VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Incidence and prevalence of target indication	schizophrenia Schizophrenia is a mental disorder characterized by a breakdown of thought processes and by impaired emotional responses. Common symptoms are delusions including paranoia and auditory hallucinations, disorganized thinking reflected in speech, and a lack of emotional intelligence. It is accompanied by significant social or vocational dysfunction. The onset of symptoms typically occurs in young adulthood, with a global lifetime prevalence of about 0.3–0.7%. Diagnosis is based on observed behavior and the patient's reported experiences. bipolar disorder; moderate to severe manic episodes Bipolar disorder, also known as bipolar affective disorder, manic-depressive disorder, or manic depression, is a mental illness classified by psychiatry as a mood disorder. Individuals with bipolar disorder experience episodes of an elevated or agitated mood known as mania alternating with episodes of depression. 2.4 percent of the world's population may have some form of the disease. Mania can occur with different levels of severity. At milder levels of mania, known as hypomania, individuals appear energetic, excitable, and may be highly productive. As mania becomes more severe, individuals begin to behave erratically and impulsively, often making poor decisions due to unrealistic ideas about the future, and may have great difficulty with sleep. At the most severe level, individuals can experience very distorted beliefs about the world known as psychosis. bipolar disorder; major depressive episodes 2.4 percent of the world's population may have some form of bipolar disorder. Signs and symptoms of the depressive phase of bipolar disorder include persistent feelings of sadness, anxiety, guilt, anger, isolation, or hopelessness; disturbances in sleep and appetite; fatigue and loss of interest in usually enjoyable activities; problems concentrating; loneliness, self-loathing, apathy or indifference; depersonalization; loss of interest in sexual activity; shyness or social anxiety; irritability, chronic pain (with or without a known cause); lack of motivation; and morbid suicidal thoughts. In severe cases, the individual may become psychotic, a

condition also known as severe bipolar depression with psychotic features. These symptoms include delusions or, less commonly, hallucinations, usually unpleasant. A major depressive episode persists for at least two weeks, and may continue for over six months if left untreated.

Prevention of recurrence in patients with bipolar disorder, in patients whose manic, mixed or depressive episode has responded to quetiapine treatment

A naturalistic study from first admission for mania or mixed episode (representing the hospitalized and therefore most severe cases) found that 50% achieved syndromal recovery (no longer meeting criteria for the diagnosis) within six weeks and 98% within two years. Within two years, 72% achieved symptomatic recovery (no symptoms at all) and 43% achieved functional recovery (regaining of prior occupational and residential status). However, 40% went on to experience a new episode of mania or depression within 2 years of syndromal recovery, and 19% switched phases without recovery.

Add-on treatment of major depressive episodes in patients with Major Depressive Disorder (MDD) who have had sub-optimal response to antidepressant monotherapy

Major depressive disorder (MDD) is a mental disorder characterized by a pervasive and persistent low mood which is accompanied by low self-esteem and by a loss of interest or pleasure in normally enjoyable activities. Major depressive disorder is a disabling condition that adversely affects a person's family, work or school life, sleeping and eating habits, and general health. It is believed to currently affect approximately 298 million people as of 2010 (4.3% of the global population). Lifetime prevalence varies widely, from 3% in Japan to 17% in the US. In the United States, around 3.4% of people with major depression commit suicide, and up to 60% of people who commit suicide had depression or another mood disorder.

VI.2.2 Summary of treatment benefits

Clinical studies show that patients can be switched to and from quetiapine without much difficulty. Quetiapine’s efficacy is clearly superior to that of placebo, is similar to that of haloperidol or chlorpromazine, and appears to have similar efficacy to risperidone and olanzapine. It has a benign side-effect profile, particularly regarding to extrapyramidal symptoms and therefore good compliance is expected. Generally quetiapine is considered a safe drug. Although quetiapine was introduced as an atypical antipsychotic drug with clinical efficacy in schizophrenic patients, there is also new evidence from studies regarding its efficacy in treating mood disorders (bipolar disorder). To date, quetiapine has demonstrated efficacy in both acute

