Floriva®-F Respicap

Salmeterol Xinafoate and
Fluticasone Propionate

Description: Floriva®-F Respicap is a combination of Salmeterol Xinafoate and Fluticasone Propionate. Salmeterol Xinafoate is a selective, long acting β2 agonist; it attaches to β2 receptors on the smooth muscle cells that surround the airways, causing the muscle cells to relax and opening the airways. Fluticasone Propionate is a synthetic corticosteroid which is a glucocorticoid receptor agonist with mainly potent anti-inflammatory activity.

Mode of action: Salmeterol Xinafoate is a selective, long acting beta-2 agonist; it attaches to beta-2 receptors on the smooth muscle cells that surround the airways, causing the muscle cells to relax and opening the airways. Fluticasone Propionate is a synthetic corticosteroid, which is a glucocorticoid receptor agonist with mainly potent anti-inflammatory activity. Fluticasone Propionate is stated to exert a topical effect on the lungs without systemic effects at usual dose.

Pharmacokinetics:

Absorption

Fluticasone Propionate is acts locally in the lung; therefore, plasma levels may not predict therapeutic effect. Trials using oral dosing of labeled and unlabeled drug have demonstrated that the oral systemic bioavailability of fluticasone propionate was negligible (<1%), primarily due to incomplete absorption and presystemic metabolism in the gut and liver. In contrast, the majority of the fluticasone propionate delivered to the lung was systemically absorbed. After administration of 232/14 mcg to patients aged 12 years and older with persistent asthma in a clinical trial, the mean Cmax value of fluticasone propionate was 66 pg/mL with a median tmax value of approximately 2 hour.

After administration of Salmeterol, 232/14 mcg to patients aged 12 years and older with persistent asthma, the mean Cmax values of salmeterol was 60 pg/mL. The median tmax was 5 minutes.

Distribution

Following intravenous administration of Fluticasone Propionate, the initial disposition phase for fluticasone propionate was rapid and consistent with its high lipid solubility and tissue binding. The volume of distribution averaged 4.2 L/kg. The percentage of fluticasone propionate bound to human plasma proteins averages 99%. Fluticasone propionate is weakly and reversibly bound to erythrocytes and is not significantly bound to human transcortin.

Volume of distribution data are not available for salmeterol. The percentage of salmeterol bound to human plasma proteins averages 96% in vitro over the concentration range of 8 to 7,722 ng of salmeterol base per milliliter, much higher concentrations than those achieved following therapeutic doses of salmeterol.

Elimination

Following intravenous dosing, fluticasone propionate showed polyexponential kinetics and had a terminal elimination half-life of approximately 7.8 hours. Terminal half-life estimates of fluticasone propionate following oral inhalation administration were approximately 10.8 hours.

Terminal half-life estimates for salmeterol were approximately 12.6 hours. The xinafoate moiety has no apparent pharmacologic activity. The xinafoate moiety is highly protein bound (greater than 99%) and has a long elimination half-life of 11 days.

Metabolism

Salmeterol base is extensively metabolized by hydroxylation. An in vitro study using human liver microsomes showed that salmeterol is extensively metabolized to Î± hydroxysalmeterol (aliphatic oxidation) by CYP3A4. Ketoconazole, a strong inhibitor of CYP3A4, essentially completely inhibited the formation of Î± hydroxysalmeterol in vitro.

Composition: Floriva®-F 50/100 Respicap Inhaler: Each Respicap (Dry Powder Inhaler) capsule contains Salmeterol Xinafoate BP equivalent to 50 µg Salmeterol and Fluticasone Propionate BP 100 µg.

Floriva®-F 50/250 Respicap Inhaler: Each Respicap (Dry Powder Inhaler) capsule contains Salmeterol Xinafoate BP equivalent to 50 µg Salmeterol and Fluticasone Propionate BP 250 µg.

Floriva®-F 50/500 Respicap Inhaler: Each Respicap (Dry Powder Inhaler) capsule contains Salmeterol Xinafoate BP equivalent to 50 µg Salmeterol and Fluticasone Propionate BP 500 µg.

Indications: Floriva®-F Respicap is indicated for the regular treatment of asthma where use of a combination (inhaled corticosteroid and long acting β2 adrenoceptor agonist) is appropriate and in patients with severe COPD.

Dosage & administration

Asthma

Adult and Child over 5 years:

- Floriva-F 50/100 Respicap Inhaler-1 Respicap twice daily.

Adult and Child over 12 years:

- Floriva-F 50/100 Respicap Inhaler-1 Respicap twice daily.
- Floriva-F 50/250 Respicap Inhaler-1 Respicap twice daily.
- Floriva-F 50/500 Respicap Inhaler-1 Respicap twice daily.

