Johnson syndrome; SmPC Summary of Product Characteristics; TD Tardive dyskinesia; VTE Venous thromboembolism; XR Extended release.

VI: 2 ELEMENTS FOR A PUBLIC SUMMARY

Quetiapine is a type of medication known as an antipsychotic medicine. The medicine is available in two forms: SEROQUEL and SEROQUEL XR/XL (a slow-releasing form), hereafter SEROQUEL/SEROQUEL XR. SEROQUEL/SEROQUEL XR works by correcting imbalances of chemical substances which act on the brain and nervous system. SEROQUEL/SEROQUEL XR is used to treat schizophrenia, bipolar disorder, and Major Depressive Disorder.

Inclusion of information relating to a potential risk should not be taken to imply that causal association with the use of SEROQUEL/SEROQUEL XR has been established.

VI: 2.1 Overview of disease epidemiology

VI: 2.1.1 Schizophrenia

Schizophrenia is a serious mental health condition that causes disordered ideas, beliefs and experiences. Symptoms include hearing, seeing, or sensing things that are not real, having mistaken beliefs, and feeling unusually suspicious. The incidence of schizophrenia is variable across countries, but tends to be higher in more developed countries. In men, the highest risk of developing schizophrenia is between 18 and 25 years of age; women aged between 26 and 45 years, and between 55 to 64 years have a higher risk of developing schizophrenia. People who have other family members with schizophrenia have a higher risk of developing the condition, and schizophrenia tends to be more common in people with lower family incomes. If untreated, people with schizophrenia have a higher risk of death.

Schizophrenia may be treated with antipsychotics medicines, as well as non-drug treatments such as behavioural therapy and counselling.

VI: 2.1.2 Bipolar disorder

Bipolar disorder is a life-long illness that causes periods of depression (lows) and periods of mania (highs), affecting mood, energy, and ability to function. Bipolar I patients have intense mania, while Bipolar II patients have less severe mania (known as hypomania). All bipolar patients spend more time depressed than manic or hypomanic.

People aged around 20 years old have the highest risk of developing bipolar disorder; risk reduces with increasing age. Bipolar I occurs in men and women equally: Bipolar II is more common in women. The chances of developing bipolar disorder are unrelated to race or family income. If untreated, bipolar patients have a higher risk of other mental health and medical conditions, and a higher risk of death, especially suicide.

Bipolar patients may be treated with various medications or combinations of medications including antipsychotics, antidepressants, mood stabilisers such as lithium, anti-epileptic medicines and non-drug treatments such as behavioural therapy and counselling.

VI: 2.1.3 Major Depressive Disorder

Major depression is a medical illness that causes a continual feeling of sadness and loss of interest, usually requiring long-term treatment. The incidence of major depression is variable across European countries. People aged between 18 and 30 have the highest risk of developing major depression: it is also more common in women than in men, and in people with other long-term diseases such as Parkinson's disease, chronic pain, stroke, heart disease, AIDS, lung diseases, thyroid diseases and cancer. Having other mental health problems such as anxiety or personality disorders, or abusing drugs or alcohol, may also increase the risk of developing major depression. If untreated, major depression can increase the risk of death.

Major depression may be treated with antidepressants (sometimes in combination with other medicines, including antipsychotics). Electric shock treatment is an option for patients who do not respond to standard drug treatments.

VI: 2.2 Summary of treatment benefits

SEROQUEL/SEROQUEL XR is a type of medication known as an antipsychotic medicine which works by correcting imbalances of chemical substances which act on the brain and nervous system. Because SEROQUEL/SEROQUEL XR only acts specifically with certain chemicals in the brain, patients taking SEROQUEL/SEROQUEL XR may experience a lower level of certain side effects, such as muscle spasms, restlessness, shaking or rigidity.

Over 28,000 adult patients have received SEROQUEL or SEROQUEL XR in clinical studies. SEROQUEL XR releases medicine more slowly than SEROQUEL.

There have been five clinical studies in schizophrenia which showed that SEROQUEL XR treatment significantly increased the time to a schizophrenic episode in clinically stable patients treated for up to 9 months. Data from clinical studies demonstrate that SEROQUEL is effective in the dose range of 150 to 750 mg daily (400 to 800 mg daily for SEROQUEL XR).