mania and bipolar depression, with a safety and tolerability profile superior to other medications in its class.
Quetiapine has also demonstrated efficacy in treating bipolar disorder in paediatric and geriatric populations. Quetiapine has been examined in children and adolescents in randomized clinical trials, open-label studies and several chart review studies. Most studies indicate that quetiapine is effective and well tolerated in paediatric population.
Also, in long-term studies (up to 2 years treatment) evaluating recurrence prevention in patients with manic, depressed or mixed mood episodes quetiapine was superior to placebo in increasing the time to recurrence of any mood event (manic, mixed or depressed), in patients with bipolar I disorder.
Also, two short-term (6 week) studies enrolled patients who had shown an inadequate response to at least one antidepressant. Quetiapine prolonged release 150 mg and 300 mg/day, given as add-on treatment to ongoing antidepressant therapy demonstrated superiority over antidepressant therapy alone in reducing depressive symptoms.

VI.2.3 Unknowns relating to treatment benefits
Not applicable. This is a generic application.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
<Safety concern in lay language (medical term)>	<Brief summary in lay language>	<Whether risk can be minimised or mitigated, and how>
Life-threatening neurological disorder (Neuroleptic malignant syndrome)	Neuroleptic malignant syndrome (NMS) is a life-threatening neurological disorder most often caused by an adverse reaction to neuroleptic or antipsychotic drugs. NMS typically consists of muscle rigidity, fever, autonomic instability, and cognitive changes such as delirium, and is associated with elevated plasma creatine phosphokinase.	The patient needs to tell his/her doctor immediately if he/she experiences a combination of high temperature (fever), severe muscle stiffness, sweating or lowered level of consciousness (a disorder called ˝neuroleptic malignant syndrome˝). Immediate medical treatment may be needed.
Reduction in number of white blood cells (Neutropenia)	A reduction in number of white blood cells makes infections more likely. Most cases of neutropenia have occurred within a couple of months of starting therapy with quetiapine. Possible risk factors for neutropenia include pre-existing low white cell count (WBC) and history of drug induced neutropenia.	The patient needs to tell his/her doctor if he/she has signs and symptoms of infection or if he had a decreased white blood cell count previously while taking some medications. The doctor may ask the patient to have blood tests from time to time, especially if there are signs and symptoms of infection present.
Change in electrical activity of the heart seen on ECG (QT prolongation)	The prolonged QT interval is widely seen and associated with the potentially deadly rhythm, *Torsades de Pointes* (TdP) and is therefore associated with the risk of sudden cardiac death. While it can occur spontaneously in the congenital form, there is a wide array of drugs that have been implicated in the prolongation of the QT interval.	Before taking this medicine, the doctor needs to be told if the patient or someone in his/her family has any heart problems, for example heart rhythm problems or if the patient is taking any medicines that may have an impact on the way the heart beats. The doctor will then make some additional tests and decide if this medicine is the right one to be used.

Blood clots (Venous thromboembolism)	Blood clots can form in the veins especially in the legs (symptoms include swelling, pain and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing. If you notice any of these symptoms seek medical advice immediately.	Before taking this medicine, the doctor needs to be told if the patient or someone in his/her family has a history of blood clots, as medicines like these have been associated with formation of blood clots with symtoms such as swelling, pain and redness in the leg as well as chest pain and difficulty in breathing. If the patient notices any of these symptoms, medical advice needs to be sought immediately.
Inflammation of the pancreas (Pancreatitis)	Pancreatitis has been reported in clinical trials and during the post marketing experience with quetiapine. Among the post marketing reports, while not all cases were confounded by risk factors, many patients had factors which are known to be associated with pancreatitis such as increased triglycerides, gallstones, and alcohol consumption.	Before taking this medicine, the doctor needs to be told if the patient has risk factors associated with inflammation of the pancreas (increased triglycerides, gallstones or alcohol consumption)
Blockage of bowel (Intestinal obstruction)	Constipation represents a risk factor for intestinal obstruction. Constipation and intestinal obstruction have rarely been reported with quetiapine. Patients who are receiving multiple concomitant medications that decrease intestinal motility are at increased risk.	The doctor needs to be told as soon as possible if the patient has constipation along with persistent abdominal pain, or constipation which has not responded to treatment, as this may lead to a more serious blockage of the bowel. Patients with blockage of bowel (intestinal obstruction) should be managed with close monitoring and urgent care.

