Only for the use of Medical Professionals

Combair® HFA

Inhalation Aerosol
Salbutamol Sulphate and Ipratropium Bromide

Description
Combair® HFA inhalation aerosol is a combination of Salbutamol Sulphate and Ipratropium Bromide. Salbutamol, a short acting β_2 agonist bronchodilator and Ipratropium Bromide, an anticholinergic bronchodilator produce greater bronchodilator effect when used in combination than either agent alone. It is an environment friendly inhaler which does not contain chlorofluorocarbons (CFCs) as propellant. It uses hydrofluoroalkane (HFA) as propellant which is environment friendly. This combination is expected to maximize the response to treatment in patients with chronic obstructive pulmonary disease (COPD) by reducing bronchospasm through two distinctly different mechanisms, anticholinergic (parasympatholytic) and sympathomimetic.

Indications
Combair® HFA inhalation aerosol is indicated as a bronchodilator for the treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD) in patients who require regular treatment with both Salbutamol and Ipratropium. It is also useful in patients having asthma featuring COPD symptoms & in patients having history of smoking over 10 pack-years.

Dosage and Administration
The dosage of **Combair® HFA** should be individualized according to the requirement of patient.
Adults (including elderly and adolescents >12 years of age): 2 inhalations (puffs) four times a day. Additional inhalations (puffs) may be taken if required; however, maximum number of inhalations (puffs) should not exceed 12 inhalations (puffs) in 24 hours.
Children and Pediatric patients: Safety and effectiveness of patients below 12 years of age have not been established.
Use in hepatic or renal disease: This combination has not been studied in patients with hepatic or renal insufficiency. It should be used with caution in those patients.

Side Effects
As the combination inhaler contains Salbutamol and Ipratropium Bromide, the type and severity of adverse reactions associated with each of the compounds may be expected. The following adverse events may be observed:

Salbutamol: There have been rare reports of mild tremor and headache. These usually disappear with continuous treatment. Transient muscle cramp has been reported very rarely. There have been very rare reports of hypersensitivity reactions such as angio-oedema, urticaria, bronchospasm, hypotension and collapse.

Ipratropium: There have been reports of headache, pain, influenza, coughing, pneumonia, chest pain, nausea, bronchitis, dyspnea, and bronchospasm in lower part, and pharyngitis, sinusitis and rhinitis in the upper part.

Precautions
As this preparation contains Ipratropium Bromide and, therefore, caution should be exercised in patients having narrow-angle glaucoma, prostatic hypertrophy or bladder-neck obstruction.

Since this preparation also contains sympathomimetic amines such as Salbutamol Sulphate, therefore, caution should be taken in patients having convulsive disorders, hyperthyroidism, or diabetes mellitus and in patients who are unusually responsive to sympathomimetic amines. Significant hypokalaemia may also be produced by β adrenergic agents (possibly through intracellular shunting) in some patients which has the potential to produce adverse cardiovascular effects. This hypokalaemia is usually transient, not requiring supplementation.
Paradoxical bronchospasm: This inhalation aerosol can produce paradoxical bronchospasm that can be life threatening. If it occurs, immediate discontinuation of the preparation is advised and alternative therapy should be instituted. It should be recognized that paradoxical bronchospasm, when associated with inhaled formulations, frequently occurs with the first use of a new canister.
Cardiovascular effect: Like other β adrenergic agonists, Salbutamol Sulphate can produce a clinically significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure and/or other symptoms. Although such effects are uncommon after administration of this inhalation aerosol at recommended doses, if they occur, the preparation may be discontinued. In addition, β adrenergic agents have been reported to produce electrocardiogram (ECG) changes, such as flattening of the T wave, prolongation of the QTC interval, and ST segment depression. Therefore, caution should be exercised in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmia and hypertension.
Immediate hypersensitivity reactions: Immediate hypersensitivity reactions may occur after administration of Ipratropium Bromide or Salbutamol Sulphate, as demonstrated by rare cases of urticaria, angio-oedema, rash, bronchospasm, anaphylaxis and oropharyngeal oedema.

Pregnancy and Lactation
This combination (Salbutamol Sulphate and Ipratropium Bromide) inhalation aerosol is pregnancy Category C.
Ipratropium: Pregnancy Category B. Animal studies have demonstrated no evidence of teratogenic effects as a result of Ipratropium bromide.
Salbutamol: Pregnancy Category C. Salbutamol has been shown to be teratogenic in mice. There are, however, no adequate and well controlled studies of this inhalation aerosol of Ipratropium bromide or Salbutamol Sulphate in pregnant women. Because animal reproduction studies are not always predictive of human response, this inhalation aerosol should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.
It is not known whether the components of this inhalation aerosol are excreted in human milk. This inhalation aerosol should be used in lactating mother only if the potential benefit justifies the potential risk to the neonate.

Contraindications
This combination inhalation aerosol is contraindicated in patients with a history of hypersensitivity to any of the ingredients. It is contraindicated in patients with hypertrophic obstructive cardiomyopathy or tachyarrhythmia, and in patients hypersensitive to any components of the product or to atropine or its derivatives. It is also contraindicated in patients with a history of hypersensitivity to soya lecithin or related food products such as soyabean and peanut.

Drug Interactions
This inhalation aerosol has been used concomitantly with other drugs, including sympathomimetic bronchodilators, methylxanthines and steroids, commonly used in the treatment of COPD, without adverse drug reactions.
Anticholinergic agents: Caution is advised in the co-administration of this inhalation aerosol with other anticholinergic drugs, as there is potential for an additive interaction.

Beta-adrenergic agents: There is an increased risk of adverse cardiovascular effects. Caution is therefore, advised in the co-administration of this inhalation aerosol and other sympathomimetic agents. β-receptor blocking agents and Salbutamol inhibit the effect of each other. β-receptor blocking agents should be used cautiously in patients with hyperreactive airways.

Diuretics: Caution is advised in the co-administration of β agonist containing drugs with non potassium sparing diuretics. β-adrenergic agonists should be administered with extreme caution in patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants or within two weeks of discontinuation of such agents because the action of β-adrenergic agonists may be enhanced.

Overdosage

The effects of overdosage are expected to be related primarily to Salbutamol. Acute overdosage with ipratropium bromide by inhalation is unlikely since ipratropium bromide is not well absorbed systemically after aerosol or oral administration. Manifestations of overdosage with Salbutamol may include anginal pain, hypertension, hypokalemia, and tachycardia with rates up to 200 beats per minute. As with all sympathomimetic aerosol medications, cardiac arrest and even death may be associated with abuse. Dialysis is not appropriate treatment for overdosage of salbutamol as an inhalation aerosol; the judicious use of a cardiovascular β-receptor blocker, such as metoprolol tartrate may be indicated.

Pharmaceutical Precaution

Do not puncture, break or incinerate pressurized canister even when apparently empty.
Avoid storage in direct sunlight or heat.
Store below 30°C.
Keep away from eyes.
Keep away from children.

Package Quantities

Combair® HFA Inhalation Aerosol: Each canister contains 200 metered doses, each actuation (Puff) delivers 100 microgram of Salbutamol Sulphate BP and 20 microgram of Ipratropium Bromide BP.

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