticosteroids, Bexitrol® F should be administered with caution in patients with active or quiescent pulmonary tuberculosis and fungal, viral or other infections of the airway. Appropriate treatment should be promptly instituted, if indicated.

Cardiovascular effects: Rarely, Bexitrol® F may cause cardiac arrhythmias e.g. supraventricular tachycardia, extra systoles and atrial fibrillation, and a mild transient reduction in serum potassium at high therapeutic doses. Bexitrol® F should be used with caution in patients with severe cardiovascular disorders or heart rhythm abnormalities and in patients with diabetes mellitus, thyrotoxicosis, uncorrected hypokalaemia or patients predisposed to low levels of serum potassium.

Hyperglycemia: There have been very rare reports of increases in blood glucose levels and this should be considered when prescribing to patients with a history of diabetes mellitus.

Paradoxical bronchospasm: As with other inhalation therapy paradoxical bronchospasm may occur with an immediate increase in wheezing and shortness of breath after dosing. Paradoxical bronchospasm responds to a rapid-acting bronchodilator and should be treated straightaway. Bexitrol® F Maxhaler® should be discontinued immediately, the patient assessed and alternative therapy instituted if necessary.

The pharmacological side effects of β_2 agonist treatment, such as tremor, palpitations and headache, have been reported, but tend to be transient and reduce with regular therapy.

Systemic Corticosteroid Effects: Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, cataract and 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 patient is reviewed regularly and the dose of inhaled corticosteroid is reduced 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. Very rare cases of adrenal suppression and acute adrenal crisis have also been described with doses of fluticasone propionate between 500 and less than 1000 micrograms. 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.

The benefits of inhaled fluticasone propionate therapy should minimise the need for oral steroids, but patients transferring from oral steroids may remain at risk of impaired adrenal reserve for a considerable time. Therefore these patients should be treated with special care and adrenocortical function regularly monitored. Patients who have required high dose emergency corticosteroid therapy in the past 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.

Ritonavir can greatly increase the concentration of fluticasone propionate in plasma. Therefore, concomitant use should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects. There is also an increased risk of systemic side effects when combining fluticasone propionate with other potent CYP3A inhibitors.

Pneumonia in patients with COPD: An increase in the incidence of pneumonia, including pneumonia requiring hospitalization, 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.

Interactions with potent CYP3A4 inhibitors: Concomitant use of systemic ketoconazole significantly increases systemic exposure to Salmeterol. This may lead to an increase in the incidence of systemic effects (e.g. prolongation in the QTc interval and palpitations). Concomitant treatment with ketoconazole or other potent CYP3A4 inhibitors should therefore be avoided unless the benefits outweigh the potentially increased risk of systemic side effects of Salmeterol treatment.

Paediatric Population

Children and adolescents <16 years taking high doses of fluticasone propionate (typically ≥ 1000 micrograms/day) may be at particular risk. Systemic effects may occur, particularly at high doses prescribed for long periods. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, acute adrenal crisis and growth retardation in children and adolescents and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression. Consideration should be given to referring the child or adolescent to a paediatric respiratory specialist.

It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroid is regularly monitored. The dose of inhaled corticosteroid should be reduced to the lowest dose at which effective control of asthma is maintained.

Drug Interaction

β adrenergic blockers may weaken or antagonize the effect of Salmeterol. Both non-selective and selective β blockers should be avoided unless there are compelling reasons for their use. Potentially serious hypokalaemia may result from β_2 agonist therapy. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics. Concomitant use of other β adrenergic containing drugs can have a potentially additive effect.

Fluticasone propionate and Salmeterol are substrates of CYP3A4. The use of strong CYP3A4 inhibitors (e.g. ritonavir, clarithromycin, nelfinavir, ketokonazole etc.) with Bexitrol® F Maxhaler® is not recommended because increased systemic corticosteroid and increased cardiovascular adverse effects may occur.

Pregnancy and Lactation

Pregnancy

A large amount of data on pregnant women (more than 1000 pregnancy outcomes) indicates no malformative or neonatal toxicity related to Bexitrol® F. Animal studies have shown reproductive toxicity after administration of β_2 adrenoreceptor agonists and glucocorticosteroids.

Administration of Bexitrol® F to pregnant women should only be considered if the expected benefit to the mother is greater than any possible risk to the fetus. The lowest effective dose of fluticasone propionate needed to maintain adequate asthma control should be used in the treatment of pregnant women.

Breastfeeding

It is unknown whether Salmeterol and fluticasone propionate/metabolites are excreted in human milk. Studies have shown that Salmeterol and fluticasone propionate, and their metabolites, are excreted into the milk of lactating rats. A risk to breastfed newborns/infants cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue Bexitrol® F therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Side Effects

As Bexitrol® F Maxhaler® contains salmeterol and fluticasone propionate, the type and severity of adverse reactions associated with each of the compounds may be expected. There is no incidence of additional adverse events following concurrent administration of the two compounds.