Abnoramal muscle movement/symptoms similar to Parkinson's disease (Extrapyramidal symptoms)	In placebo controlled clinical trials of adult patients quetiapine was associated with an increased incidence of extrapyramidal symptoms (EPS) compared to placebo in patients treated for major depressive episodes in bipolar disorder.	Extrapyramidal symptoms include difficulty starting muscle movements, shaking, feeling restless or muscle stiffness without pain and other symptoms similar to Parkinson's disease.
Movement disorder (Tardive diskinesia)	If signs and symptoms of the movement disorder (tardive diskinesia) appear, dose reduction or discontinuation of quetiapine should be considered. The symptoms of tardive dyskinesia can worsen or even arise after discontinuation of treatment.	The doctor needs to be told if the patient is experiencing uncontrollable movements, mainly of the face or tongue. Dose reduction or discontinuation of the medication should be considered.
Feeling sleepy (Somnolence)	Quetiapine treatment has been associated with feeling sleepy (somnolence) and related symptoms, such as sedation. In clinical trials for treatment of patients with bipolar depression, the onset was usually within the first 3 days of treatment and was predominantly of mild to moderate intensity. In patients experiencing somnolence of severe intensity discontinuation of quetiapine may need to be considered.	Feeling sleepy (this may go away with time) (may lead to falls); however, in more severe cases discontinuation of quetiapine may need to be considered.

Fainting and low blood pressure when standing up (Syncope and orthostatic hypotension)	Quetiapine treatment has been associated with orthostatic hypotension that can result in syncope (low blood pressure when standing up and fainting) and which, usually occurs within the first 3 days of treatment. This could increase the occurrence of accidental injury (fall), especially in the elderly population. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medication.	The patient needs to exercise caution until he/she is familiar with the potential effects of the medication as low blood pressure potentially caused by this medication could lead to fainting and/or falls.
Convulsions or fits (Seizures)	In controlled clinical trials, there was no difference in the incidence of seizures in patients treated with quetiapine or placebo. No data is available about the incidence of seizures in patients with a history of seizure disorder. As with other antipsychotics, caution is recommended when treating patients with a history of seizures.	Before taking thismedicine, the patient needs to tell the doctor if he/she has ever had a fit.
Severe reduction/Lack of white blood cells (Agranulocytosis)	A severe reduction in number of white blood cells makes infections more likely. Most cases of severe neutropenia have occurred within a couple of months of starting therapy with quetiapine. Possible risk factors for neutropenia include pre-existing low white cell count (WBC) and history of drug induced neutropenia.	The doctor needs to be told if the patient has signs and symptoms of infection or if he/she had a decreased white blood cell count previously while taking some medications. The doctor may ask the patient to have blood tests from time to time, especially if the patient has signs and symptoms of infection.

Weight gain	Weight gain has been reported in patients who have been treated with quetiapine, and should be monitored and managed as clinically appropriate.	Weight gain has been seen in patients taking quetiapine. The patient and his/her doctor should check the patient's weight regularly.
Changes/increases in the content of certain fats in blood (Lipid changes (increased cholesterol, increased triglycerides, or decreased HDLs))	Changes/increases in the content of certain fats in blood (Increases in triglycerides, LDL cholesterol and total cholesterol, and decreases in HDL cholesterol) have been observed in clinical trials with quetiapine. Lipid changes should be managed as clinically appropriate.	The doctor may weigh the patient and may be checking for certain fats in the blood while the patient is receiving quetiapine therapy.
Increases in blood sugar (Hyperglycemia) and diabetes mellitus	Increases in blood sugar (Hyperglycaemia) and/or development or exacerbation of diabetes occasionally associated with a very severe consequences, called ketoacidosis or coma, has been reported rarely, including some fatal cases. In some cases, a prior increase in body weight has been reported which may be a predisposing factor.	Before taking the medicine, the doctor needs to be told if the patient has diabetes or a risk of getting diabetes. If this is the case, the doctor may check the patient's blood sugar levels while the patient is taking quetiapine.
Risk factors that make you prone to gain weight, develop diabetes and increase the content of different fats in blood (Metabolic risk factors, metabolic syndrome)	Given the observed changes in weight, blood glucose and lipids seen in clinical studies, patients (including those with normal baseline values) may experience worsening of their metabolic risk profile, which should be managed as clinically appropriate.	The doctor may weigh the patient and may be checking his/her blood sugar and certain fats in his/her blood while the patient is taking quetiapine.

