Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for QUETIAPINE 50 mg, 150 mg, 200 mg, 300 mg and 400 mg prolonged- release tablets

This is a summary of the risk management plan (RMP) for QUETIAPINE 50 mg, 150 mg, 200 mg, 300 mg and 400 mg prolonged- release tablets, (hereinafter referred to as Quetiapine). The RMP details important risks of Quetiapine, how these risks can be minimised, and how more information will be obtained about Quetiapine's risks and uncertainties (missing information).

Quetiapine's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Quetiapine should be used.

Important new concerns or changes to the current ones will be included in updates of Quetiapine's RMP.

I. The Medicine and What It is used for

Quetiapine is authorised for:

- Treatment of schizophrenia
- Treatment of bipolar disorder:
  - For the treatment of moderate to severe manic episodes in bipolar disorder
  - For the treatment of major depressive episodes in bipolar disorder
  - For the prevention of recurrence of manic or depressed episodes in patients with bipolar disorder who previously responded to quetiapine treatment
- Add-on treatment of major depressive episodes in patients with Major Depressive Disorder (MDD) who have had sub-optimal response to antidepressant monotherapy.

It contains Quetiapine as the active substance and it is given orally.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Quetiapine, together with measures to minimise such risks and the proposed studies for learning more about Quetiapine's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Quetiapine these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Quetiapine is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Quetiapine are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Quetiapine. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 8: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• Extrapyramidal symptoms (EPS) • Somnolence • Weight gain • Lipid changes (Increased cholesterol [including increased LDLs], increased triglycerides, and decreased HDLs) • Hyperglycemia and diabetes mellitus • Metabolic risk factors • Suicide and suicidality
Important potential risks	• Cerebrovascular adverse events in the elderly • Cerebrovascular adverse events in non-elderly patients • Torsades de Pointes • Ischemic heart disease • Abuse and misuse • Potential for off-label use and misdosing
Missing information	• Use in pregnant or breast feeding women • Use in patients on concomitant cardiovascular medications • Use in patients on concomitant valproic acid

II.B Summary of Important Risks

Table 9: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important identified risk: Extrapyramidal symptoms (EPS)	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4, 4.5, 4.8 and 5.1. PL sections 2 and 4. Prescription only medicine Additional risk minimisation measures Educational materials for physicians
Important identified risk: Somnolence	
Risk minimisation	Routine risk minimisation measures

measures	SmPC sections 4.2, 4.4, 4.7 and 4.8. PL section 4. Prescription only medicine Additional risk minimisation measures Educational materials for physicians
Important identified risk: Weight gain	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4, 4.8 and 5.1. PL sections 2 and 4. Prescription only medicine Additional risk minimisation measures Educational materials for physicians
Important identified risk: Lipid changes (Increased cholesterol [including increased LDLs], increased triglycerides, and decreased HDLs)	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4 and 4.8. PL section 4. Prescription only medicine Additional risk minimisation measures Educational materials for physicians
Important identified risk: Hyperglycaemia and diabetes mellitus	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4 and 4.8. PL section 2 and 4. Additional risk minimisation measures Educational materials for physicians
Important identified risk: Metabolic risk factors	
Risk minimisation measures	Routine risk minimisation measures SmPC section 4.4. PL sections 2 and 4. Prescription only medicine Additional risk minimisation measures Educational materials for physicians
Important potential risk: Potential for off-label use and misdosing	
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.2 and 4.4 PL section 3. Prescription only medicine Additional risk minimisation measures Educational materials for physicians

II.C Post-Authorisation Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Quetiapine.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Quetiapine.