COPD

- Floriva-F 50/250 Respicap Inhaler-1 Respicap twice daily.
- Floriva-F 50/500 Respicap Inhaler-1 Respicap twice daily.

Contraindications: The use of Fluticasone Propionate & Salmeterol Xinafoate combination is contraindicated in the following conditions: Primary treatment of status asthmaticus or other acute episodes of asthma or COPD where intensive measures are required. Severe hypersensitivity to milk proteins.

Side effects: As the combination inhaler 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. Adverse events, which have been associated with Salmeterol or Fluticasone Propionate, are given below:

Salmeterol: The pharmacological side effects of β2 agonist treatment, such as tremor, subjective palpitations and headache have been reported but tend to be transient and reduce with regular therapy. Cardiac arrhythmia (including atrial fibrillation, supraventricular tachycardia and extra systoles) may occur, usually in susceptible patients. There have been reports of arthralgia and hypersensitivity reactions including rash, oedema and angio-oedema and oropharyngeal irritation.

Fluticasone Propionate: Hoarseness and candidiasis (thrush) of the mouth and throat can occur in some patients. Cutaneous hypersensitivity reactions have been reported. Rare cases of facial and oropharyngeal oedema have been reported. Only for the use of medical professional Contraindications This combination inhaler is contraindicated in patients with a known history of hypersensitivity to any of the ingredients. Precautions Consideration should be given to additional corticosteroid therapies and to including administration of antibiotics if an infection is present. As with all inhaled medication containing corticosteroids, this combination inhaler should be administered with caution in patients with active or quiescent pulmonary tuberculosis. This combination inhaler should be administered with caution in patients with thyrotoxicosis. Pregnancy and lactation. There is insufficient experience of the use of this combination in human pregnancy & lactation. Administration of this combination during pregnancy and lactation should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus or child.

Use in pregnancy & lactation: Pregnancy category C. It should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Administration of Fluticasone Propionate & Salmeterol Xinafoate combination to women who are breastfeeding should only be considered if the expected benefit to the mother is greater than any possible risk to the child.

Precautions: Floriva®-F Respicap must not be swallowed and can be used with any inhaler device. Remove Respicap capsule from the blister pack just prior to use, as Respicap exposed to moisture may not tear easily. Avoid storage in direct sunlight or heat. Store below 30°C. Keep away from children.

Drug interactions: Care should be taken when co administering known strong CYP3A4 inhibitors (e.g., Ketoconazole, Ritonavir), as there is potential for increased systemic exposure to Fluticasone Propionate. Both non-selective and selective β blockers should be avoided in patients with asthma, unless there are compelling reasons for their use. Due to the very low plasma concentrations achieved after inhaled dosing clinically significant drug interactions are unlikely.

Over dosage: No human over dosage data has been reported for this combination inhaler; however data on overdose with both drugs are given below: Salmeterol: The signs and symptoms of Salmeterol overdose are seizures, angina, hypertension or hypotension, tachycardia, arrhythmias, nervousness, headache, tremor, muscle cramps, dry mouth, palpitation, nausea, dizziness, fatigue, malaise, and insomnia. Other signs of over dosage may include hypokalemia and hyperglycemia. Treatment consists of discontinuation of Salmeterol together with appropriate cardio selective beta-blocking agents, which should be used with caution in patients with a history of bronchospasm. Fluticasone Propionate: Acute inhalation of Fluticasone Propionate doses in excess of those recommended may lead to temporary suppression of adrenal function. This does not need emergency action as adrenal function is recovered in a few days. Chronic overdose of inhaled Fluticasone Propionate may lead to adrenal suppression. Monitoring of adrenal reserve may be necessary. In cases of Fluticasone Propionate overdose this combination inhaler therapy may still be continued at a suitable dosage for symptom control.

Storage: Keep out of reach of children. Store in a dry place, below 25˚C temperature and protected from light.

Packaging

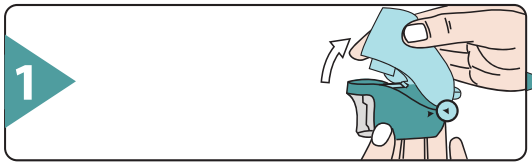
Floriva®-F 50/100 Respicap Inhaler: Each box contains 10X3 inhalation capsules in alu-alu blister strips.

Floriva®-F 50/250 Respicap Inhaler: Each box contains 10X3 inhalation capsules in alu-alu blister strips.

Floriva®-F 50/500 Respicap Inhaler: Each box contains 10X3 inhalation capsules in alu-alu blister strips.