A syndrome that controls urine volume and thereby causes a decrease in blood sodium levels (Syndrome of inappropriate antidiuretic hormone (SIADH) and hyponatremia)	Syndrome of inappropriate antidiuretic hormone (SIADH) secretion and hyponatremia (decrease in blood sodium levels) are very rare/uncommon adverse events.	Decrease in blood sodium levels is an uncommon adverse event that may affect up to 1 in 100 people. SIADH (Inappropriate secretion of a hormone that controls urine volume) is a very rare adverse event that may affect up to 1 in 10,000 people.
Decrease in thyroid hormones (Hypothyroidism)	Quetiapine treatment was associated with small dose-related decreases in thyroid hormone levels. For about 2/3 of all cases, cessation of quetiapine treatment was associated with a reversal of the effects irrespective of the duration of treatment.	Underactive thyroid gland which can cause tiredness or weight gain (hypothyroidism) is an uncommon adverse event (may affect up to 1 in 100 people).
Increase in the concentration of the milk-forming hormone prolactin in the blood (Hyperprolactinemia)	Quetiapine treatment was associated with an increase in the amount of a hormone called prolactin in the blood.	An increase in the amount of a hormone called prolactin in the blood is a common adverse event in adults (it may affect up to 1 in 10 people) and a very common adverse event in children and adolescents (may affect more than 1 in 10 people). This can lead to swelling of breasts and unexpected production of breast milk in boys and girls as well as irregular or no monthly period in girls.
Inflammation of the liver with or without yellowing of the skin and eyes (Hepatitis with or without jaundice)	Quetiapine treatment was rarely associated with yellowing of the skin and eyes (Jaundice) or inflammation of the liver (Hepatitis), while increases in liver enzymes occur commonly.	Yellowing of the skin and eyes (Jaundice) or inflammation of the liver (Hepatitis) are rare adverse events that may affect up to 1 in 1,000 people, while increases in liver enzymes are a common adverse event that may affect up to 1 in 10 people.

Very severe form of allergic reaction (Anaphylactic reaction) which may cause difficulty in breathing or shock.	Quetiapine treatment is very rarely associated with a very severe form of allergic reaction (Anaphylactic reaction).	The very severe form of allergic reaction (Anaphylactic reaction) is a very rare adverse event that may affect up to 1 in 10,000 people.
Serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome)	Quetiapine treatment is very rarely associated with a serious illness with blistering of the skin, mouth, eyes and genitals (Stevens-Johnson syndrome) and other serious skin reactions.	Stevens-Johnson syndrome, a serious illness with blistering of the skin, mouth, eyes and genitals and other serious skin reactions are very rare adverse events that may affect up to 1 in 10,000 people.
Withdrawal (discontinuation) symptoms	Acute withdrawal symptoms such as insomnia, nausea, headache, diarrhoea, vomiting, dizziness, and irritability have been described after abrupt cessation of quetiapine. Gradual withdrawal over a period of at least one to two weeks is advisable as withdrawal (discontinuation) symptoms are very common adverse events and may affect more than 1 in 10 people. Withdrawal may also occur in newborn babies, of mothers that have used quetiapine in the last trimester (last three months of their pregnancy). The newborns may display shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty in feeding.	Discontinuation symptoms (symptoms which occur when stopping quetiapine therapy include not being able to sleep (insomnia), feeing sick (nausea), headache, diarrhoea, being sick (vomiting), dizziness, and irritability. Gradual withdrawal over a period of at least 1 to 2 weeks is advisable as withdrawal (discontinuation) symptoms may affect more than 1 in 10 people. If the patient's newborn develops withdrawal symptoms, the patients may need to contact her doctor.

