Part VI: Summary of the risk management plan

Summary of risk management plan for Lenvatinib

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

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

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

I. The medicine and what it is used for

Lenvatinib is authorised for the treatment of adult patients:

- As monotherapy, for the treatment of patients with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine;
- As monotherapy, for the treatment of patients with advanced or unresectable hepatocellular carcinoma who have received no prior systemic therapy;
- In combination with pembrolizumab, for the treatment of patients with advanced or recurrent endometrial carcinoma who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and are not candidates for curative surgery or radiation.

The Applicant's Lenvatinib contains lenvatinib as the active substance and it is taken orally.

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

Important risks of Lenvatinib, together with measures to minimise such risks and the proposed studies for learning more about Lenvatinib'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*.

II.A List of important risks and missing information

Important risks of Lenvatinib 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 Lenvatinib. 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	Arterial thromboembolic events
	Cardiac failure
	Gastrointestinal perforation and fistula formation
	Haemorrhagic events
	Hepatotoxicity
	Hypothyroidism
	Non-gastrointestinal fistula formation (any fistula which does not involve the stomach or intestine) and pneumothorax
	Posterior reversible encephalopathy syndrome
	Proteinuria and nephrotic syndrome
	QTc prolongation
	Renal failure or impairment
Important potential risks	Abnormal pregnancy outcome, excretion of lenvatinib in breast milk
	Bone and teeth abnormalities in the paediatric population
	Impaired wound healing
	Interstitial lung disease-like conditions
	Male and female fertility
	Venous thromboembolic events
Missing information	None

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 the Applicant's Lenvatinib.

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

There are no studies required for the Applicant's Lenvatinib.