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combivair rotacaps

(Budesonide + Formoterol Fumarate)

COMPOSITION

Combivair 200 Rotacaps: Each capsule contains:
Budesonide B.P. 200 mcg
Formoterol Fumarate (as Dihydrate) B.P. 6 mcg
Combivair 400 Rotacaps: Each capsule contains:
Budesonide B.P. 400 mcg
Formoterol Fumarate (as Dihydrate) B.P. 6 mcg

DESCRIPTION

Combivair Rotacaps is a combination of budesonide, a potent glucocrticoid and formoterol, a selective long-acting beta$_2$-agonist. Budesonide is a potent glucocorticoid that binds with high affinity to the glucocorticoid receptor. It has a high ratio of topical to systemic activity. Formoterol is a very potent long-acting beta$_2$-agonist with a high intrinsic activity and a rapid onset of action.

MECHANISM OF ACTION

Budesonide is an anti-inflammatory corticosteroids that exhibits potent glucocorticoid activity and weak mineralocorticoid activity. It has demonstrated a reduction in the number and activation of inflammatory cells in the epithelium and sub-mucosa after regular Inhaled corticosteroids, together with healing of damaged epithelium.

Inflammation is an important component in the pathogenesis of COPD and asthma. Budesonide potentially inhibit the formation of cytokines (e.g. IL-1, IL3, IL4, IL5, IL9, IL-13, TNF and granulocyte-macrophages colony-stimulating factor, GM-CSF) that are secreted in asthma by T-lymphocytes, macrophages and mast cells. Budesonide also decreases eosinophils survival by inducing apoptosis. Budesonide inhibit the expression of multiple inflammatory genes in airway epithelial cells, probably the most important action of Budesonide in suppressing asthmatic inflammation. These anti-inflammatory actions of corticosteroids may contribute to their efficacy in COPD and asthma.

Formoterol is a long acting selective beta$_2$ adrenergic agonist (beta$_2$ agonist) with a rapid onset of action. Inhaled Formoterol fumarate acts locally in the lungs as a bronchodilator. The long duration of Formoterol action occurs because Formoterol molecules initially diffuses into the plasma membrane of the lung cells and then are slowly released back outside, where they can come into contact with beta$_2$ adrenergic receptors. The pharmacological effect of beta$_2$ adrenoceptor agonist drugs, including Formoterol are at least in part attributable to stimulation of intracellular adenyle cyclase, the enzyme that catalyze the conversion of adenosine triphosphate (ATP) to cyclic-3', 5'- adenosine monophosphate(cyclic AMP). Increased cyclic AMP levels cause relaxation of smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

PHARMACOKINETIC

Orally inhaled Budesonide is rapidly absorbed in the lungs and peak concentration is typically reached with in 20 minutes and peak plasma concentration was achieved in about 1-2 hours. The pharmacokinetics of Budesonide is important in relation to the systemic effects. The fraction of drug that is inhaled into the lungs acts locally on the airway mucosa but may be absorbed from the airway and alveolar surface. Thus a portion of inhaled dose reaches the systemic circulation. Furthermore, the fraction of inhaled drug that is deposited in the oropharynx is swallowed and absorbed from the gut. The absorbed fraction may be metabolized in the liver (first pass metabolism) before reaching the system circulation. Budesonide has a lower oral bioavailability.

The volume of distribution of Budesonide was approximately 3L/kg. It is 80 to 90% bound to the plasma proteins. Budesonide is rapidly and extensively metabolized by liver isoenzymes.

Inhaled Formoterol is rapidly absorbed and peak plasma concentration is typically reached with in 5-10 minutes after dosing. It is likely that the majority of inhaled Formoterol delivered is swallowed and then absorbed from the gastrointestinal tract.

The Budesonide was excreted in the urine and feces in the form of metabolites.

INDICATION

Combivair Rotacap is indicated in the regular treatment of asthma, where use of a combination (long acting beta$_2$-agonist and inhaled corticosteroid) has been found to be appropriate.

Symptomatic treatment of severe chronic obstructive pulmonary disease (COPD) with a history of repeated exacerbations despite regular therapy with long acting bronchodilators.

It is not indicated for the relief of acute bronchospasm.

DOSAGE AND ADMINISTRATION

Capsules are intended for use through Revolizer or Rotahaler only and are not to be swallowed. Dosage is individual and adjusted according to disease severity. When control has been achieved, the dose should be titrated to the lowest effective dose, which could include Combivair Rotacap given once daily.

ASTHMA

Combivair Recommended Dose in Asthma			
Age Group	**Condition**	**Combivair 200**	**Combivair 400**
Adults (18 years and older)	**Based upon patient's asthma severity**	**1-2 Rotacaps twice daily, maximum dose is 4 Rotacaps twice daily**	**1- Rotacap twice daily, maximum dose is 2 Rotacaps twice daily**
Adolescent (12-17 years)		**1-2 Rotacaps twice daily**	**1- Rotacap twice daily**
Children (6-11 years)		**1- Rotacaps twice daily**	**1- Rotacap twice daily**
Children (6-11 years)	**Chronic obstructive pulmonary disease (COPD)**	**2- Rotacaps twice daily**	**1- Rotacap twice daily**

Combivair Rotacap should only be inhaled with the Revolizer or Rotahaler device.

Combivair Rotacap must not be swallowed.

CONTRAINDICATIONS

Combivair Rotacap is contraindicated in patients with a history of hypersensitivity to any of the component of the drug product.