Difficulty swallowing (Dysphagia)	Difficulty swallowing (dysphagia) has been reported with quetiapine. Quetiapine should be used with caution in patients at risk for aspiration pneumonia. An increase in the rate of dysphagia with quetiapine vs. placebo was only observed in the clinical trials in bipolar depression.	Difficulty swallowing (dysphagia) is an uncommon adverse event that may affect up to 1 in 100 people.
Increased blood pressure in pediatric patients	Clinical trials have shown that in addition to the known safety profile identified in adults certain adverse events occurred at a higher frequency in children and adolescents compared to adults. Additionally, increase in blood pressure is an adverse event that has not been previously seen in adult studies.	Increased blood pressure is an adverse event very commonly seen in pediatric patients as it (may affect more than 1 in 10 children and adolescents).

Important potential risks:

Risk	What is known (Including reason why it is considered a potential risk)
Stroke in elderly patients (Cerebrovascular AEs in elderly patients)	An approximately 3-fold increased risk of cerebrovascular adverse events has been seen in randomised placebo controlled trials in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. An increased risk cannot be excluded for other antipsychotics or other patient populations. Quetiapine should be used with caution in patients with risk factors for stroke.
Stroke in non-elderly patients (Cerebrovascular AEs in the non-elderly patients)	As some cases have been identified, this adverse event is considered a potential risk.
Life-threatening arrhythmia (Torsade de Pointes)	Neuroleptics have been associated with the development of various life-threatening arrhythmias (such as QT-prolongation, ventricular arrhythmia, sudden unexplained death, cardiac arrest and torsades de pointes), which can lead to sudden death. This is considered a class effect.

Heart disease caused by a decrease in blood perfusion (Ischemic heart disease)	As some cases have been identified, this adverse event is considered a potential risk.
Higher likelihood of death in patients, who are suffering from dementia (loss of brain function) (Increased mortality in elderly demented patients)	In a meta-analysis of atypical antipsychotic drugs, it has been reported that elderly patients with dementia-related psychosis are at an increased risk of death compared to placebo. However in two 10-week placebo-controlled quetiapine studies in the same patient population the incidence of mortality in quetiapine-treated patients was 5.5% versus 3.2% in the placebo group. The patients in these trials died from a variety of causes that were consistent with expectations for this population. These data do not establish a causal relationship between quetiapine treatment and death in elderly patients with dementia.
Aggression/agitation	There have been reports of agitation in newborns exposed to antipsychotics (including quetiapine) in the third trimester of pregnancy. Also, effects of overdose include agitation.
Abuse and misuse	As some cases have been identified, this adverse event is considered a potential risk.
Likelihood of wanting to kill yourself and actually killing yourself (Suicide and suicidality)	Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery. In addition, physicians should consider the potential risk of suicide-related events after abrupt cessation of quetiapine treatment, due to the known risk factors for the disease being treated. Other psychiatric conditions for which quetiapine is prescribed can also be associated with an increased risk of suicide related events. In shorter-term placebo controlled clinical studies of patients with major depressive episodes in bipolar disorder an increased risk of suicide-related events was observed in young adult patients (younger than 25 years of age) who were treated with quetiapine as compared to those treated with placebo (3.0% vs. 0%, respectively).
Fall (Accidental injury)	Quetiapine treatment has been associated with orthostatic hypotension that can result in syncope (low blood pressure when standing up and fainting) and which, usually occurs within the first 3 days of treatment. This could increase the occurrence of accidental injury (fall), especially in the elderly population. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medication.