There have been eleven clinical studies of SEROQUEL and SEROQUEL XR in the treatment of bipolar disorder which showed that SEROQUEL and SEROQUEL XR are effective in the treatment of both depressive and manic episodes and that continued treatment, either alone or in combination with other mood stabilisers such as lithium or valproate, increased the time to an episode of depression or mania taking place. A study on long term treatment showed that benefits were maintained for up to one year. Data showed that a range of 300 to 800 mg daily was effective.

There have been eight clinical studies in major depression which showed that giving SEROQUEL XR at a dose of 150 to 300 mg daily was effective in patients who had not responded to initial treatment with standard antidepressants.

VI: 2.3 Unknowns relating to treatment benefits

Most clinical studies excluded seriously ill patients (heart, liver or kidney failure; uncontrolled diabetes), pregnant women and patients with recent suicide attempts. Reduced doses are recommended in patients with liver damage and standard doses in patients with kidney damage. Babies of women using SEROQUEL/SEROQUEL XR during pregnancy may experience withdrawal effects.

VI: 2.4 Summary of safety concerns

This section presents a summary of important identified risks, important potential risks and missing information; these are defined as follows:

- An important identified risk is an important side effect that is known to be related to the medicine of interest.
- An important potential risk is an important side effect that is suspected to be related to the medicine of interest but a connection has not been confirmed. It is not known whether the potential risks described in this summary are due to the use of SEROQUEL/SEROQUEL XR.
- Missing information is information about the safety of a medicine that is not available when the medicine was approved for sale. This may be unknown information about the safety of the medicine for conditions for which it is not approved for use.

Inclusion of information relating to a potential risk should not be taken to imply that causal association with the use of SEROQUEL/SEROQUEL XR has been established.

For SEROQUEL/SEROQUEL XR, important identified risks, important potential risks and missing information are provided in Table VI-3, Table VI-4, and Table VI-5, respectively.

Table VI-3 Important identified risks

Risk	What is known	Preventability
Abnormal muscle movements such as muscle spasms, restlessness, shaking, rigidity, muscle stiffness without pain.	Approximately 1 in 10 of all patients in SEROQUEL/SEROQUEL XR clinical studies experienced uncontrollable muscle movements resulting from drug treatment. Patients with bipolar disorder appeared to be more likely to experience these effects compared with patients with schizophrenia	Doctors and patients are made aware of the increased risk of abnormal muscle movements in the SEROQUEL/SEROQUEL XR product information. Medication adjustments may be necessary.

Table VI-3 Important identified risks

Risk	What is known	Preventability
Feeling sleepy	Approximately 42 in 100 of all patients in SEROQUEL/SEROQUEL XR clinical studies reported feeling sleepy after starting treatment with SEROQUEL/SEROQUEL XR.	Patients should be aware of the risk of feeling more sleepy when starting SEROQUEL/SEROQUEL XR treatment. The effect of feeling sleepy may be reduced by using a lower dose. The effects may also reduce with time, if SEROQUEL/SEROQUEL XR is continued. Patients should not drive or use any tools or machines until they know how the tablets affect them.
Weight gain	Approximately 1 in 5 of all patients in SEROQUEL/ SEROQUELXR clinical studies had weight gain of 7% or more compared with baseline.	A healthy diet and exercise are recommended for patients at risk for weight gain.
Changes in cholesterol levels	The following changes in cholesterol levels were seen in patients in SEROQUEL/ SEROQUEL XR clinical studies: increases in total cholesterol (approximately 1 in 10 patients), triglycerides (approximately 1 in 5 patients), and LDL (bad) cholesterol (approximately 7 in 100 patients), with decreases in HDL (good) cholesterol (approximately 15 in 100 patients).	A healthy diet and exercise are recommended for patients at risk for increased cholesterol. For some patients, a cholesterol lowering medication may be required.
High blood sugar levels and diabetes	Approximately 3 in 100 patients in SEROQUEL SEROQUELXR / clinical studies developed high blood sugar levels after starting treatment with SEROQUEL/ SEROQUELXR.	Weight reduction, blood pressure control, cholesterol control, diet, and exercise are recommended in patients at risk for development of diabetes.
Metabolic syndrome risk factors (metabolic syndrome describes a combination factors that, when occurring together, increase the risk of developing heart disease and diabetes)	Approximately 1 in 10 patients in SEROQUEL/ SEROQUELXR clinical studies shifted their risk score for metabolic syndrome from less than 3 (low risk) to 3 or more (high risk) after starting treatment with SEROQUEL/SEROQUELXR.	Weight reduction, blood pressure control, cholesterol control, diet, and exercise are recommended in patients at risk for development of metabolic syndrome.