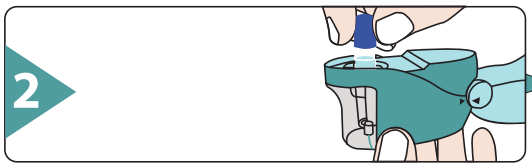
Instruction for use of **Respihaler**

রেসপিহেলার ব্যবহারবিধি



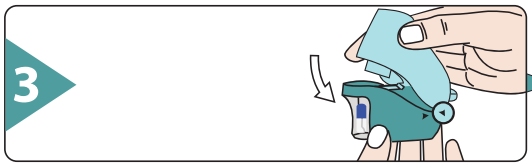
To open the **Respihaler**, hold the base of the **Respihaler** with one hand and pull up the mouthpiece till the direction two arrows meet.

রেসপিহেলার খোলার জন্য নিচের অংশ এক হাতে ধরুন এবং মাউথপিসটি উপরের দিকে টানুন যাতে নির্দেশিত দু'টি তীর একত্রে মিলিত হয়।



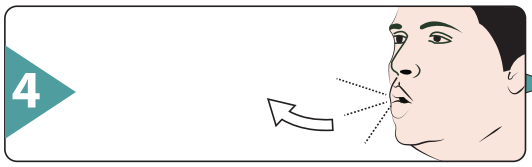
Place the Respicap into the capsule chamber so that the transparent part stays down.

রেসপিক্যাপটি ক্যাপসুল চেম্বারে এমনভাবে স্থাপন করুন যাতে স্বচ্ছ অংশ নিচে থাকে।



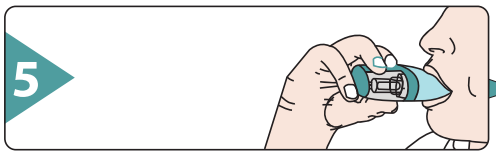
Close the mouthpiece firmly until a click sound is heard which indicates proper locking of the **Respihaler**.

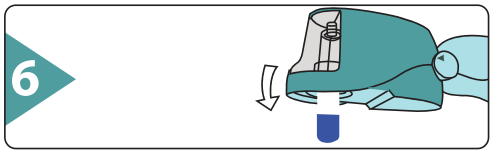
মাউথপিসটি দৃঢ়ভাবে বন্ধ করুন যতক্ষণ না ক্লিক শব্দ হয়, যা নির্দেশনা দেয় **রেসপিহেলার** সঠিকভাবে লক হয়েছে।



Breathe out completely.

পুরোপুরি শ্বাস ছাড়ুন।





Grip the mouthpiece between your mouth and close your lips around it. Keep your head upright and breathe as deeply as you can, if done correctly, the Respicap will vibrate inside the **Respihaler**. Remove the **Respihaler** from your mouth & hold your breath as long as comfortable then resume normal breathing. At times, step 5 may be repeated to ensure that all the powder has been inhaled.

রেসপিহেলার মুখের কাছে নিন এবং আপনার ঠোঁট মাউথপিসের চারপাশে ভালোভাবে বন্ধ করুন। আপনার মাথা সোজাভাবে রাখুন এবং মুখ দিয়ে জোরে শ্বাস নিন, যদি সঠিকভাবে সম্পন্ন হয়, রেসপিহেলারের ভেতর রেসপিক্যাপটির কম্পনের শব্দ পাওয়া যাবে। **রেসপিহেলার** মুখের ভেতর থেকে বের করুন এবং যতক্ষণ সহজে শ্বাস ধরে রাখা যায় ধরে রাখুন, এই সময় রেসপিক্যাপের পাউডার পুরোপুরি শ্বাস নেওয়ার সাথে খালি না হওয়া পর্যন্ত ৫ম ধাপ পুনরায় করুন।

After every use, open the mouthpiece again to discard the used Respicap. Then close the mouthpiece and store in the pouch provided for the next use.

প্রতিবার ব্যবহারের পর মাউথপিসটি খুলুন এবং ব্যবহৃত রেসপিক্যাপটি ফেলে দিন। এরপর মাউথপিসটি বন্ধ করুন এবং পরবর্তী ব্যবহারের জন্য পাউচের ভেতর সংরক্ষণ করুন ।

সাবধানতা: ভেজা অবস্থায় রেসপিহেলার ব্যবহার করবেন না।

কিভাবে রেসপিহেলার পরিষ্কার করতে হবে:

যখন প্রয়োজন হবে, তখন একটি শুকনো কাপড় দিয়ে রেসপিহেলারের মাউথপিস্ এবং ক্যাপসুল চেম্বারটি পরিষ্কার করে নিন ।

Opsonin Pharma
Ideas for healthcare

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