Inflammation of the lungs because of food gowing down the »wrong pipe« (Aspiration pneumonia)	Difficulty swallowing (Dysphagia) has been reported with quetiapine. Quetiapine should therefore be used with caution in patients at risk for aspiration pneumonia.
Potential for using the drug different than what it is intended for (Potential for off label and misdosing)	There is clear guidance provided on the usage of quetiapine. However, there have been cases when quetiapine has been used for indications and at dosages it is not approved for.
Use in elderly patients	The mean plasma clearance of quetiapine was reduced by 30% to 50% in elderly patients when compared to younger patients. Therefore, quetiapine should be used with caution in elderly patients, especially during the initial dosing period. The rate of dose titration may need to be slower, and the daily therapeutic dose lower, than that used in younger patients.

Important missing information

Risk	**What is known**
Pregnant or lactating women	Pregnancy: The safety and efficacy of quetiapine during human pregnancy have not yet been established. Up to now there are no indications for harmfulness in animal tests, possible effects on the foetal eye have not been examined, though. Therefore, quetiapine should only be used during pregnancy if the benefits justify the potential risks. Following pregnancies in which quetiapine was used, neonatal withdrawal symptoms were observed. Neonates exposed to antipsychotics (including quetiapine) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully. Breast-feeding: There have been published reports of quetiapine excretion into human breast milk, however the degree of excretion was not consistent. Women who are breast-feeding should therefore be advised to avoid breast-feeding while taking quetiapine.

	If the patient is pregnant or breast-feeding, thinks she may be pregnant or is planning to have a baby, she needs to ask her doctor or pharmacist for advice before taking this medicine. The patient should not take quetiapine during pregnancy unless this has been discussed with her doctor. Quetiapine should not be taken if the patient is breast-feeding. The following symptoms may occur in newborn babies, of mothers that have used quetiapine in the last trimester (last three months of their pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty in feeding. If the patient's baby develops any of these symptoms the patient may need to contact her doctor.
Patients on concomitant cardiovascular medications	Formal interaction studies with commonly used cardiovascular medicinal products have not been performed.
Patients on concomitant valproic acid	The pharmacokinetics of sodium valproate and quetiapine were not altered to a clinically relevant extent when co-administered. A retrospective study of children and adolescents who received valproate, quetiapine, or both, found a higher incidence of leukopenia and neutropenia in the combination group versus the monotherapy groups.

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

The following additional risk minimisation measures are considered necessary.

Risk: Weight gain
Risk minimization measure: Healthcare Professional education
Objective and rationale: To inform all prescribing physicians, prior to launch of quetiapine by Krka, that weight gain can occur with quetiapine use and that patients need to be counseled, monitored and treated accordingly.
Main additional risk minimization measures: HCP educational materials to be provided to all prescribing physicians prior to launch of Quetiapine by Krka.

Risk: Lipid changes (increased cholesterol, increased triglycerides, or decreased HDLs)
Risk minimization measure: Healthcare Professional education
Objective and rationale: To inform all prescribing physicians, prior to launch of quetiapine by Krka, that lipid changes (increased cholesterol, increased triglycerides, or decreased HDLs) can occur with quetiapine use and that patients need to be counseled, monitored and treated accordingly.
Main additional risk minimization measures:

HCP educational materials to be provided to all prescribing physicians prior to launch of Quetiapine by Krka.

Risk: Hyperglycemia and diabetes mellitus
Risk minimization measure: Healthcare Professional education
Objective and rationale: To inform all prescribing physicians, prior to launch of quetiapine by Krka, that hyperglycemia and diabetes mellitus can occur with quetiapine use and that patients need to be counseled, monitored and treated accordingly.
Main additional risk minimization measures: HCP educational materials to be provided to all prescribing physicians prior to launch of Quetiapine by Krka.

Risk: Metabolic risk factors, metabolic syndrome
Risk minimization measure: Healthcare Professional education
Objective and rationale: To inform all prescribing physicians, prior to launch of quetiapine by Krka, that metabolic risk factors, metabolic syndrome can occur with quetiapine use and that patients need to be counseled, monitored and treated accordingly.
Main additional risk minimization measures: HCP educational materials to be provided to all prescribing physicians prior to launch of Quetiapine by Krka.

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

Not applicable. No postauthorisation studies are planned.