Part VI: Summary of the risk management plan

Summary of risk management plan for Leflunomide 10 mg, 15 mg and 20 mg film-coated tablets

This is a summary of the risk management plan (RMP) for Leflunomide 10 mg, 15 mg and 20 mg film-coated tablets (hereinafter referred to as Leflunomide). The RMP details important risks of leflunomide, how these risks can be minimized, and how more information will be obtained about leflunomide's risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Leflunomide is indicated for the treatment of adult patients with:

- Active rheumatoid arthritis as a "disease-modifying antirheumatic drug" (DMARD),
- Active psoriatic arthritis.

Recent or concurrent treatment with hepatotoxic or haematotoxic DMARDs (e.g. methotrexate) may result in an increased risk of serious adverse reactions; therefore, the initiation of leflunomide treatment has to be carefully considered regarding these benefit/risk aspects.

Moreover, switching from leflunomide to another DMARD without following the washout procedure may also increase the risk of serious adverse reactions even for a long time after the switching.

(See SmPC for full indication). It contains leflunomide as an active substance and is given orally.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of leflunomide, together with measures to minimize such risks and the proposed studies for learning more about leflunomide's 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 leaflet and SmPC 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 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 minimisation measures.

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

In addition to these measures, information about the adverse reactions is collected continuously and regularly analysed, and are assessed 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 leflunomide is not yet available, it is listed under missing information below.

II.A List of important risks and missing information

Important risks of leflunomide 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 leflunomide. 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	Hepatic reactions
	Blood cytopenia
	Infections
	Teratogenicity
Important potential risks	Male-mediated foetal toxicity
	Progressive multifocal leukoencephalopathy
Missing information	None

II.B Summary of important risks

Important Identified risk information	
Hepatic reactions	
Risk minimisation measures	**Routine risk minimisation measures** Listings in SmPC section 4.1 Therapeutic indications, 4.3 Contraindications, 4.4 Special warnings and precautions for use, 4.5 Interaction with other medicinal products and other forms of interaction, 4.8 Undesirable effects, 5.1 Pharmacodynamic properties and 5.3 Preclinical safety data Listings in PIL section 2. What you need to know before you take leflunomide and 4. Possible side effects **Additional risk minimisation measures** Educational material Consists of the following elements: ➢ The SmPC

Important Identified risk information	
Hepatic reactions	
	➢ The PIL ➢ A physician leaflet

Important Identified risk information	
Blood cytopenia	
Risk minimisation measures	**Routine risk minimisation measures** Listings in SmPC section 4.1 Therapeutic indications, 4.2 Posology and method of administration, 4.3 Contraindications, 4.4 Special warnings and precautions for use, 4.5 Interaction with other medicinal products and other forms of interaction and 4.8 Undesirable effects Listings in PIL section 2. What you need to know before you take leflunomide and 4. Possible side effects **Additional risk minimisation measures** Educational material Consists of the following elements: ➢ The SmPC ➢ The PIL ➢ A physician leaflet

Important Identified risk information	
Infections	
Risk minimisation measures	**Routine risk minimisation measures** Listings in SmPC section 4.3 Contraindications, 4.4 Special warnings and precautions for use, 4.8 Undesirable effects and 5.3 Preclinical safety data Listings in PIL section 2. What you need to know before you take leflunomide and 4. Possible side effects **Additional risk minimisation measures** Educational material Consists of the following elements: ➢ The SmPC ➢ The PIL ➢ A physician leaflet

Important Identified risk information	
Teratogenicity	
Risk minimisation measures	**Routine risk minimisation measures** Listings in SmPC section 4.3 Contraindications, 4.6 Fertility, Pregnancy and lactation and 5.3 Preclinical safety data Listings in PIL section 2. What you need to know before you take leflunomide **Additional risk minimisation measures** Educational material Consists of the following elements: ➢ The SmPC ➢ The PIL ➢ A physician leaflet

Important potential risks information	
Male-mediated foetal toxicity	
Risk minimisation measures	**Routine risk minimisation measures** Listings in SmPC section 4.4 Special warnings and precautions for use and 4.6 Fertility, Pregnancy and lactation Listings in PIL section 2. What you need to know before you take leflunomide **Additional risk minimisation measures** Educational material Consists of the following elements: ➢ The SmPC ➢ The PIL ➢ A physician leaflet

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 leflunomide.

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

There are no studies required for leflunomide.