VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Salmex is used to treat asthma and Chronic Obstructive Pulmonary disease (COPD).

Asthma is a lung disease that is caused by inflammation of the small tubes (bronchi) which carry air in and out of the lungs. The airways become narrow and the muscles around them tighten (bronchoconstriction) when patients are exposed to triggers (e.g. house dust mites, pollen). Symptoms include shortness of breath, wheezing, chest tightness and cough. Asthma can develop at any age and is more likely to happen in patients who have a family history of asthma.

In Europe about 30 million children and adults less than 45 years old have asthma. The amount of people with asthma tends to be higher in northern and western European countries with more than 10% of the adults aged between 18 and 44 years affected by asthma in these countries.

Chronic obstructive pulmonary disease is the name for a number of lung diseases including chronic bronchitis and emphysema. People with COPD have difficulty breathing because of a narrowing of their airways. Symptoms include increasing breathlessness when active, a persistent cough with phlegm and frequent chest infections. The main cause of COPD is smoking because it irritates and inflames the lungs. Over many years, the inflammation leads to permanent changes in the lung. The walls of the airways thicken and more mucus is produced. Damage to the delicate walls of the air sacs in the lungs causes emphysema and the lungs lose their normal elasticity. The smaller airways also become scarred and narrowed. Other causes of COPD include long-term exposure to fumes, dust and air pollution and genetic disorders.

It is estimated that approximately 8% of the population have COPD and it is the fourth leading cause of death in Europe.

VI.2.2 Summary of treatment benefits

Salmex is a 'generic medicine'. This means that Salmex is similar to a 'reference medicine' already authorised in the European Union (EU) and studies have been carried out to confirm that these two products produce the same amounts of the active substances (salmeterol and fluticasone) in the body. The benefits of salmeterol/fluticasone have been established during clinical studies and clinical experience with the reference medicine.

VI.2.3 Unknowns relating to treatment benefits

Breast feeding women, patients with liver problems and children less than 4 years of age were not included in clinical studies with the reference product.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Lung infections especially pneumonia in patients having asthma or obstructive disease of the respiratory tract (Pneumonia in COPD and asthma patient population)	In clinical studies, patients with Chronic Obstructive Pulmonary Disease (COPD) taking salmeterol/fluticasone were more likely to get pneumonia (swelling of lung tissue caused by an infection) compared with patients taking placebo (inactive treatment) or salmeterol only. Pneumonia and bronchitis may occur in up to 1 in 10 people taking salmeterol/fluticasone.	Doctors should look out for the possible development of pneumonia and other lung infections in patients with COPD as the symptoms of such infections are similar to those due to a worsening of COPD. Patients should tell their doctor if they notice any of the following symptoms: increase in sputum production, change in sputum colour, fever, chills, increased cough, increased breathing problems.
Serious events or death related to respiratory disorders or diseases (Respiratory-related events and deaths)	A clinical study of one of the drugs (salmeterol) contained in Salmex showed an increased risk in some asthma patients of severe outcomes including death.	Patients should tell their doctor straight away if their asthma or breathing gets worse whilst using Salmex.

Risk	What is known	Preventability
Production of very high level of hormone cortisol in the body (Cushing's syndrome) or inability of adrenal glands to produce enough amount of cortisol (adrenal suppression)	One of the drugs (fluticasone) contained in Salmex is a corticosteroid. Whole body (systemic) effects may occur when inhaled corticosteroids are taken in high doses for a long time. Possible effects include symptoms caused by very high levels of a hormone called cortisol in the body (Cushing's syndrome), a condition where the adrenal glands are unable to produce sufficient amounts of cortisol (adrenal suppression), slowing of growth in children and adolescents, thinning of the bones, cloudiness in the clear structure of the eye (cataract), an eye condition caused by damage to the optic nerve (glaucoma) and more rarely, effects on mental health/behaviour, mainly in children. Stopping taking Salmex or reducing the dose of Salmex may cause you to have problems with your adrenal gland. These problems can also occur when your body is under stress such as from fever, infection or surgery. Symptoms include: stomach pain tiredness and loss of appetite, feeling sick, diarrhoea, weight loss, headache, drowsiness, low levels of sugar in your blood, low blood pressure and fits.	Doctors should check patients regularly for any of these side effects and make sure that the lowest dose of Salmex is used to effectively control asthma. Doctors should monitor levels of the hormone cortisol in patients switching from oral to inhaled corticosteroids. Doctors should measure the height of children regularly.

Risk	What is known	Preventability
Increased side effects of Salmex when taken with some other medicines (Drug interaction with CYP450 3A4 inhibitors)	Some medicines used to treat viruses, bacterial and fungal infections (e.g. ritonavir, telithromycin, ketoconazole, itraconazole) may increase the amount of Salmex in a patient's body. This can increase the risk of side effects of Salmex including irregular heart beats.	Patients should tell their doctor if they are taking or have recently taken any other medicines.
Allergic reactions (Hypersensitivity reactions including anaphylactic reactions)	Severe allergic reactions have been reported in patients taking Salmex. In addition, Salmex also contains lactose. There have been reports of serious allergic reactions in patients with severe milk protein allergy. Signs of serious allergic reactions can include rash, swelling of the face, mouth and/or tongue and breathing problems.	Patients should not take Salmex if they are allergic to salmeterol, fluticasone or to the other ingredient lactose. Patients should not take any more Salmex if they develop any signs of a serious allergic reaction and they should seek medical attention immediately.
Heart rhythm problems (Arrhythmias)	Patients treated with Salmex may be at increased risk of developing problems with their heart rhythm.	Patients should tell their doctor before taking Salmex if they have heart disease, an abnormal heart rhythm, diabetes mellitus, overactive thyroid gland or low levels of potassium in their blood.
Chest pain (Angina pectoris)	Patients treated with Salmex may encounter chest pain.	Patients should tell their doctor before taking Salmex if they have heart disease or low levels of potassium in their blood. In case of chest pain, immediate medical attention must be sought.

Important potential risks

Risk	What is known
None.	Not applicable.

Missing information

Risk	What is known
Use during breastfeeding	It is not known whether the medicines in Salmex are transferred in the mother's breast milk, therefore, a risk to breast fed babies cannot be ruled out. Patients should seek their doctor's advice before taking this medicine.
Use in patients with liver problems	No information is available concerning the use of Salmex in patients with liver problems.
Use in children < 4 years	There is no data available concerning the use of Salmex in children under 4 years of age.

VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Salmex can be found in the EPAR page.

This medicine has no additional risk minimization measures.

VI.2.6 Planned post authorisation development plan (if applicable)

None are planned.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable (first version of RMP).