Table VI-3 Important identified risks

Risk	What is known	Preventability
Changes in electrical activity of the heart	Approximately 1 in 1,000 patients in the SEROQUEL/SEROQUEL XR clinical studies had changes in electrical activity of the heart after starting treatment with SEROQUEL/SEROQUEL XR.	SEROQUEL/SEROQUEL XR should be used with care in patients with heart disease or a family history of changes in the electrical activity of the heart. Caution should also be taken when SEROQUEL/SEROQUEL XR is given at the same time as other medicines known to affect the electrical activity of the heart, including other antipsychotic medicines. This is especially true for patients with heart electrical activity abnormalities or a family history of such abnormalities, elderly patients, patients with low levels of sodium or magnesium in the blood, and patients with heart failure or an increased heart size. Patients who have taken an overdose of SEROQUEL/SEROQUEL XR should be observed for any changes in the electrical activity of the heart.

XR extended release.

Table VI-4 Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Stroke	In clinical studies, stroke was seen in approximately 1 in 50 elderly patients (more than 65-years-old) after starting treatment with SEROQUEL/SEROQUEL XR. In non-elderly patients, the frequency of patients experiencing stroke was approximately 1 in 1,000.
Reduced blood supply to the heart (ischemic heart disease)	Reduced blood supply to the heart (ischemic heart disease) is considered an effect which is observed with other antipsychotic medicines of the same type as SEROQUEL/SEROQUEL XR. In the SEROQUEL/SEROQUEL XR clinical studies, approximately 1 in 375 patients had ischemic heart disease.
Abuse and misuse	Abuse/misuse is considered an effect which is observed with other antipsychotic medicines of the same type as SEROQUEL/SEROQUEL XR. In the SEROQUEL/SEROQUEL XR clinical studies, approximately 7 in 10,000 patients had an event of abuse or misuse.
Potential for off-label use and misdosing	Antipsychotic medicines like SEROQUEL/SEROQUEL XR are often used in situations that have not been tested in clinical studies, and therefore to treat patients or diseases, or to use doses, that they are not specifically approved for. Although AstraZeneca does not support the use of its products for off-label or unapproved uses, there is a potential that SEROQUEL/SEROQUEL XR will be used in such situations.

Table VI-5 Missing information

Risk	What is known
Use in pregnant or breast feeding women	Women were not allowed to take part in the SEROQUEL/SEROQUEL XR clinical studies if they were pregnant. However, some women became pregnant during clinical studies. Following pregnancies in which SEROQUEL/SEROQUEL XR was used, some babies displayed withdrawal symptoms. If you are pregnant or breast feeding, think you may be pregnant or planning to have a baby ask your doctor for advice before taking Seroquel XR. You should not take Seroquel XR during pregnancy unless this has been discussed with your doctor. Seroquel XR should not be taken if you are breast-feeding.
Use in patients taking medications for heart conditions	The effects of SEROQUEL/SEROQUEL XR when given at the same time as other medicines which affect the heart have not been formally studied. Because some patients in the SEROQUEL/SEROQUEL XR clinical studies had changes in electrical activity of the heart after starting treatment, SEROQUEL/SEROQUEL XR should be used with care in patients with heart disease or a family history of changes in the electrical activity of the heart. Caution should also be taken when SEROQUEL/SEROQUEL XR is given at the same time as other commonly used medicines taken for heart conditions, or other medicines known to affect the electrical activity of the heart, including other antipsychotic medicines. This is especially true for patients with heart electrical activity abnormalities or a family history of such abnormalities, elderly patients, patients with low levels of sodium or magnesium in the blood and patients with heart failure or an increased heart size.
Use in patients taking the anti-epileptic medicine valproic acid (valproate)	A small study of SEROQUEL and valproate taken at the same time found that the combination of the two products was generally safe and well tolerated.

