VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Asthma

CHF 1535 pressurised metered dose inhaler (pMDI) and CHF 1535 NEXThaler® are approved for regular treatment of adult patients with asthma in whom:

• asthma is not adequately controlled by using inhaled corticosteroids and "as needed" short-acting bronchodilators, or

• asthma is responding well to treatment with both corticosteroids and long-acting bronchodilators.

Asthma is one of the most common long-term (chronic) diseases in the world. It is estimated that approximately 300 million people of all ages and all ethnic backgrounds suffer from asthma. Asthma has become more common in both children and adults around the world in recent decades mainly because of a rise in allergic diseases. Moreover cases of asthma increase as more people adopt western lifestyles and live in town or cities.

It is estimated that asthma accounts for about 1 in every 250 deaths worldwide. Many of the deaths are preventable, being due to either poor long-term medical care or delay in obtaining help during a final attack.

Chronic Obstructive Pulmonary Disease (COPD)

CHF 1535 pMDI is approved for the treatment of symptoms of severe chronic obstructive pulmonary disease (COPD) in adult patients.

COPD is the sixth commonest case of death worldwide, and set to become the third commonest cause by the year 2020. The main cause of COPD is smoking. The likelihood of developing COPD increases the more people smoke and the longer people have been smoking. This is because smoking irritates and inflames the lungs, which results in scarring. When the smaller airways become scarred and narrowed they cause the symptoms of shortness of breath (breathlessness), cough and phlegm associated with COPD.

COPD mainly affects people over the age of 40 and becomes more common with increasing age. It is more common in men than women.

VI.2.2 Summary of treatment benefits

Asthma

Main results of Pivotal studies conducted with CHF 1535 pMDI

CHF 1535 pMDI as maintenance treatment
CHF 1535 pMDI improved asthma symptoms and lung function and reduced flare ups (exacerbations).
In a 24-week study involving 645 patients the effect on lung function of CHF 1535 pMDI (2 puffs twice a day) was the same as that when using its components in separate inhalers, and was better than using beclometasone alone.

CHF 1535 pMDI used as maintenance and reliever treatment
In a 48-week study involving 1701 adult patients with asthma, the effectiveness of CHF 1535 pMDI used as maintenance (1 puff twice a day) and as reliever treatment (up to 8 puffs per day) was compared to CHF 1535 pMDI used as maintenance treatment (1 puff twice a day) plus another reliever inhaler containing salbutamol used as needed. The results demonstrated that CHF 1535 pMDI used as maintenance and reliever treatment when compared with CHF 1535 pMDI used as maintenance treatment plus salbutamol as reliever as needed:
- significantly delayed the time to first severe flare up;
- has a lower rate of severe asthma flare ups.

CHF 1535 pMDI high dose-strength formulation, used as maintenance treatment
CHF 1535 pMDI in the 200/6 formulation had a better effect on lung function and similar benefits in terms of symptoms-based parameters than beclometasone (same dose) alone. The same effect is expected for the CHF 1535 NEXThaler® 200/6 formulation.

Main results of Pivotal studies conducted with CHF 1535 NEXThaler®

CHF 1535 NEXThaler® has been studied in 3 pivotal clinical trials in which the effects of CHF 1535 NEXThaler® were compared to CHF 1535 pMDI (first trial), to CHF 1535 pMDI and placebo (second trial) and to CHF 1535 pMDI and beclometasone dipropionate 100 micrograms per dose inhalation powder (third trial). In the first study, where both products were taken as 1 and 2 puffs twice a day for up to three months, CHF 1535 NEXThaler® was not worse than CHF 1535 pMDI in improving the lung function and the asthma symptoms in 696 patients.

In the second study, where CHF 1535 pMDI and CHF 1535 NEXThaler® were taken as 1 or 4 puffs as a single dose, the NEXThaler® formulation was not worse than the pMDI formulation in improving the lung function in 69 partly controlled asthmatic patients and they were both better than placebo.

In the third clinical trial involving 755 controlled asthmatic patients, after 2 months of treatment with 1 puff twice a day, no difference was seen between CHF 1535 pMDI and NEXThaler® in controlling asthma symptoms.

