Part VI: Summary of the risk management plan

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

This is a summary of the risk management plan (RMP) for [Leflunomide] 10, 15 and 20mg film coated tablets. This RMP details important risks of [Leflunomide] 10, 15 and 20mg film coated tablets, how these risks can be minimised, and how more information will be obtained about [Leflunomide] 10, 15 and 20mg film coated tablets risks and uncertainties (missing information).

[Leflunomide] 10, 15 and 20mg film coated tablets summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how these products are used.

Important new concerns or changes to the current ones will be included in updates of [Leflunomide] 10, 15 and 20mg film coated tablets's RMP.

I. The medicine and what it is used for

[Leflunomide] 10, 15 and 20mg film coated tablets, is indicated for the treatment of adult patients with:
• active rheumatoid arthritis as a "disease-modifying antirheumatic drug" (DMARD)
• active psoriatic arthritis
It contains leflunomide 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 [Leflunomide] 10, 15 and 20mg film coated tablets, together with measures to minimise such risks and the proposed studies for learning more about [Leflunomide] 10, 15 and 20mg film coated tablets, are outlined below.

Measures to minimise the risks for [Leflunomide] 10, 15 and 20mg film coated tablets include:

- 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 the case of [Leflunomide] 10, 15 and 20mg film coated tablets, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of [Leflunomide] 10, 15 and 20mg film coated tablets is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of [Leflunomide] 10, 15 and 20mg film coated tablets 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 of [Leflunomide] 10, 15 and 20mg film coated tablets 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 [Leflunomide] 10, 15 and 20mg 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);

List of important risks and missing information	
Important identified risks	• Hepatic reactions • Blood cytopenia • Severe skin reactions • Infections • Interstitial lung disease • Teratogenicity • Hypertension • Concomitant use of other disease modifying antirheumatic drugs (DMARDs) (methotrexate)
Important potential risks	• Male-mediated foetal toxicity • Renal failure • Lymphoproliferative disorders • Progressive multifocal leukoencephalopathy • Peripheral neuropathy • Risk of interaction (with CYP2C8 substrates, CYP1A2 substrates, BCRP substrates, OATP1B1/B3 substrates, OAT3 substrates, warfarin and oral contraceptives)
Missing information	• Use in children • Concomitant use of biologic DMARDs

II.B Summary of important risks

Hepatic reactions	
Evidence for linking the risk to the medicine	Considered 'important' as a change in the risk could have an impact on the risk-benefit balance of the product.
Risk factors and risk groups	Not applicable
Risk minimisation measures	*Routine Risk minimization measures:* SmPC sections 4.3, 4.4 and 4.8, PL sections 2 and 4 Restrictions on distribution of the product through the legal status

	Additional risk minimization measures: Communication and educational program
Blood cytopenia	
Evidence for linking the risk to the medicine	Considered 'important' as a change in the risk could have an impact on the risk-benefit balance of the product
Risk factors and risk groups	Not applicable
Risk minimisation measures	*Routine Risk minimization measures:* SmPC sections 4.3, 4.4, 4.8, PL sections 2 and 4. Restrictions on distribution of the product through the legal status *Additional risk minimization measures:* Communication and educational program
Infections	
Evidence for linking the risk to the medicine	Considered 'important' as a change in the risk could have an impact on the risk-benefit balance of the product
Risk factors and risk groups	Not applicable
Risk minimisation measures	*Routine Risk minimization measures:* SmPC sections 4.3, 4.4 and 4.8, PL sections 2 and 4 Restrictions on distribution of the product through the legal status *Additional risk minimization measures:* Communication and educational program
Teratogenicity	
Evidence for linking the risk to the medicine	Considered 'important' as a change in the risk could have an impact on the risk-benefit balance of the product.
Risk factors and risk groups	Not applicable
Risk minimisation measures	*Routine Risk minimization measures:* SmPC sections 4.3, 4.6. and 5.3, PL section 2 Restrictions on distribution of the product through the legal status *Additional risk minimization measures:* Communication and educational program Ad hoc advisory service
Concomitant use of other disease modifying antirheumatic drugs (DMARDs) (methotrexate)	
Evidence for linking the risk to the medicine	Considered 'important' as a change in the risk could have an impact on the risk-benefit balance of the product
Risk factors and risk groups	Not applicable
Risk minimisation measures	*Routine Risk minimization measures:* SmPC sections 4.1, 4.4 and 4.8 Restrictions on distribution of the product through the legal status *Additional risk minimization measures:* Communication and educational program

Male-mediated foetal toxicity	
Evidence for linking the risk to the medicine	Considered 'important' as a change in the risk could have an impact on the risk-benefit balance of the product
Risk factors and risk groups	Not applicable
Risk minimisation measures	*Routine Risk minimization measures:* SmPC sections 4.4 and 4.8, PL section 2 Restrictions on distribution of the product through the legal status *Additional risk minimization measures:* Communication and educational program Ad hoc advisory service

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] 10, 15 and 20mg film coated tablets.

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

There are no studies required for [Leflunomide] 10, 15 and 20mg film coated tablets.