Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for AXITINIB 1 mg, 3 mg, 5 mg, 7 mg film-coated tablets

This is a summary of the risk management plan (RMP) for AXITINIB 1 mg, 3 mg, 5 mg, 7 mg film-coated tablets (hereinafter referred to as Axitinib). The RMP details important risks of Axitinib, how these risks can be minimised, and how more information will be obtained about product's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Axitinib is authorised for the treatment of adult patients with advanced renal cell carcinoma after failure of prior treatment with sunitinib or a cytokine (see SmPC for the full indication). It contains Axitinib 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 Axitinib, together with measures to minimise such risks and the proposed studies for learning more about Axitinib's risks, if any, 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 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 Axitinib is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Axitinib 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 Axitinib. 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 4: Summary of Safety Concerns

Summary of safety concerns	
Important identified risks	• Arterial embolic and thrombotic events • Gastrointestinal perforation and fistula • Haemorrhage • Posterior reversible encephalopathy syndrome • Venous embolic and thrombotic event • Effects on the exocrine pancreas • Renal failure • Congestive heart failure/cardiomyopathy
Important potential risks	• Torsade de pointes due to QT prolongation • Reproductive and developmental toxicity • Carcinogenicity • Osteonecrosis of the jaw
Missing information	• Risks in pregnant and lactating women • Risks in paediatric subjects • Risks in subjects with moderate and severe renal impairment (serum creatinine >1.5 times the ULN or calculated creatinine clearance <60 mL/min) • Risks in subjects with severe hepatic impairment (Child-Pugh Class C) • Risks in subjects with brain metastasis, spinal cord compression, or carcinomatous meningitis • Risks in subjects with active peptic ulcer disease • Risks in subjects with a recent major surgery (within 4 weeks) or radiation therapy (within 2 weeks)

II.B Summary of Important Risks

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

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 Axitinib.

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

There are no studies required for Axitinib.