Chronic Obstructive Pulmonary Disease (COPD)

Pivotal studies conducted with CHF 1535 pMDI

CHF 1535 pMDI was not worse than the combination budesonide plus formoterol and was better than formoterol alone in terms of improvement of lung function. It significantly reduced the risk of flare ups compared to formoterol alone. The same effect is expected for the CHF 1535 NEXThaler® formulation.

VI.2.3 Unknowns relating to treatment benefits

Mainly Caucasian and Chinese patients were enrolled into the clinical trials with CHF 1535, but it is not expected an influence of the racial group on the product's effect.

No data are available for use of CHF 1535 in patients with reduced liver or kidney function, but there is no theoretical reason to suggest that CHF 1535 dose need to be adjusted in these patients.

VI.2.4 Summary of safety concerns

The following safety concerns relate to CHF 1535 pMDI. Common and Uncommon frequencies derive from clinical trials experience:

Important identified risks

Risk	What is known	Preventability
Low potassium levels in the blood (Hypokalaemia)	Cases of low potassium levels in the blood have been uncommonly reported in clinical trials with CHF 1535 pMDI (affecting less than 1 in 100 people). None of these were serious and none of the patients needed to stop their medication. However, it may be more serious in patients who already have low potassium levels, have a heart attack or are taking certain medicines that may cause a fall in potassium level.	Special care should be taken in patients who already have low potassium levels and are not taking medicines to control it, in patients suffering from severe asthma or in patients who are taking other medicines which may lower potassium levels such as other asthma medicines (theophylline, aminophylline or steroids) or diuretics (water tablets) or medicines for treating heart diseases (digoxin). Levels of potassium in the blood will be monitored.
Problems with the adrenal glands (Adrenal suppression)	The adrenal glands release hormones, such as glucocorticoids, in the body. Very rarely (affecting less than 1 in 10,000 people), problems of suppression of adrenal glands work may occur particularly if high doses of inhaled corticosteroids like beclometasone (one of the medicines in CHF 1535 pMDI) are taken for long periods of time. However, inhaled corticosteroids are less likely to cause problems with the adrenal glands than when they are taken by mouth.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
High blood sugar levels (Hyperglycaemia)	Formoterol (one of the medicines in CHF 1535 pMDI) is known to cause high blood sugar levels.	Additional blood tests to check blood sugar at the beginning of treatment and from time to time

Risk	What is known	Preventability
	Cases of hyperglycaemia have been uncommonly reported with CHF 1535 pMDI (affecting less than 1 in 100 people). This can make it more difficult for diabetic patients to control their blood sugar.	during treatment for diabetic patients.
Asthma attack (Asthmatic crisis)/ worsening shortness of breath, cough and wheezing immediately after using (Paradoxical bronchospasm)	All patients with asthma are at risk of having a worsening of asthma symptoms, with worsening of shortness of breath, cough, wheezing or tightness in the chest. The severity of the attacks may vary from mild to life-threatening. Bronchospasm is an abnormal contraction of the smooth muscle of the bronchi, resulting in an acute narrowing and obstruction of the respiratory airways. As with other inhalation therapies, there is the possibility that drugs such as CHF 1535 pMDI cause rarely (affecting less than 1 in 1,000 people) bronchospasm.	Asthmatic attacks and paradoxical bronchospasm are not preventable, but severity can be mitigated by quick medical intervention. If asthma symptoms get worse or are difficult to control or the reliever inhaler does not improve symptoms, the doctor must be contacted as soon as possible. In case of paradoxical bronchospasm, treatment must be stopped and a quick-acting "reliever" inhaler should be used straightaway to treat the symptoms.
Changes in the electrocardiogram (ECG QTc prolongation)/ Heart problems such as a very fast heart beat and disorders of heart rhythm (Tachycardia/Tachyarrhythmia)	Formoterol may cause abnormalities in electrocardiogram (QTc prolongation). Patients with (or at risk of) this electrocardiogram abnormality from other causes and heart problems might be at risk of more significant QTc prolongation and serious heart rhythm disorders when exposed to CHF 1535 pMDI. Cases of heart rhythm disorders, fast heart beat and QTc prolongation have been reported uncommonly (affecting less than 1 in 100 people) with CHF 1535 pMDI.	Use with caution (which may include monitoring) in patients with disorders of heart rhythm such as increased or irregular heart rate, a fast pulse rate or palpitations or if the heart trace is abnormal. Use with caution with other medicines used for treating abnormal heart rhythms (quinidine, disopyramide, procainamide), antihistamines for allergic reactions, medicines to treat depression or mental disorders such as monoamine oxidase inhibitors (phenelzine, isocarboxazid), tricyclic antidepressants (amitriptyline, imipramine), phenothiazines (which may cause changes in

