13 Part VI: Summary of the risk management plan for Quetiapine fumarate, 50 mg, 150 mg, 200 mg, 300 mg, 400 mg and 600 mg, Prolonged-release tablets and 25 mg, 50 mg, 100 mg, 150 mg, 200 mg, 300 mg and 400 mg, Film-coated tablets

This is a summary of the risk management plan (RMP) for quetiapine fumarate, 50 mg, 150 mg, 200 mg, 300 mg, 400 mg and 600 mg, prolonged-release tablets and 25 mg, 50 mg, 100 mg, 150 mg, 200 mg, 300 mg and 400 mg, film-coated tablets. The RMP details important risks of quetiapine fumarate, prolonged-release tablets and film-coated tablets, how these risks can be minimized, and how more information will be obtained about quetiapine fumarate, prolonged-release tablets and film-coated tablet's risks and uncertainties (missing information).

Quetiapine fumarate, prolonged-release tablets and film-coated tablet's summary of product characteristics (SmPCs) and its package leaflets give essential information to healthcare professionals and patients on how quetiapine fumarate, prolonged-release tablets and film-coated tablets should be used.

13.1 Part VI: I. The medicine and what it is used for

Quetiapine fumarate prolonged-release tablets and film-coated tablets are indicated for the:

- 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 associated with bipolar disorder
  - For the prevention of recurrence of manic or depressed episodes in patients with bipolar disorder who previously responded to quetiapine treatment.

Quetiapine fumarate prolonged-release tablets are additionally indicated for:

- Add-on treatment of major depressive episodes in patients with Major Depressive Disorder (MDD) who have had sub-optimal response to antidepressant monotherapy. Prior to initiating treatment, clinicians should consider the safety profile of quetiapine.

It contains quetiapine fumarate as the active substance and is given orally as prolonged-release tablets (50 mg, 150 mg, 200 mg, 300 mg, 400 mg and 600 mg) and film-coated tablets (25 mg, 50 mg, 100 mg, 150 mg, 200 mg, 300 mg and 400 mg).

13.2 Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of quetiapine fumarate, prolonged-release tablets and film-coated tablets, together with measures to minimize such risks and the proposed studies for learning more about quetiapine fumarate, prolonged-release tablets' and film-coated tablets' risks are outlined below.

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

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflets and SmPCs addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorized 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 minimize its risks.

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

In the case of quetiapine fumarate, prolonged-release tablets and film-coated tablets, these measures are supplemented with *additional risk minimization measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, 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 fumarate, prolonged-release tablets and film-coated tablets, is not yet available, it is listed under 'missing information' below.

13.2.1 Part VI – II.A: List of important risks and missing information

Important risks of quetiapine fumarate, prolonged-release tablets and film-coated tablets are risks that need special risk management activities to further investigate or minimize 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 fumarate, prolonged-release tablets and film-coated tablets. 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 13-1 List of important risks and missing information

List of important risks and missing information	
Important identified risks	Extrapyramidal symptoms (EPS)
	Somnolence
	Weight gain
	Lipid changes (Increased cholesterol (including low density lipoproteins (LDLs)), increased triglycerides, and decreased high density lipoproteins (HDLs))
	Hyperglycemia and diabetes mellitus
	Metabolic risk factors
	Suicide and suicidality
Important potential risks	Cerebrovascular adverse events in elderly
	Cerebrovascular adverse events in non-elderly patients
	Torsade 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

13.2.2 Part VI – II.B: Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Table 13-2 Important identified risk: EPS

Risk minimization measures	**Routine risk minimization measures** SmPC sections 4.4, 4.5, 4.6, 4.8 and 5.1 PL sections 2 and 4 Legal status: Prescription only **Additional risk minimization measures:** Physician's leaflet

Table 13-3 Important identified risk: Somnolence

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4, 4.5, 4.6, 4.7, 4.8 and 5.1 PL sections 2, 3 and 4 Legal status: Prescription only **Additional risk minimization measures:** Physician's leaflet

Table13-4 Important identified risk: Weight gain

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4, 4.5, 4.8, 5.1 and 5.3 PL sections 2 and 4 Legal status: Prescription only **Additional risk minimization measures:** Physician's leaflet

Table 13-5 Important identified risk: Lipid changes (Increased cholesterol, including LDLs, increased triglycerides, and decreased HDLs)

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4 and 4.8 PL section 4 Legal status: Prescription only **Additional risk minimization measures:** Physician's leaflet

Table 13-6 Important identified risk: Hyperglycemia and diabetes mellitus

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4 and 4.8

	PL sections 2 and 4 Legal status: Prescription only **Additional risk minimization measures:** Physician's leaflet

Table 13-7 Important identified risk: Metabolic risk factors

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4 and 4.8 PL sections 2 and 4 Legal status: Prescription only **Additional risk minimization measures:** Physician's leaflet

Table 13-8 Important potential risk: Potential for off-label use and misdosing

Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.1 and.4.2 PL section 3 Legal status: Prescription only **Additional risk minimization measures:** Physician's leaflet

13.2.3 Part VI – II.C: Post-authorization development plan

13.2.3.1 II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligations for quetiapine fumarate, prolonged-release tablets and film-coated tablets.

13.2.3.2 II.C.2. Other studies in post-authorization development plan

There are no studies required for quetiapine fumarate, prolonged-release tablets and film-coated tablets.