The following side effects were commonly reported: Candidiasis of the mouth and throat, Pneumonia (in COPD patients), Bronchitis, Hypokalaemia, Headache, Nasopharyngitis, Throat irritation, Hoarseness/dysphonia, Sinusitis, Contusions, Muscle cramps, Traumatic fractures, Arthralgia and Myalgia.

The following side effects were rarely reported: Paradoxical bronchospasm, Oesophageal candidiasis, Angioedema (mainly facial and oropharyngeal oedema), Respiratory symptoms (bronchospasm), Anaphylactic reactions including anaphylactic shock, Cushing's syndrome, Cushingoid features, Adrenal suppression, Growth retardation in children and adolescents, Decreased bone mineral density, Behavioural changes, including psychomotor hyperactivity and irritability (predominantly in children), Glaucoma, Cardiac arrhythmias (including supraventricular tachycardia and extrasystoles).

Overdosage

There are no data available from clinical trials on overdose with Bexitrol® F Maxhaler®.

Pharmaceutical Precautions

Avoid storage in direct sunlight or heat. Do not store above 30°C. Store in a dry place. Keep away from children. Store your Maxhaler® in Carry-bag and always keep your information leaflet inside.

Special precautions for disposal and other handling

Do not open until you ready to inhale it because after each opening of mouthpiece cover one dose is opened and your device will be clogged if it is not inhaled. If you accidentally open mouthpiece cover/ lever make sure to gently shaking by holding mouthpiece downward to remove extra powder.

The Maxhaler® releases a powder which is inhaled into the lungs. A dose indicator on the Maxhaler® indicates the number of doses left.

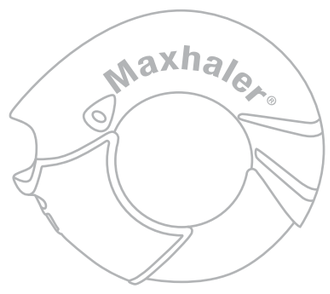
Commercial Pack

Bexitrol® F 50/100 Maxhaler®: One Maxhaler® contains 60 doses and each dose contains Salmeterol Xinafoate BP equivalent to Salmeterol 50 μg and Fluticasone Propionate BP 100 μg.

Bexitrol® F 50/250 Maxhaler®: One Maxhaler® contains 60 doses and each dose contains Salmeterol Xinafoate BP equivalent to Salmeterol 50 μg and Fluticasone Propionate BP 250 μg.

Bexitrol® F 50/500 Maxhaler®: One Maxhaler® contains 60 doses and each dose contains Salmeterol Xinafoate BP equivalent to Salmeterol 50 μg and Fluticasone Propionate BP 500 μg.

BEXIMCO PHARMA
Manufactured by
BEXIMCO PHARMACEUTICALS LTD.
126, Kathaldia, Auchpara, Tongi, Gazipur, Bangladesh
3020006533 270319



INSTRUCTIONS FOR USE
ব্যবহারবিধি

What is Maxhaler®?

This is a patient friendly, ready to use and easy to grip Pre-dispensed Inhalation Powder Device.

ম্যাক্সহেলার® কি?

ম্যাক্সহেলার® একটি পূর্বপ্রস্তুতকৃত/প্রি-ডিসপেনসড ড্রাই পাউডার ইনহেলার (শ্বাসের মাধ্যমে ওষুধ নেওয়ার) ডিভাইস, যা সহজে এবং তৎক্ষনাৎ ব্যবহারযোগ্য।

বেক্সিট্রল® এফ ম্যাক্সহেলার® এর সরবরাহকৃত মাত্রা সমূহ

আপনার ম্যাক্সহেলার® এর অংশগুলো চিনে নিন:

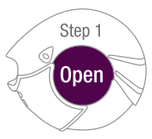
Important information while using Bexitrol® F Maxhaler®

- **Bexitrol® F Maxhaler®** is for oral inhalation use only.
- Take **Bexitrol® F Maxhaler®** out of the foil pouch just before you use it for the first time. Safely throw away the pouch. The **Maxhaler®** will be in the closed position. The counter should read 60.
- You should consider getting a replacement when the counter shows the number 05. Do not use your **Maxhaler®** if the counter shows 00 and must dispose of your **Maxhaler®**.
- Do not open unless use. Otherwise, there will be a chance of wasting a dose which may retain inside the device and leading to cause overdose in next dose.
- However, if there is an accidental opening of mouthpiece cover, you must hold the device downward and then gently shake to clear the powder from mouthpiece.
- You will get a carry bag to store your **Maxhaler®** device.