Risk	What is known	Preventability
		heart trace and increase the risk of disorders of heart rhythm) and certain anaesthetics.
Increased pressure in the eye (Glaucoma)	Very rarely (affecting less than 1 in 10,000 people) CHF 1535 pMDI may cause glaucoma, an increased pressure in the eye that may occur when high doses of inhaled corticosteroids are taken over a long period of time. Over time, the pressure in the eye causes damage to the optic nerve fibers.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
A clouding of the lens within the eye, causing blurred vision (Cataract)	Very rarely (affecting less than 1 in 10,000 people) CHF 1535 pMDI may cause cataracts, a clouding of the lens within the eye causing blurred vision that may occur when taking high doses of inhaled corticosteroids over a long period of time.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
Irregular heart beat (Atrial fibrillation)	Atrial fibrillation is the most common type of arrhythmia and might have serious outcomes. Cases of irregular heart beat were reported uncommonly (affecting less than 1 in 100 people) in patients taking CHF 1535 pMDI. Patients suffering from other heart conditions may be more likely to develop an irregular heart beat.	Use with caution and monitoring in patients with heart problems.
A reduction in white blood cells (Granulocytopenia)	Uncommonly (affecting less than 1 in 100 people) CHF 1535 pMDI may cause a reduction in white blood cells.	This side effect is listed in the SmPC and PIL.
A reduction in blood platelets (Thrombocytopenia)	This is a very rare blood side effect which is not normally worrying unless it causes serious haemorrhages, but they have never been reported with CHF 1535 pMDI. Cases of reduction in blood platelets have been reported very rarely (affecting	This side effect is listed in the SmPC and PIL.

Risk	What is known	Preventability
	less than 1 in 10,000 people) with CHF 1535 pMDI and in other medicines containing formoterol.	
Chest/heart pain (Angina pectoris)	Angina pectoris is a pain in the chest that is caused by ischaemia, an insufficient supply of oxygen-rich blood to the heart muscle. Cases of angina have been reported rarely (affecting less than 1 in 1,000 people) with CHF 1535 pMDI.	Use with caution and monitor in patients with heart problems.
Sleeping problems, depression or feeling worried, restless, nervous, over-excited or irritable, abnormal behaviour (Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes) predominantly in children	High doses of inhaled corticosteroids taken for a long period of time may cause some psychological and behavioural problems. These events are more likely to occur in children but the frequency is unknown.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
Thinning of the bones (Bone density decreased)	Even if no cases have been observed so far with CHF 1535 pMDI, a review of published literature suggests that there is a link between inhaled corticosteroids and a thinning of the bones when high doses of inhaled corticosteroids are taken over a long period of time.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
Very high levels of a hormone called cortisol in the blood (Cushing's syndrome)	A few cases of Cushing's syndrome have been reported in patients using inhaled corticosteroids. The risk of having this side effect is greater if high doses of inhaled corticosteroids are taken for a long period of time.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
Swelling of the skin or mucous membranes especially of the eyes, face, lips and throat (Angioedema)	CHF 1535 pMDI may rarely (affecting less than 1 in 1,000 people) cause symptoms of allergic reactions such as swelling of the skin or mucous membranes especially of the	Patients who are allergic to any of the ingredients in this medicine should not use CHF 1535 pMDI.

