13.2 Part VI.2 Elements for a Public Summary

13.2.1 Part VI.2.1 Overview of disease epidemiology

Asthma

Asthma is a disease of the airways in the lungs. Its symptoms are caused by inflammation, which makes the airways red, swollen, narrower and extra-sensitive to irritants. This leads to recurrent attacks of wheezing, breathlessness, chest tightness and coughing. Mild attacks can settle down without treatment, but treatment usually helps them to resolve more quickly. Appropriate treatment can also reduce the risk of further attacks. If you experience a serious attack you should seek emergency help.

Asthma is a long-term (chronic) disease. Your asthma does not stay the same, but changes over time, and every person with asthma has good and bad days (or longer periods of time).

Asthma is very common. Around one out of every ten people in the Western World develops asthma at some stage in their life.

Chronic obstructive pulmonary disease (COPD) – for Salmeterol xinafoate / Fluticasone propionate 50/250 µg and 50/500 µg pre-dispensed inhalation powder only

COPD is a progressive disease that makes it hard to breathe. Other symptoms are e.g. cough, mucus, chest tightness. COPD is a major cause of disability and the third leading cause of death in the United States. COPD develops slowly. Symptoms often worsen over time and can limit your ability to do routine activities. Mostly COPD is diagnosed in middle-aged or older adults. COPD has no cure yet. However, treatments and lifestyle changes can help you feel better, stay more active, and slow the progress of the disease.

Cigarette smoking is the leading cause of COPD. Most people who have COPD smoke or used to smoke. Long-term exposure to other lung irritants—such as air pollution, chemical fumes, or dust—also may contribute to COPD.

13.2.2 Part VI.2.2 Summary of treatment benefits

This medicine contains two active substances.

- Salmeterol: a long-acting substance that widens the airways
- Fluticasone: a cortisone which reduces swelling and inflammation in the lungs

A study has been conducted with 150 participants. The goal was to show comparable efficacy and safety of the test product in comparison with a reference product already marketed in adults and adolescents who suffer from a moderate or severe form of asthma

13.2.3 Part VI.2.3 Unknowns relating to treatment benefits

In the supporting study, adults and adolescents with a moderate or severe form of asthma have been studied. No data from pregnant women and children below 4 years of age have been collected.

13.2.4 Part VI.2.4 Summary of safety concerns

Table 13-5 Important identified risks

Risk	What is known	Preventability
Respiratory-related events or deaths	Data from a large clinical trial suggested African-American patients were at increased risk of serious respiratory-related events or deaths when using salmeterol compared with placebo.	Yes, patients of black African or Afro-Caribbean ancestry should therefore be asked to continue treatment but to seek medical advice if asthma symptoms remained uncontrolled or worsen whilst using.
Inflammation of the lungs (Pneumonia)	Acute or chronic inflammation of one or both lungs, in which the air sacs (alveoli) become filled with liquid, which renders them useless for breathing. It is usually caused by bacterial (especially pneumococcal) or viral infection	No, physicians should remain vigilant for the possible development of pneumonia and other lower respiratory tract infections in patients with COPD as the clinical features of such infections and exacerbation frequently overlap. If a patient with severe COPD has experienced pneumonia the treatment with salmeterol-fluticasone should be re-evaluated.
A syndrome caused by an excess of corticosteroids in the blood usually caused by a tumor (Cushing's syndrome and adrenal suppression)	It is characterized by obesity, muscle and skin atrophy, facial fullness (known as *moon facies*), hypertension, and other physical changes	Yes, the patient needs to be reviewed regularly and the dose of inhaled corticosteroid needs to be reduced to the lowest dose at which effective control of asthma is maintained
Slowing of growth in children and adolescents (Growth retardation in pediatrics)	Children and adolescents might grow slower than normal.	Yes, the patient needs to be reviewed regularly and the dose of inhaled corticosteroid needs to be reduced to the lowest dose at which effective control of asthma is maintained
Medicines to treat viruses, such as ritonavir (Drug-interaction with CYP450 3A4 inhibitors)	Ritonavir can increase the concentration of fluticasone in the blood. This may lead to increased side effects.	Yes, avoid concomitant use.
Serious allergic reactions which causes difficulty in breathing or dizziness (Hypersensitivity reactions including anaphylactic reactions)	The breathing might suddenly get worse after using salmeterol-fluticasone or the patient may be very wheezy and cough, may notice itching and swelling (usually of the face, lips, tongue, or throat).	No.

Risk	What is known	Preventability
Irregularity in the force or rhythm of the heartbeat (Arrhythmias)	The heart might have a faster or uneven beat.	No.
Constricting chest pain (Angina)	Chest pain, often radiating to the left shoulder and down the left arm, caused by an insufficient supply of blood to the heart.	No.

Table 13-6 Important potential risks

Risk	What is known
Off-label use in children below 12 years old	Children and adolescents might grow slower than normal and have an increased risk for depression or aggression and behavioural changes, such as being unusually active and irritable.

Table 13-7 Missing information

Risk	What is known
Patients with hepatic impairment	There are no data available for use of salmeterol-fluticasone in patients with hepatic impairment.
Pregnant and breastfeeding women	It is not known whether salmeterol-fluticasone passes into breast-milk. A risk to breastfed newborns/infants cannot be excluded.

13.2.5 Part VI.2.5 Summary of additional risk minimization 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 minimizing 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 minimization measures.

No special important risks or potential risks have been identified for salmeterol-fluticasone, which require additional risk minimization activities other than routine.

13.2.6 Part VI.2.6 Planned post authorization development plan

None.

13.2.7 Part VI.2.7 Summary of changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	24.09.2013	**Identified risks:** - Respiratory-related events or deaths - Pneumonia - Cushing's syndrome and adrenal suppression - Growth retardation in pediatrics - Drug-interaction with CYP450 3A4 inhibitors - Hypersensitivity reactions including anaphylactic reactions - Arrhythmias - Angina **Potential risks:** None **Missing information:** - Patients with hepatic impairment - Breastfeeding women - Use in children 4-12 years of age	
1.1	22.05.2014	**Based on the RMS Day 100 Preliminary Assessment report, date 09/05/2014 the following changes to the safety concerns were made:** "Use in children 4-12 years of age" was **reworded** to "Off-label use in children below 12 years old" and was **moved** from "Missing information" to "Potential risk". Breastfeeding women" was **reworded** to " Pregnant and breastfeeding women" **Based on the CMS (IMB) Day 70 draft assessment report:**	

Version	Date	Safety Concerns	Comment
		Medication error was included as a "Potential risk". The 'Before using the inhaler' instructions (the requirement to remove the foil strip) are significantly different to instructions for other inhaler devices on the Irish market and therefore the potential for medication errors exists.	
1.2	10 Jul 2014	**Based on the RMS Day 120 Draft Assessment Report in SE/H/1405; 1407-08/01-02/DC:** Medication error was deleted as "potential risk" throughout the RMP.	
			The Marketing Status (Annex 2) was updated as the product in the meantime is approved.
2.0	20 May 2016	N/A	For a new registration of 25/125 µg and 25/250 µg, Pressurized inhalation, suspension, the following changes were made in the existing, approved RMP v.1.2 for 50/250 µg and 50/500 µg, Inhalation powder, pre-dispensed:
		N/A	25/125 µg and 25/250 µg, Pressurized inhalation, suspension addressed in all relevant RMP parts (Cover page, Part I Product(s) overview, Part II modules SI, III, IV, VI, VII)
		N/A	Inclusion of Part II Module SV
		N/A	MA status updated