

Combivent®

metered aerosol



Boehringer
Ingelheim

Composition

Each metered dose contains: 21 micrograms ipratropium bromide corresponding to 20 micrograms ipratropium bromide anhydrous, 120 micrograms salbutamol sulphate.

Indications

COMBIVENT is indicated as a bronchodilator for treatment of bronchospasm associated with moderate to severe chronic obstructive airway disease in patients who require more than a single bronchodilator.

Dosage and Administration

Adults (including elderly patients): Two inhalations four times a day. The dose may be increased as required up to a limit of 12 inhalations in 24 hours.

Children: Not recommended for children under 12 years of age.

Patients should be advised to consult a doctor or the nearest hospital immediately in the case of acute or rapidly worsening dyspnoea (difficulty in breathing) if additional inhalations do not produce an adequate improvement.

Administration

The correct operation of the metered aerosol apparatus is essential for successful therapy. **Shake the aerosol canister and depress the valve two times before the apparatus is initially used.**

Before each use the following rules should be observed:



Fig. 1



Fig. 2

1. Remove protective cap.
2. **Shake the metered aerosol well before each use (see fig. 1)**
3. Breathe out deeply.
4. Hold the metered aerosol as shown in fig. 2, and close lips over the mouthpiece. The arrow and the base of the container should be pointing upwards.
5. Breathe in as deeply as possible, pressing the base of the container firmly at the same time, this releases one

metered dose. Hold the breath for a few seconds, then remove the mouthpiece from the mouth and breathe out.

6. Replace the protective cap after use. The container is under pressure and should on no account be opened by force or exposed to temperatures exceeding 50°C. As the container is not transparent it is not possible to see when

the contents are used up, but shaking the container will show if there is any remaining fluid. The mouthpiece should always be kept clean and can be washed with warm water. If soap or detergent is used, the mouthpiece should be thoroughly rinsed in clear water.

Contraindications

COMBIVENT is contraindicated in patients with a history of hypersensitivity to any of its components, or to atropine or its derivatives.

Special Precautions

Ocular complications: There have been rare reports of ocular complications (i.e. mydriasis, eye pain) when the contents of ipratropium bromide containing metered aerosols have been inadvertently sprayed in the eye. Care must be taken not to allow the aerosol to enter the eye. Should eye complications develop, treatment with miotic drops should be initiated immediately and specialist advice sought. Patients must be instructed in the correct administration of COMBIVENT metered aerosol. In the following conditions COMBIVENT should only be used after careful risk/benefit assessment, especially when doses higher than recommended are used: Hypertrophic obstructive cardiomyopathy, tachyarrhythmia, insufficiently controlled diabetes mellitus, recent myocardial infarction and/or severe organic heart or vascular disorders, hyperthyroidism. In the case of acute, rapidly worsening dyspnoea (difficulty in breathing) a doctor should be consulted immediately.

Prolonged use: If bronchial obstruction deteriorates it is inappropriate and possibly hazardous to simply increase the use of COMBIVENT beyond the recommended dose over extended periods of time. If higher than recommended doses of COMBIVENT are required to control symptoms, the patient's therapy plan should be reviewed.

Potentially serious hypokalaemia may result from beta₂-agonist therapy. Particular caution is advised in severe airways obstruction, as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics.

Additionally, hypoxia may aggravate the effects of hypokalaemia on cardiac rhythm. It is recommended that serum potassium levels are monitored in such situations.

Drug Interactions

Beta-adrenergics, xanthine derivatives and corticosteroids may enhance the effect of COMBIVENT.

The concurrent administration of other beta-mimetics, systemically absorbed anticholinergics and xanthine derivatives may increase the side effects. A potentially serious reduction in effect may occur during concurrent administration of beta-blockers. Anticholinergic effects of other drugs can be enhanced.

Pregnancy and Lactation

COMBIVENT should only be used in pregnancy and during lactation period if the potential benefit justifies the potential risks.

Side Effects

In common with other beta-agonists more frequent undesirable effects of COMBIVENT are fine tremor of skeletal muscles and nervousness, less frequent are tachycardia, dizziness, palpitations or headache, especially in hypersensitive patients.

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In isolated cases there may be local reactions such as dryness of the mouth, throat irritation, or allergic reactions.

As with other bronchodilators, in some cases cough, in very rare instances paradoxical bronchoconstrictions have been observed.

Use of anticholinergic agents (like e.g. ipratropium bromide) may precipitate urinary retention, in particular in patients with pre-existing outflow tract obstruction.

Overdosage

The effects of overdosage are expected to be primarily related to salbutamol because acute overdosage with ipratropium bromide is unlikely as it is not well absorbed systemically after inhalation or oral administration.

Manifestations of overdosage with salbutamol may include anginal pain, hypertension, hypokalaemia and tachycardia. The preferred antidote for overdosage with salbutamol is a cardio-selective beta-blocking agent but due care and attention should be used in administering these drugs in patients with a history of bronchospasm.

Properties

Ipratropium bromide is an anticholinergic agent which inhibits vagally mediated reflexes by antagonising the action of acetylcholine, the transmitter agent released from the vagus nerve. The bronchodilation following inhalation of ipratropium bromide is primarily local and site specific to the lung and not systemic in nature.

Salbutamol sulphate is a beta₂-adrenergic agent which acts on airway smooth muscle

resulting in relaxation. Salbutamol relaxes all smooth muscle from the trachea to the terminal bronchioles and protects against all bronchoconstrictor challenges.

COMBIVENT metered aerosol provides the simultaneous release of ipratropium bromide and salbutamol sulphate allowing the synergistic efficacy on the muscarinic and beta₂-adrenergic receptors in the lung to cause bronchodilation.

Pharmacokinetics

Ipratropium bromide is not readily absorbed into the systemic circulation either from the surface of the lung or from the gastrointestinal tract as confirmed by blood level and renal excretion studies. The half-life elimination is about 3–4 hours after inhalation or intravenous administration. Ipratropium bromide does not penetrate the blood brain barrier.

Salbutamol sulphate is rapidly and completely absorbed following oral administration either by the inhaled or gastric route. Peak plasma salbutamol concentrations are seen within three hours of administration and is excreted unchanged in the urine after 24 hours.

Intravenous salbutamol will cross the blood brain barrier reaching concentrations amounting to about five percent of the plasma concentrations.

From a pharmacokinetic perspective, the additive activity of COMBIVENT is due to the local effect of the fixed dose of the active components (ipratropium bromide and salbutamol sulphate) on the muscarinic and beta₂-adrenergic receptor in the lung.

Availability

Metered aerosol

Manufacturer:

Boehringer Ingelheim France
Reims, France

for
Boehringer Ingelheim
International GmbH

This is a medicament

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of the reach of children!