Risk	What is known	Preventability
	eyes, face, lips and throat. It might have serious outcomes.	
Slowing or halting of labour during birth (Tocolytic effect)/ abnormalities in babies (Foetal malformation)	There is no data on the use of CHF 1535 pMDI in pregnant women. However, animal studies have shown that high doses of corticosteroids cause abnormalities in babies and it is known that medicines of the same class of formoterol can slow or halt labour.	CHF 1535 pMDI must not be used during/at the end of pregnancy or during labour unless advised by the treating physician.
Trembling (Tremor)	Cases of trembling have been reported in some patients taking CHF 1535 pMDI and this is considered an uncommon side effect of this medicine (affecting less than 1 in 100 people). It is not in general a serious disorder and the major impact is on activities of daily life (e.g. eating, shaving or writing may be impacted).	This side effect is listed in the SmPC and PIL.
Infection of the lungs (Pneumonia)	Pneumonia is an infection of the lungs that in most of the cases reported during clinical trials with CHF 1535 pMDI in COPD patients had serious outcomes. Published literature suggests that there is an increased risk of pneumonia in patients with COPD treated with inhaled corticosteroids. In clinical trials with CHF 1535 pMDI in COPD patients, pneumonia has been uncommonly observed as side effect (affecting less than 1 in 100 people).	This side effect is listed in the SmPC and PIL.

Important potential risk

Risk	What is known (Including reason why it is considered a potential risk)
Slow growth in children and adolescents (Growth retardation	Children and adolescents may be at an increased risk of slow growth particularly if high doses of inhaled corticosteroids are taken for a

Risk	What is known (Including reason why it is considered a potential risk)
in children and adolescents).	long period of time. However it is not clear whether this affects the long term growth of the child/adolescent. There have been no cases of growth retardation from the clinical trials conducted up to now in children and adolescents. It is estimated this event may occur very rarely in patients exposed to CHF 1535 pMDI (affecting less than 1 in 10,000 people).

Missing information

Risk	What is known
Effects in the breast-fed baby	There is no information on the use of the medicine in breast-feeding. Therefore, it is advised not use CHF 1535 pMDI during breast-feeding.
Safety in children aged 5-11 and in adolescents aged 12-17 with asthma	There is no or limited information in children and adolescents aged 5 to 17 years old. Therefore, the medicine should not be used in children or adolescents under the age of 18 until further data become available.
Use in patients with reduced liver or kidney function	No clinical data have been generated to support the use of CHF 1535 pMDI in patients with reduced liver or kidney function, but there is no theoretical reason to suggest that CHF 1535 dose need to be adjusted in these patients.

The following safety concerns relate to CHF 1535 NEXThaler®. Common and uncommon frequencies derive from clinical trial experience.

Important identified risks

Risk	What is known	Preventability
Low potassium levels in the blood (Hypokalaemia)	Even if no cases of low potassium levels in the blood were reported as side effect during clinical trials, CHF 1535 NEXThaler® may cause a sharp fall in the serum potassium level. This side effect may be more serious in patients who already have low potassium levels, have a heart attack or are taking certain medicines that may cause a fall in potassium level.	Special care should be taken in patients who already have low potassium levels and are not taking medicines to control it, in patients suffering from severe asthma or in patients who are taking other medicines which may lower potassium levels such as other asthma medicines (theophylline, aminophylline or steroids) or diuretics (water tablets) or medicines for treating heart

Risk	What is known	Preventability
		diseases (digoxin). Levels of potassium in the blood will be monitored.
Problems with the adrenal glands (Adrenal suppression)	The adrenal glands release hormones, such as glucocorticoids, in the body. Problems of suppression of adrenal glands work may occur, particularly if high doses of inhaled corticosteroids like beclometasone (one of the medicines in CHF 1535 NEXThaler®) are taken for long periods of time. However, inhaled corticosteroids are less likely to cause problems with the adrenal glands than when they are taken by mouth. Cases of decreased blood cortisol level have been uncommonly observed with CHF 1535 NEXThaler® (affecting less than 1 in 100 people).	Regular monitoring of patients and reducing, when applicable, the dose of medicine.
High blood sugar levels (Hyperglycaemia)	Formoterol (one of the medicines in CHF 1535 NEXThaler®) is known to cause high blood sugar levels. Cases have been observed uncommonly (affecting less than 1 in 100 people) with CHF 1535 NEXThaler®. This can make it more difficult for diabetic patients to control their blood sugar.	Additional blood tests to check blood sugar at the beginning of treatment and from time to time during treatment for diabetic patients.
Asthma attack (Asthmatic crisis)/ worsening shortness of breath, cough and wheezing immediately after using (Paradoxical bronchospasm)	All patients with asthma are at risk of having a worsening of asthma symptoms, with worsening of shortness of breath, cough, wheezing or tightness in the chest. The severity of the attacks may vary from mild to life-threatening. Bronchospasm is an abnormal contraction of the smooth	Asthmatic attacks and paradoxical bronchospasm are not preventable, but severity can be mitigated by quick medical intervention. If asthma symptoms get worse or are difficult to control or the reliever inhaler does not improve symptoms, the doctor must be contacted as soon as

