

## ***VI.2 Elements for a public summary***

### **VI.2.1 Overview of disease epidemiology**

#### **Chronic obstructive pulmonary disease (COPD):**

Chronic obstructive pulmonary disease (COPD) is an umbrella term for people with chronic bronchitis, emphysema, or both. With COPD the airflow to the lungs is restricted (obstructed). COPD is usually caused by smoking. Symptoms include cough and breathlessness. The most important treatment is to stop smoking. Inhalers are commonly used to ease symptoms. Other treatments such as steroids, antibiotics, oxygen, and mucolytic (mucus-thinning) medicines are sometimes prescribed in more severe cases, or during a flare-up (exacerbation) of symptoms. COPD is one of the leading causes of morbidity and mortality in the industrialized and the developing countries. According to the prediction of the World Health Organization, COPD will become the third leading cause of mortality and the fifth cause of disability in 2020 worldwide.

Chronic obstructive pulmonary disease (COPD) is a general term which includes the conditions chronic bronchitis and emphysema. COPD is the preferred term, but you may still hear it called chronic obstructive airways disease (COAD).

Chronic means persistent. Bronchitis is inflammation of the bronchi (the airways of the lungs). Emphysema is damage to the smaller airways and air sacs (alveoli) of the lungs. Pulmonary means 'affecting the lungs'. Chronic bronchitis or emphysema can cause obstruction (narrowing) of the airways. Chronic bronchitis and emphysema commonly occur together. The term COPD is used to describe airflow obstruction due to chronic bronchitis, emphysema, or both.

COPD is usually caused by smoking. COPD should be considered as a possible diagnosis in anyone aged over 35 years old who smokes, or has ever smoked *and* has persistent problems such as cough with lots of phlegm, breathlessness or wheeze, and recurrent chest infections. Symptoms usually become worse if you continue to smoke. Symptoms are unlikely to get much worse if you stop smoking. Treatment with inhalers often eases symptoms, but no treatment can reverse the damage to the airways. A flare-up of symptoms, often during a chest infection, may be helped by increasing the dose of usual treatments. This may be combined with a short course of steroid tablets and/or antibiotics.<sup>5</sup>

### **VI.2.2 Summary of treatment benefits**

None of the drugs currently available for chronic obstructive pulmonary disease (COPD) are able to reduce the progressive decline in lung function which is the hallmark of this disease. Smoking cessation is the only intervention that has proved effective. The current pharmacological treatment of COPD is symptomatic and is mainly based on bronchodilators, such as selective  $\beta_2$ -adrenergic agonists (short- and long-acting), anticholinergics, theophylline, or a combination of these drugs.

Glucocorticoids are not generally recommended for patients with stable mild to moderate COPD due to their lack of efficacy, side effects, and high costs. However glucocorticoids are recommended for severe COPD and frequent exacerbations of COPD.

New

pharmacological strategies for COPD need to be developed because the current treatment is inadequate.

The objective of pharmacological treatment of chronic obstructive pulmonary disease (COPD) is to prevent and control symptoms, reduce the frequency and severity of exacerbations, and improve general health status and exercise tolerance.

It is important to try to control symptoms of COPD with pharmacological treatment using the following general proposals:

- 1) There should be a stepwise increase in treatment, according to the severity of the disease. The step-down approach used in the chronic treatment of asthma is not applicable to COPD.
- 2) Treatment needs to be chronic and maintained at the same level for long periods of time, unless significant side effects or exacerbations occur.
- 3) Since individual patient response to the pharmacological treatment is variable, it is important to monitor pharmacological treatment closely and, if necessary, adjust it frequently.

Drugs currently recommended for the treatment of COPD are:

- 1) Bronchodilators (selective  $\beta$ 2-agonists, anticholinergic antimuscarinic agents and methylxanthines); 2) glucocorticoids; 3) other types of medication (vaccines, antibiotics,  $\alpha$ 1- antitrypsin augmentation therapy, mucolytic agents, antioxidants, immunoregulators, antitussives and vasodilators).<sup>3</sup>

### VI.2.3 Summary of safety

#### concerns Important identified

#### risks

Risk	What is known	Preventability
Whole body allergic reaction (Anaphylactic reaction)	Whole body allergic reaction is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, Any occurrence of allergic reaction should be immediately informed to the treating doctor. The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
		bromide/ salbutamol and initiate remedial therapy.
Low potassium in blood (Hypokalaemia)	Low potassium in blood is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, It is recommended that regular blood tests should be performed to check serum levels of potassium. The doctor should monitor patient's levels of potassium on a regular basis. If low potassium is observed, the doctor should decide to discontinue ipratropium bromide/ salbutamol treatment. They should stringently monitor the potassium levels in patients who are also receiving steroids, water-pills (diuretics) and xanthenes.
Headache	Headache is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any occurrence of headache should be informed to the treating doctor. . The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.
Inability of the eye to automatically change focus from distance to near objects (Accomodation disorders)	Inability of the eye to automatically change focus from distance to near objects is known to be associated with use of Ipratropium bromide	Yes, any eye discomfort should be informed to the doctor. The treating doctor should check the patient. The doctor should decide to

