Combivent Inhaler

1. Name of the medicinal product

Combivent

2. Qualitative and quantitative composition

Each 2.5 ml single dose unit contains 500 micrograms ipratropium bromide (as 520 micrograms ipratropium bromide monohydrate) and 3 mg salbutamol sulfate (corresponds to 2.5mg salbutamol base).

3. Pharmaceutical form

Nebuliser solution.

A clear, colourless or almost colourless solution.

4. Clinical particulars
4.1 Therapeutic indications

The management of bronchospasm in patients suffering from chronic obstructive pulmonary disease who require regular treatment with both ipratropium and salbutamol.

4.2 Posology and method of administration

COMBIVENT Inhalers are intended for inhalation only and may be administered from a suitable nebuliser or an intermittent positive pressure ventilator. The single dose units must not be taken orally or administered parenterally.

Treatment should be initiated and administered under medical supervision, e.g. in the hospital setting. Home based treatment can be recommended in exceptional cases (severe symptoms or experienced patients requiring higher doses) when a low dose rapid acting beta-agonist bronchodilator has been insufficient in providing relief after consultation with an experienced physician.

The treatment with the nebuliser solution in Inhalers should always be started with the lowest recommended dose. In very severe cases two unit dose vials may be required for symptom relief. Administration should be stopped when sufficient symptom relief is achieved.

The recommended dose is:

Adults (including elderly patients and children over 12 years):

1 single dose unit three or four times daily.

Children under 12 years:

There is no experience of the use of COMBIVENT Inhalers in children under 12 years.

Administration:

Please refer to the patient information leaflet for instructions for use with a nebuliser.

Since the single dose units contain no preservatives, it is important that the contents are used immediately after opening and that a fresh vial is used for each administration to avoid microbial contamination. Partly used, open or damaged single dose units should be discarded.

It is strongly recommended not to mix COMBIVENT Inhalers with other drugs in the same nebuliser.

4.3 Contraindications

COMBIVENT Inhalers are contraindicated in patients with hypertrophic obstructive cardio- myopathy or tachyarrhythmia. COMBIVENT Inhalers are also contraindicated in patients with a history of hypersensitivity to ipratropium bromide, salbutamol sulfate or to atropine or its derivatives.

4.4 Special warnings and precautions for use

Hypersensitivity

Immediate hypersensitivity reactions may occur after administration of COMBIVENT Inhalers, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm and oropharyngeal oedema.

Paradoxical bronchospasm

As with other inhalation therapy paradoxical bronchospasm may occur with an immediate increase in wheezing and shortness of breath after dosing. Paradoxical bronchospasm responds to a rapid-acting inhaled bronchodilator and should be treated straightaway. COMBIVENT should be discontinued immediately, the patient should be assessed and alternative therapy instituted if necessary.

Ocular complications

There have been rare cases of ocular complications (i.e. mydriasis, blurring of vision, narrow-angle glaucoma and eye pain) when the contents of metered aerosols containing ipratropium bromide have been sprayed inadvertently into the eye.

Patients must be instructed in the correct use of COMBIVENT Inhalers and warned not to allow the solution or mist to enter the eyes. This is particularly important in patients who may be pre-disposed to glaucoma. Such patients should be warned specifically to protect their eyes. Eye pain or discomfort, blurred vision, visual halos or coloured images, in association with red eyes from conjunctival congestion and corneal oedema may be signs of acute narrow-angle glaucoma. Should any combination of these symptoms develop, treatment with miotic drops should be initiated and specialist advice sought immediately.

Systemic effects

In the following conditions COMBIVENT Inhalers should only be used after careful risk/benefit assessment: insufficiently controlled diabetes mellitus, recent myocardial infarction and/or severe organic heart or vascular disorders, hyperthyroidism, pheochromocytoma, risk of narrow-angle glaucoma, prostatic hypertrophy or bladder-neck obstruction.

Cardiovascular effects

Cardiovascular effects may be seen with sympathomimetic drugs including COMBIVENT.There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol for respiratory disease, should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

Hypokalaemia

Potentially serious hypokalaemia may result from beta2-agonist therapy. Particular caution is advised in severe airway 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 (especially in patients receiving digoxin). It is recommended that serum potassium levels are monitored in such situations.

Gastro-intestinal motility disturbances

Patients with cystic fibrosis may be more prone to gastro-intestinal motility disturbances.

Dyspnoea

The patient should be instructed to consult a doctor immediately in the event of acute, rapidly worsening dyspnoea. In addition, the patient should be warned to seek medical advice should a reduced response become apparent.

Interference with laboratory tests or other diagnostic measures

The use of COMBIVENT may lead to positive results with regards to salbutamol in tests for non clinical substance abuse, e.g. in the context of athletic performance enhancement (doping).

4.5 Interaction with other medicinal products and other forms of interaction

The chronic co-administration of COMBIVENT with other anticholinergic drugs has not been studied. Therefore, the chronic co-administration of COMBIVENT with other anticholinergic drugs is not recommended.

The use of additional beta-agonists, xanthine derivatives and corticosteroids may enhance the effect of COMBIVENT Inhalers. The concurrent administration of other beta-mimetics, systemically absorbed anticholinergics and xanthine derivatives may increase the severity of side effects. A potentially serious reduction in effect may occur during concurrent administration of beta-blockers.

Beta2-adrenergic agonists should be administered with caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of beta2-adrenergic agonists may be enhanced.

Inhalation of halogenated hydrocarbon anaesthetics such as halothane, trichloroethylene and enflurane may increase the susceptibility to the cardiovascular effects of beta-agonists.

4.6 Pregnancy and lactation

Ipratropium bromide has been in general use for several years and there is no definite evidence of ill-consequence during pregnancy; animal studies have shown no hazard.

Salbutamol has been in widespread use for many years without apparent ill- consequence during pregnancy. There is inadequate published evidence of safety in the early stages of human pregnancy but in animal studies there has been evidence of some harmful effects on the foetus at very high dose levels.

As with all medicines, COMBIVENT Inhalers should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus. Similarly, COMBIVENT Inhalers should not be administered to breast-feeding mothers unless the expected benefit is thought to outweigh any possible risk to the neonate.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be advised that they may experience undesirable effects such as dizziness, accommodation disorder, mydriasis and blurred vision during treatment with COMBIVENT. If patients experience the above mentioned side effects they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8 Undesirable effects

Many of the listed undesirable effects can be assigned to the anticholinergic and beta2 –sympathomimetic properties of COMBIVENT. As with all inhalation therapy COMBIVENT may show symptoms of local irritation. Adverse drug reactions were identified from data obtained in clinical trials and pharmacovigilance during post approval of the drug.

The most frequent side effects reported in clinical trials were headache, throat irritation, cough, dry mouth, gastrointestinal motility disorders (including constipation, diarrhoea and vomiting), nausea and dizziness.