Risk	What is known	Preventability
	muscle of the bronchi, resulting in an acute narrowing and obstruction of the respiratory airways. Although no cases were observed in the clinical trial experience, as with other inhalation therapies, there is the possibility that drugs such as CHF 1535 NEXThaler® cause bronchospasm.	possible. In case of paradoxical bronchospasm, treatment must be stopped and a quick-acting "reliever" inhaler should be used straightaway to treat the symptoms.
Changes in the electrocardiogram (ECG QTc prolongation)/ heart problems such as a very fast heart beat and disorders of heart rhythm (Tachycardia/Tachyarrhythmia)	Formoterol may cause abnormalities in electrocardiogram (QTc prolongation). Patients with (or at risk of) this electrocardiogram abnormality from other causes and heart problems might be at risk of more significant QTc prolongation and serious heart rhythm disorders when exposed to CHF 1535 NEXThaler®. QTc prolongation and very fast heart beat have been reported uncommonly (affecting less than 1 in 100 people) during clinical trials with CHF 1535 NEXThaler®.	Use with caution (which may include monitoring) in patients with disorders of heart rhythm such as increased or irregular heart rate, a fast pulse rate or palpitations or if the heart trace is abnormal. Use with caution with other medicines used for treating abnormal heart rhythms (quinidine, disopyramide, procainamide), antihistamines for allergic reactions, medicines to treat depression or mental disorders such as monoamine oxidase inhibitors (phenelzine, isocarboxazid), tricyclic antidepressants (amitriptyline, imipramine), phenothiazines (which may cause changes in heart trace and increase the risk of disorders of heart rhythm) and certain anaesthetics.
Increased pressure in the eye (Glaucoma)	Even if no cases were observed during clinical trials, CHF 1535 NEXThaler® may cause glaucoma, an increased pressure in the eye that may occur when high doses of inhaled corticosteroids are taken over a long period of time. Over time, the pressure in the eye causes damage to the optic nerve fibers.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.

Risk	What is known	Preventability
A clouding of the lens within the eye, causing blurred vision (Cataract)	Even if no cases were observed during clinical trials, CHF 1535 NEXThaler® may cause cataracts, a clouding of the lens within the eye causing blurred vision that may occur when taking high doses of inhaled corticosteroids over a long period of time.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
Irregular heart beat (Atrial fibrillation)	Atrial fibrillation is the most common type of arrhythmia and might have serious outcomes. Even if no cases were observed during clinical trials, this effect may occur in patients taking CHF 1535 NEXThaler®. Patients suffering from other heart conditions may be more likely to develop an irregular heart beat.	Use with caution and monitoring in patients with heart problems.
Chest/heart pain (Angina pectoris)	Angina pectoris is a pain in the chest that is caused by ischaemia, an insufficient supply of oxygen-rich blood to the heart muscle. Cases of angina have been reported uncommonly (affecting less than 1 in 100 people) with CHF 1535 NEXThaler® during clinical trials.	Use with caution and monitoring in patients with heart problems.
Sleeping problems, depression or feeling worried, restless, nervous, over-excited or irritable, abnormal behaviour (Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes) predominantly in children	High doses of inhaled corticosteroids taken for a long period of time may cause some psychological and behavioural problems. These events are more likely to occur in children but the frequency is unknown.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
Thinning of the bones (Bone density decreased)	Even if no cases have been reported so far with CHF 1535 NEXThaler®, a review of published literature suggests that there is a link between	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.