WARNINGS AND PRECAUTIONS

Patients should be made aware that Combivair Rotacap must be used daily for optimum benefit, even when asysptomatic. Combivair Rotacap should be used to treat acute asthma symptoms for which a fast and short-acting bronchodilator is required. Patients should be advised to have their relief medication available at all times. Sudden and progressive deterioration in control of asthma is potentially life threatening and consideration should be given to the need for increased therapy with corticosteroid. As with all inhaled medication containing corticosteroids, Combivair Rotacap should be administered with caution in patients with pulomonary tuberculosis, in patients with severe cardiovascular disorders, including heart rhythm abnormalities, diabetes mellitus, untreated hypokalaemia or thyrotoxicosis. Potentially serious hypokalaemia may result from high doses of beta$_2$-agonists.

Paradoxical bronchospasm may occur. In such case Combivair Rotacap should be discontinued immediately, the patient assessed and alternative therapy instituted if necessary. The local effect includes development of localized infections of the mouth and pharynx, the candida albicans has occurred in patients treated with Combivair. When such infections develops, it should be treated with appropriate local or systemic therapy, while treatment with Combivair continues, but at times therapy with Combivair may need to be interrupted. Physician should remain vigilant for the possible development of pneumonia in patient with COPD as the clinical features of pneumonia and exacerbation frequently overlap. Patients who are on drugs that suppress the immune system are more susceptible to infection than health individuals. Systemic effects are much less likely to occur with inhaled corticosteroids than with oral corticosteroids. Possible systemic effects include adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. It is important, therefore, That the dose is titrated to the lowest dose at which effective control is maintained.

LABA increases the risk of asthma related hospitalization in pediatric and adolescent patients. Therefore, when treating patients with asthma Combivair should only be used for patients not adequately controlled on a long term asthma control medication.

The safety and effectiveness of the drug in asthma patients 6 to <12 years of age has not been established. The potential growth effects of prolong treatment should be weighed against the clinical benefits obtained before prescribing the drug in children 6 < 12 years of age.

Drug interactions

Even though plasma levels of Combivair are very low, potential interactions with other substrates or inhibitors of CYP3A4 cannot be excluded, both non-selective and selective beta-blockers should be avoided in patients with asthma, unless there are compelling reasons for their use. Concomitant use of other beta-adrenergic containing drugs can have a potentially additive effect. Electrocardiographic changes and or hypokalemia associated with non potassium sparing diuretics may worsen with concomitant beta agonist. Monoamine Oxidase Inhibitors and tricyclic antidepressant may potentiate effect of Formoterol on vascular system. Caution should be exercised when considering co-administration of Combivair with long-term ketoconazole, and other known strong CYP3A4 inhibitors (e.g. ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, saquinavir, telithromycin).

Pregnancy

Pregnancy Category C

There are no adequate and well controlled studies of Combivair in pregnant women. Administration of Combivair Rotacaps in pregnant woman should only be considered if the potential benefit justifies the potential risk of fetus.

Lactation

There are no adequate and well controlled studies of Combivair in nursing mothers, a decision should be made whether to discontinue nursing or to discontinue Combivair, taking into account the importance of Combivair to mothers.

ADVERSE EFFECTS

As Combivair Rotacaps contain formoterol and budesonide the type and severity of side effects associated with each of the compounds may be expected. There is no incidence of additional side effects following concurrent administration of the two compounds. Side effects associated with

Formoterol

Tremor, palpitation and headache, have been reported, but tend to be transient and reduce with regular therapy. Cardiac arrhythmias, muscle cramps and hypersensitivity reaction, including rash, oedema and angioedema may occur in some patients.

Budesonide

Hoarseness and candidiasis (thrush) of the mouth and throat can occur in some patients. Cutaneous hypersensitivity reactions have been reported. Both hoarseness and incidence of candidiasis may be relieved by gargling with water after use of Combivair Rotacaps. Symptomatic candidiasis can be treated with topical anti-fungal therapy whilst continuing with Combivair Rotacaps.

OVERDOSAGE

The sign and symptoms of Combivair overdose are tremor, headache and tachycardia. The preferred antidotes are cardio selective beta-blocking agents, which should be used with caution in patients with a history of bronchospasm. If higher than recommended dosage is continued over prolonged periods, some degree of adrenal suppression may result. Monitoring of adrenal reserve may be necessary.

PRESENTATION

1. **Combivair 200 Rotacaps:** Blister pack of 3 X 10's Rotacaps.
2. **Combivair 400 Rotacaps:** Blister pack of 3 X 10's Rotacaps.

DOSAGE & INSTRUCTIONS:

To be sold and used on the prescription of a registered medical practitioner only.
Keep out of the reach of children.
Store below 25°C in a dry place.
Protect from light.

CAPSULES ARE INTENDED FOR USE THROUGH REVOLIZER OR ROTAHALER ONLY AND ARE NOT TO BE SWALLOWED.

کومبی وائیر

(بیوڈیسونائیڈ + فارموٹیرول فیوماریٹ)

روٹا کیپس

خوراک وہدایات

صرف مستندڈاکٹر کےنسخہ کےمطابق ہی دوافروخت اوراستعمال کی جائے۔

بچوں کی پہنچ سے دور رکھیں۔ دوا کو 25°C سے کم درجہ حرارت پر خشک جگہ پر رکھیں۔

روشنی سے بچائیں۔

کیپسولز کھانے کے لیے نہیں۔

صرف روٹا ہیلر یا ریوولائزر کے ذریعے استعمال کریں۔

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