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 reducing them. An easier-to-read summary of this information is provided in the form of the patient information leaflet (PIL). The information in these documents is known as routine risk minimisation (reduction) measures.

SEROQUEL/SEROQUEL XR has special conditions and restrictions for its safe and effective use (additional risk reduction measures). The way in which these special conditions are put into practice across the European Union may be different for different countries.

These additional risk reduction measures are for the risks described in Table VI-6 to Table VI-11.

Table VI-6 Abnormal muscle movements

Risk minimisation measure(s): Healthcare Professional education
Objective and rationale To reduce the known risk that SEROQUEL/SEROQUEL XR can cause abnormal muscle movement, clear guidelines are needed for physicians to enable early detection of any abnormal muscle movement and to ensure the appropriate actions are taken to treat any changes that do occur.
Main additional risk minimisation measures • Provide additional printed information (eg a laminated card, brochure, or similar document) to remind physicians of the risks of SEROQUEL/SEROQUEL XR treatment on abnormal muscle movement with a reference to the local prescribing information for details • Educational programmes on the risks and benefits of SEROQUEL/SEROQUEL XR, delivered by company sales representatives

Table VI-7 Sleepiness

Risk minimisation measure(s): Healthcare Professional education
Objective and rationale To reduce the known risk that SEROQUEL/SEROQUEL XR can cause sleepiness, clear guidelines are needed for physicians to enable early detection of any problems with patients' sleep patterns and to ensure the appropriate actions are taken to treat any changes that do occur
Main additional risk minimisation measures • Provide additional printed information (eg a laminated card, brochure, or similar document) to remind physicians of the risks of SEROQUEL/SEROQUEL XR treatment on sleep patterns with a reference to the local prescribing information for details • Educational programmes on the risks and benefits of SEROQUEL/SEROQUEL XR, delivered by company sales representatives

Table VI-8 Weight gain

Risk minimisation measure(s): Healthcare Professional education
Objective and rationale To reduce the known risk that SEROQUEL/SEROQUEL XR can cause weight gain, clear guidelines are needed for physicians to enable early detection of any problems with patients' weight and to ensure the appropriate actions are taken to treat any changes that do occur
Main additional risk minimisation measures • Provide additional printed information (eg a laminated card, brochure, or similar document) to remind physicians of the risks of SEROQUEL/SEROQUEL XR treatment on patients' weight • Educational programme describing the effects of SEROQUEL/SEROQUEL XR treatment on the metabolism, including weight gain

Table VI-9 High blood sugar levels and diabetes

Risk minimisation measure(s): Healthcare Professional education

Objective and rationale

To reduce the known risk that SEROQUEL/SEROQUEL XR can cause increases in blood sugar and diabetes, clear guidelines are needed for physicians to enable early detection of any problems with patients' blood sugar levels and to ensure the appropriate actions are taken to treat any changes that do occur

Main additional risk minimisation measures

- Provide additional printed information (eg a laminated card, brochure, or similar document) to remind physicians of the risks of SEROQUEL/SEROQUEL XR treatment on patients' blood sugar levels
- Educational programme describing the effects of SEROQUEL/SEROQUEL XR treatment on the metabolism, including high blood sugar levels and diabetes

Table VI-10 Changes in blood cholesterol levels

Risk minimisation measure(s): Healthcare Professional education

Objective and rationale

To reduce the known risk that SEROQUEL/SEROQUEL XR can cause changes in blood cholesterol levels, clear guidelines are needed for physicians to enable early detection of any problems with patients' cholesterol levels and to ensure the appropriate actions are taken to treat any changes that do occur

Main additional risk minimisation measures

Educational activities and materials

- Provide additional printed information (eg a laminated card, brochure, or similar document) to remind physicians of the risks of SEROQUEL/SEROQUEL XR treatment on patients' cholesterol levels
- Educational programme describing the effects of SEROQUEL/SEROQUEL XR treatment on the metabolism, including cholesterol levels

Table VI-11 Metabolic syndrome risk factors

Risk minimisation measure(s): Healthcare Professional education

Objective and rationale

To reduce the known risk that SEROQUEL/SEROQUEL XR can cause increase the risk factor for metabolic syndrome (a combination of factors that, when occurring together, increase the risk of developing heart disease and diabetes), clear guidelines are needed for physicians to enable early detection of any problems with patients' cholesterol levels and to ensure the appropriate actions are taken to treat any changes that do occur.