Risk	What is known	Preventability
	inhaled corticosteroids and a thinning of the bones when high doses of inhaled corticosteroids are taken over a long period of time.	
Very high levels of a hormone called cortisol in the blood (Cushing's syndrome)	A few cases of Cushing's syndrome have been reported in patients using inhaled corticosteroids, but no cases were observed in clinical trials with CHF 1535 NEXThaler®. The risk of having this side effect is greater if high doses of inhaled corticosteroids are taken for a long period of time.	Regular monitoring of patients and reducing, when applicable, the dose of the medicine.
Swelling of the skin or mucous membranes especially of the eyes, face, lips and throat (Angioedema)	Even if no cases were observed in the clinical trial experience, CHF 1535 NEXThaler® may cause symptoms of allergic reactions such as swelling of the skin or mucous membranes especially of the eyes, face, lips and throat. It might have serious outcomes.	Patients who are allergic to any of the ingredients in this medicine should not use CHF 1535 NEXThaler®.
Slowing or halting of labour during birth (Tocolytic effect)/ abnormalities in babies (Foetal malformation)	There is no data on the use of CHF 1535 NEXThaler® in pregnant women. However, animal studies have shown that high doses of corticosteroids cause abnormalities in babies and it is known that medicines of the same class of formoterol can slow or halt labour.	CHF 1535 NEXThaler® must not be used during/at the end of pregnancy or during labour unless advised by the treating physician.
Trembling (Tremor)	Cases of trembling have been commonly observed in patients treated with CHF 1535 NEXThaler® during clinical trials (affecting less than 1 in 10 people). Trembling was seen only with the highest dose (2 inhalations twice a day), appeared most frequently at the beginning of treatment and was mild in intensity. It is not in general a serious disorder and	This side effect is listed in the SmPC and PIL.

Risk	What is known	Preventability
	the major impact is on activities of daily life (e.g. eating, shaving or writing may be impacted).	
Infection of the lungs (Pneumonia)	Pneumonia is an infection of the lungs that in most of the cases reported during clinical trials with CHF 1535 pMDI in COPD patients had serious outcomes. Published literature suggests that there is an increased risk of pneumonia in patients with COPD treated with inhaled corticosteroids. No cases were reported in clinical trials with CHF 1535 NEXThaler® in COPD patients.	This side effect is listed in the SmPC and PIL.

Important potential risk

Risk	What is known (Including reason why it is considered a potential risk)
Slow growth in children and adolescents (Growth retardation in children and adolescents)	Children and adolescents may be at an increased risk of slow growth particularly if high doses of inhaled corticosteroids are taken for a long period of time. However it is not clear whether this affects the long term growth of the child/adolescent. There have been no cases of growth retardation from the clinical trials conducted up to now in children and adolescents.

Missing information

Risk	What is known
Effects in the breast-fed baby	There is no information on the use of the medicine in breast-feeding. Therefore, it is advised not use CHF 1535 NEXThaler® during breast-feeding.
Safety in children aged 5-11 and in adolescents aged 12-17 with asthma	There is no or limited information in children and adolescents aged 5 to 17 years old. Therefore, the medicine should not be used in children or adolescents under the age of 18 until further data become available.
Safety in long term use of CHF	The safety of NEXThaler® has not been studied in patients using

Risk	What is known
1535 NEXThaler®	NEXThaler® for long periods of time.
Use in patients with reduced liver or kidney function	No clinical data have been generated to support the use of CHF 1535 NEXThaler® in patients with reduced liver or kidney function, but there is no theoretical reason to suggest that CHF 1535 dose need to be adjusted in these patients.

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

No additional risk minimisation measures are planned.

VI.2.6 Planned post authorisation development plan

List of studies in post authorisation development plan

Study/activity (including study number)	Objectives	Safety concerns /efficacy issue addressed	Status	Planned date for submission of (interim and) final results
PMS study	To determine: - rate of growth in children during a 12-month observation period; - the risk of less frequent side effects such as death, broken bones, and heart problems; - the rates of asthma flare ups.	Long term safety in children and adolescents	Planned after paediatric indication approval	Unknown

Studies which are a condition of the marketing authorisation

The above study is a condition of the marketing authorisation.