বেক্সিট্রল® ম্যাক্সহেলার® ব্যবহারের প্রয়োজনীয় তথ্যাবলি:

- কেবল মাত্র মুখ দিয়ে শ্বাস গ্রহনের মাধ্যমে ব্যবহার করুন।
- প্রথমবার ব্যবহারের জন্য ফয়েল ব্যাগ থেকে **ম্যাক্সহেলার®** টি বের করুন। **ম্যাক্সহেলার®** টি বন্ধ অবস্থায় থাকবে এবং কাউন্টারে ৬০ নম্বর দেখাবে।
- যখন কাউন্টারে ০৫ দেখাবে তখন আপনার নতুন ঔষধ কিনে নেওয়া উচিত। যদি কাউন্টারে ০০ দেখায় তাহলে **ম্যাক্সহেলার®** টি আর ব্যবহার করবেন না। অবশ্যই আপনার **ম্যাক্সহেলার®** টি ফেলে দিবেন।
- অযথা মাউথপিসের কভারটি খুলবেন না, অন্যথায় ওষুধের ডোজ নষ্ট হবে এবং পরের ডোজটির মাত্রা বেশী হয়ে যেতে পারে এছাড়াও ওষুধের গুড়ো মাউথপিসের মুখটি বন্ধ করে দিয়ে বিপত্তি ঘটাতে পারে।
- যদি অসাবধানতাবশত মাউথপিসের কভারটি খোলা হয়ে থাকে তাহলে **ম্যাক্সহেলার®** এর মাউথপিসটি নিচের দিকে রেখে আলতো করে ঝাঁকিয়ে পাউডারগুলো বের করে দিন।
- আপনার **ম্যাক্সহেলার®** টি রাখার জন্য একটি ক্যারি ব্যাগও দেওয়া আছে।

3 easy steps to take your Maxhaler®

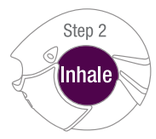


Step 1: Open your Maxhaler®
ধাপ ১: ম্যাক্সহেলার® টি খুলুন

- Hold your **Maxhaler®** in one hand and place the thumb of your other hand on sliding grip.
- **ম্যাক্সহেলার®** টি খোলার জন্য এক হাতে ডিভাইসটি ধরে অন্য হাতের বৃদ্ধাঙ্গুলটি স্লাইডিং গ্রিপে রাখুন।

- Open your **Maxhaler®** by pushing the thumb grip right around until it clicks. The mouthpiece should now be fully visible.
- বৃদ্ধাঙ্গুলটি দিয়ে মাউথপিস কভারটি টেনে খুলুন; যতক্ষণ না আপনি ক্লিক শব্দ শুনতে পাচ্ছেন। লক্ষ্য করুন এখন মাউথপিসটি পুরোপুরি দেখতে পারছেন।

- Your **Maxhaler®** is now ready to use.
- আপনার **ম্যাক্সহেলার®** টি এখন ব্যবহারের জন্য প্রস্তুত।



Step 2: Inhale your medicine
ধাপ ২: মুখ দিয়ে শ্বাসের মাধ্যমে ওষুধ নিন

- Before inhale hold the device away from your mouth, breathe out as far as is comfortable. Do not exhale into mouthpiece.
- ব্যবহারের পূর্বে ডিভাইসটি মুখ থেকে একটু দুরে রাখুন এবং যতদূর সম্ভব নিঃশ্বাস ছাড়ুন (অবশ্যই ডিভাইসের ভেতর নয়)।

- Put the mouthpiece to your lips; breathe in steadily and deeply through the device.
- এবার মাউথপিসটি ঠোঁটের মধ্যে চেপে ধরুন এবং ধীরে ধীরে, গভীরভাবে ডিভাইসের মধ্য দিয়ে শ্বাসের মাধ্যমে ফুসফুসে নিন (গিলে ফেলবেন না)।

Hold your breath for 10 Seconds

- Remove the device from your mouth. Hold your breath for as long as is comfortable (approx. 10 seconds). Breathe out slowly.
- ১০ সেকেন্ড অথবা যতক্ষণ সম্ভব শ্বাস ধরে রাখুন। ধীরে ধীরে শ্বাস ছাড়ুন।

Step 3: Close mouthpiece cover
ধাপ ৩: মাউথপিস কভারটি বন্ধ করুন

- Close your **Maxhaler®** by sliding the thumb grip back to the original position with 'Click' sound. This makes your **Maxhaler®** ready to use again next time.
- মাউথপিস কভারটি বন্ধ করার জন্য বৃদ্ধাঙ্গুল দিয়ে টেনে সামনের দিকে আনুন যতক্ষণ না আগের অবস্থায় ফেরত আসছে এবং 'ক্লিক' শব্দ শুনতে পাচ্ছেন। এখন আপনার **ম্যাক্সহেলার®** ডিভাইসটি পুনরায় ব্যবহারের জন্য প্রস্তুত।

- The dose counter on the top of the **Maxhaler®** shows how many doses are left to use.
- **ম্যাক্সহেলার®** ডিভাইসটির উপরে থাকা ডোজ কাউন্টারটি আপনাকে অবশিষ্ট ডোজ সংখ্যা দেখাবে।

- Rinse mouth with water after using **Maxhaler®**.
- **ম্যাক্সহেলার®** ব্যবহারের পর পানি দিয়ে কুলি করুন।