Main additional risk minimisation measures

Educational activities and materials

- Provide additional printed information (eg, a laminated card, brochure, or similar document) to remind physicians of the risks that SEROQUEL/SEROQUEL XR treatment may increase a patient's risk of developing metabolic syndrome
- Educational programme describing the effects of SEROQUEL/SEROQUEL XR treatment on the metabolism, including the possibility of an increased risk factor for metabolic syndrome

Table VI-12 Potential for off-label use and misdosing

Risk minimisation measure(s): Healthcare Professional education
Objective and rationale
To provide clear guidance on the safe and appropriate use of SEROQUEL/SEROQUEL XR.
Main additional risk minimisation measures
Educational activities and materials • Core guidance document ensuring consistent capture of indication from spontaneous postmarking reports • The key aim of educational activities for health care professionals is to give guidance, based on the product information, to ensure the safe and correct use of SEROQUEL/SEROQUEL XR. To ensure such use in patients with bipolar depression, AstraZeneca developed informational material to introduce physicians to the recommended dosing schedule.

VI: 2.6 Planned post authorisation development plan

There are no studies in the post authorisation development plan.

Studies which are a condition of the marketing authorisation

All studies that were conditions of the marketing authorisations for SEROQUEL and/or SEROQUEL XR have been completed.

VI: 2.7 Summary of changes to the Risk Management Plan over time

Table VI-13 Summary of changes to the Risk Management Plan over time

RMP Version number	Date of authorisation of the RMP	Formulation	Summary of changes
15		SEROQUEL and SEROQUEL XR	PASS information has been updated to reflect the finalization of SE-SLS part III study report and applicable information has been included for each outcome. Routine risk minimization activities have been updated with changes to SmPCs section 4.4 for misuse and abuse. The 2 preganncy registries were incorrectly classified as PASS.They have been removed from the applicable tables and are correctly classified under routine pharmacovigilance. Additionally, the requirement for PASS-NI-001-CRO (Croatia PASS Study) was removed by HALMED (Agency for Medicinal Products and Medical Devices of Croatia). This is an administrative update. Annex 2, 5, 6 and 9 have been updated accordingly

Table VI-13 Summary of changes to the Risk Management Plan over time

RMP Version number	Date of authorisation of the RMP	Formulation	Summary of changes
14.1 (dated |02 Dec 2016)		SEROQUEL and SEROQUEL XR	Part V has been updated to remove any reference to additional risk minimization measures being completed. Clarity has been provided throughout Part V that additional risk minimization meaures are in place for EPS, somnolence, metabolic and nutritional disorders (weight gain, lipid changes, hyperglycemia, diabetes mellitus, metabolic risk factors), off-label use and misdosing. Annex 10 (Details of proposed additional risk minimization measures) has been newly added which includes the core elements to be included in any educational materials created nationally.
14 (dated February 2016		SEROQUEL and SEROQUEL XR	The following important identified risk was deleted as a result of the preliminary assessment report of procedure number NL/H/xxxx/WS/118: QT prolongation PASS information has been updated to reflect the current status of these studies. Risk minimization measure has been added to misuse and abuse: The SEROQUEL/SEROQUEL XR MR-SmPC does not list any information about misuse and abuse at this time. However, MEB has imposed the following amendments to the Product Information in section 4.4 of the SmPC: "Misuse and abuse, Cases of misuse and abuse have been reported. Caution may be needed when prescribing quetiapine to patients with a history of alcohol or drug abuse."

