Part VI: Summary of the risk management plan

Summary of risk management plan for Sorafenib STADA 200 mg film-coated tablet (as sorafenib tosylate)

This is a summary of the risk management plan (RMP) for sorafenib. The RMP details important risks of sorafenib, how these risks can be minimised, and how more information will be obtained about sorafenib's risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Sorafenib is authorised for the treatment of hepatocellular carcinoma, and for the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy (see SmPC for the full indication). It contains sorafenib (as sorafenib tosylate), as the active substance, and it is given by oral route of administration of 200 mg film-coated tablets.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of sorafenib, together with measures to minimise such risks and the proposed studies for learning more about sorafenib'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 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 sorafenib is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of sorafenib are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 sorafenib. 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);

List of important risks and missing information	
Important identified risks	• Severe skin adverse events • Hand-foot skin reaction (HFSR) • Hypertension • Reversible posterior leukoencephalopathy syndrome (RPLS) • Hemorrhage including lung hemorrhage, gastrointestinal (GI) hemorrhage and cerebral hemorrhage • Arterial thrombosis (myocardial infarction) • Congestive heart failure (CHF) • Squamous cell cancer of the skin • Gastrointestinal perforations • Symptomatic pancreatitis and increases in lipase and amylase • Hypophosphatemia • Safety and efficacy in patients with non-small cell cancer of the lung with squamous histology • Renal dysfunction • Interstitial lung disease-like events • Drug-induced hepatitis
Important potential risks	• Arterial thrombosis (cerebral ischemia) • Wound healing complications • Microangiopathy • Torsade de Pointes • Pregnancy

List of important risks and missing information	
Missing information	• Safety in children and adolescents • Safety and efficacy in patients with hepatocellular carcinoma (HCC) and Child-Pugh B liver dysfunction

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 sorafenib.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for sorafenib.