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
	/Salbutamol	discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.. If patients experience any eye discomfort they should avoid potentially hazardous tasks such as driving or operating machinery.
Palpitations	Palpitations is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any occurrence of palpitations should be informed to the doctor. . The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.
Abnormally fast heart rate (Tachycardia)	Abnormally fast heart rate is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any occurrence of fast heart rate should be informed to the doctor. . The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.
Cough	Cough is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any occurrence of cough should be informed to the doctor. . The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
		salbutamol and initiate remedial therapy..
Dry mouth	Dry mouth is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any occurrence of dry mouth should be informed to the doctor. . The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.
Nausea	Nausea is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any occurrence of nausea should be informed to the doctor. . The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.
Unintentional shaking (Tremor)	Unintentional shaking is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any occurrence of unintentional shaking should be informed to the doctor. The treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.
Impaired voice (Dysphonia)	Impairment of voice is known to be associated with use of Ipratropium bromide /Salbutamol	Yes, any discomfort while speaking, inability to speak or change in voice should be informed to the doctor. The

Risk	What is known	Preventability
		treating doctor should check the patient. The doctor should decide to discontinue the treatment with ipratropium bromide/ salbutamol and initiate remedial therapy.

**Important potential risks:**

Risk	What is known
Constriction of the airway (Paradoxical bronchospasm)	Constriction of the airway may occur with use of Ipratropium bromide /Salbutamol. The patient may immediately experience wheezing and shortness of breath. Any occurrence of wheezing or shortness of breath should be informed to the treating doctor. The doctor should check the patient and discontinue the treatment with ipratropium bromide/ salbutamol. The doctor should place the patient on alternate treatment.
Problems with eyes (Ocular complications)	Problems with eyes such as vision blurriness, increased pressure in eye, eye pain, acute angle glaucoma and narrow angle glaucoma have been observed with the use of Ipratropium bromide /Salbutamol. The patients should take the care to avoid inadvertent entry of Ipratropium bromide /Salbutamol in eyes. It is preferable to administer Ipratropium bromide /Salbutamol using mouthpiece.
Impaired supply of blood to the heart (Ischemic heart disease)	Effects on heart have been observed with Ipratropium bromide /Salbutamol. If the patients experience chest pain, they should immediately seek medical advice.
Stomach problems (Disturbance in gastrointestinal motility)	Patients who have cystic fibrosis (inherited disease of the mucus and sweat glands) may be more prone to stomach problems and therefore ipratropium bromide/ salbutamol, should be used with caution in these patients.

**Important missing information:**

<b>Risk</b>	<b>What is known</b>
Children less than 12 years of age have not been studied.	Ipratropium bromide/Salbutamol Cipla 0.5 mg/2.5 mg per 2.5 ml Nebuliser solution is not recommended in children below 12 years of age due to lack of data on safety and efficacy
Not studied in pregnant and lactating mothers	<p><b><u>Pregnancy</u></b></p> <p>There are no adequate data from the use of ipratropium bromide and salbutamol together in pregnant women (in early stages of pregnancy). In animal studies there has been evidence of some harmful effects on the foetus at very high dose levels. The potential risk for humans is unknown. Ipratropium bromide/Salbutamol Cipla 0.5 mg/2.5 mg per 2.5 ml Nebuliser solution should not be used during pregnancy unless clearly necessary and caution should be exercised when prescribing to pregnant women (especially in the first trimester).</p> <p><b><u>Lactation</u></b></p> <p>It is unknown whether ipratropium bromide is excreted into human breast milk. Salbutamol is excreted in human breast milk. There is insufficient/limited information on the excretion of Ipratropiumbromide/Salbutamol Cipla 0,5/2,5 mg per 2,5 ml in human or animal breast milk. A risk to the suckling child cannot be excluded. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Ipratropium bromide/Salbutamol Cipla 0.5 mg/2.5 mg per 2.5 ml Nebuliser solution should be made taking into account the benefit of breast-feeding to the child and the benefit of Ipratropium bromide/Salbutamol Cipla 0.5 mg/2.5 mg per 2.5 ml Nebuliser solution to the mother.</p>

**VI.2.4 Summary of additional risk minimisation measures by safety concern**

Not applicable

**VI.2.5 Planned post authorisation development plan**

Not applicable

**VI.2.6 Summary of changes to the risk management plan over time**

Not applicable.