



IMPORTANT UPDATE:

Continued Availability of Combivent® Inhalation Aerosol

Dear Pharmaceutical Buyer:

This letter contains important information that affects patients being treated with COMBIVENT. Specifically, it addresses confusion that may exist about the availability of COMBIVENT beyond 2009.

As you may already know, the use of chlorofluorocarbons (CFCs) in metered dose inhalers (MDIs) is being phased out and eventually eliminated.^{IA}

The U.S. Food and Drug Administration (FDA) has granted “essential use” exceptions for certain medically essential products, including COMBIVENT.^{IIA}

The FDA is currently reviewing the continued “essential use” status of COMBIVENT and is expected to issue a Final Rule shortly. This Final Rule may include a date when COMBIVENT Inhalation Aerosol can no longer be sold or dispensed to patients. We anticipate that a Final Rule, when issued, will allow for sufficient time for notification and transition to alternative available products. Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI) is working closely with the FDA on a CFC-free replacement inhaler.

Once a Final Rule has been issued, we will share information on the status of COMBIVENT as appropriate. In the meantime, please be assured that COMBIVENT still is available at pharmacies for patients.

BIPI will be communicating this information to pharmacy chains and independents through multiple communications channels.

Should you have any questions please contact your National Account Director or BIPI Customer Service at 1-800-243-0127. For additional information regarding ordering our products you may log onto www.bi-touchpoint.com.

Important Safety Information

COMBIVENT Inhalation Aerosol is indicated for use in patients with chronic obstructive pulmonary disease (COPD) on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and who require a second bronchodilator.

COMBIVENT Inhalation Aerosol is contraindicated in patients with a history of hypersensitivity to soya lecithin or related food products such as soybean and peanut; and in patients hypersensitive to any other components of the drug product or to atropine or its derivatives.

COMBIVENT Inhalation Aerosol can produce paradoxical bronchospasm that can be life-threatening. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted. It should



be recognized that paradoxical bronchospasm, when associated with inhaled formulations, frequently occurs with the first use of a new canister.

Immediate hypersensitivity reactions may occur after administration of ipratropium bromide or albuterol sulfate, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis, and oropharyngeal edema.

The albuterol sulfate contained in COMBIVENT Inhalation Aerosol can produce a clinically significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure and/or symptoms. Although such effects are uncommon after administration of COMBIVENT Inhalation Aerosol at recommended doses, if they occur, discontinuation of the drug may be indicated. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischemia associated with albuterol. In addition, beta-adrenergic agents have been reported to produce ECG changes, such as flattening of the T wave, prolongation of the QTc interval, and ST segment depression. Therefore, COMBIVENT Inhalation Aerosol should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias and hypertension.

Do not exceed recommended dose. Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs, in patients with asthma. The exact cause of death is unknown, but cardiac arrest following an unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected.

Preparations containing sympathomimetic amines such as albuterol sulfate should be used with caution in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus and in patients who are unusually responsive to sympathomimetic amines. Beta-adrenergic agents may also produce significant hypokalemia in some patients (possibly through intracellular shunting) which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation.

COMBIVENT Inhalation Aerosol contains ipratropium bromide and, therefore, should be used with caution in patients with hepatic or renal insufficiency, narrow-angle glaucoma, prostatic hyperplasia or bladder-neck obstruction.

In clinical trials, the most common adverse events reported for COMBIVENT Inhalation Aerosol were bronchitis, upper respiratory tract infection, headache, dyspnea, and coughing.

Robert Belknap
Executive Director
Trade Sales & Operations

Please click on the following link [COMBIVENT Prescribing Information](#) for full prescribing information about COMBIVENT.



Boehringer Ingelheim Pharmaceuticals, Inc.

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ⁱ Federal Register Vol 72, No III, Monday, June 11, 2007.

ⁱⁱ Federal Register Vol. 70, No 63, Monday, April 4, 2005.