Table VI-13 Summary of changes to the Risk Management Plan over time

RMP Version number	Date of authorisation of the RMP	Formulation	Summary of changes
13 (dated 28 August 2015	21 October 2015	SEROQUEL and SEROQUEL XR	The following identified or potential risks or information considered missing, were deleted per procedure number NL/H/0156/001-012/IB/110 final variation assessment report: dysarthria, rhabdomyolysis, serotonin syndrome, sudden death, myocarditis, cataract, risk in patients with hepatic impairment for all SEROQUEL formulations, us in patients with renal disease, use in patients with different ethnic or racial origin, treatment emergent mania in patients with bipolar depression and use in patients with longer exposure. The following important identified or potential risks were deleted as a result of the preliminary assessment report of procedure number NL/H/xxxx/WS/118: TD, syncope and orthostatic hypotension, seizure, neutropenia, agranulocytosis, SIADH and hyponatremia, hypothyroidism, hyperprolactinemia, anaphylactic reaction, Stevens-Johnson syndrome and other serious skin reactions, neuroleptic malignant syndrome, withdrawal (discontinuation) symptoms and neonatal withdrawal, dysphagia, pancreatitis, intestinal obstruction/ileus, venous thromboembolism, increased blood pressure in the pediatric population, increased mortality in elderly demented patients, aggression/agitation, accidental injury, aspiration pneumonia, use of SEROQUEL/SEROQUEL XR in elderly patients The three risks that comprised Liver Disorder (Hepatitis, Jaundice and elevated liver enzymes have been combined into one risk, Hepatitis with or without jaundice. SEROQUEL/SEROQUEL XR clinical safety database was updated and clinical tables reflect the changes from version 26 to version 27. Experience of SEROQUEL marketed products information was updated. For the risks that contain post-marketing information, the numbers of patients experiencing adverse events was updated through 12 June 2014. PASS information has been updated to reflect the current status of these studies. Risk minimization activities have been updated. Changes to the SmPCs as a result of the harmonization process are reflected in this EU-RMP.
12	31Jan 2014	SEROQUEL and SEROQUEL XR	Blockage of bowel and withdrawal effects in babies have been added as identified risks. Risk tables have been provided in a new format. Experience of SEROQUEL marketed products information has been updated. Risk minimisation activities have been updated and Asian patients are no longer considered missing information.

Table VI-13 Summary of changes to the Risk Management Plan over time

RMP Version number	Date of authorisation of the RMP	Formulation	Summary of changes
11	13 Aug 2012	SEROQUEL and SEROQUEL XR	The following potential risks were changed to identified risks: severe reductions in a type of white blood cell called neutrophils, metabolic syndrome risk factors, muscle wasting, inflammation of the pancreas, changes in electrical activity of the heart, low blood sodium levels and harmful effects on a hormone that controls urine volume, and blood clots in the vein. Experience of SEROQUEL marketed products information was updated and risk minimisation activities were updated.
10	22 Sep 2012	SEROQUEL and SEROQUEL XR	Risk minimisation activities were updated and enhanced. The number of patients who have used SEROQUEL was updated. Information on the numbers of patients experiencing adverse events was updated, as were measures of monitoring the safety of patients using SEROQUEL, including the additional real-life clinical studies.
9	07 Dec 2009	SEROQUEL and SEROQUEL XR	Added new and newly characterised risks. Updated information from published literature. Added final results of cataract and sedation studies, and updated and enhanced risk minimisation activities.
8	19 Dec 2008	SEROQUEL and SEROQUEL XR	Bipolar depression was added to the uses of SEROQUEL (with update risk minimisation activities).
7	02 Sep 2008	SEROQUEL and SEROQUEL XR	Information was added on studies in generalised anxiety disorder and use in children.
6	21 Apr 2008	SEROQUEL XR	Severe depression added to the uses of SEROQUEL XR.
5	11 Apr 2008	SEROQUEL and SEROQUEL XR	Prevention of recurrence in bipolar disorder added to the uses of SEROQUEL.
4	15 Jan 2008	SEROQUEL and SEROQUEL XR	Update on information on bipolar depression and mania, and update on long term treatment in schizophrenia.
2	13 Jul 2007	SEROQUEL XR	Update on information on schizophrenia. Underactive thyroid was added as a potential risk and food-drug interactions were added as an identified risk (food-drug interactions were later deleted as risk, as this was no longer considered a risk). The name of the slow-releasing formulation was changed from SEROQUEL SR to SEROQUEL XR.

Table VI-13 Summary of changes to the Risk Management Plan over time

RMP Version number	Date of authorisation of the RMP	Formulation	Summary of changes
Unnumbered	18 Sep 2006	SEROQUEL SR	Schizophrenia was added to the uses of SEROQUEL SR.
Unnumbered	24 May 2006	SEROQUEL	Bipolar depression was added to the uses of SEROQUEL.

RMP Risk management plan. SR Sustained release; XR Extended release.