Safety concern	Risk minimisation measures	Pharmacovigilance activities
Missing information		
None.		

Part VI: Summary of the risk management plan

Summary of risk management plan for lenalidomide

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

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

This summary of the RMP for lenalidomide should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

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

I. The medicine and what it is used for

The Applicant's Lenalidomide is a medicine used for the treatment of

- Multiple myeloma, which is a cancer of a type of white blood cells called plasma cells;
- Myelodysplastic syndromes, which are a collection of many different blood and bone marrow diseases;
- Mantle cell lymphoma, which is a cancer of a type of white blood cell called 'B-lymphocytes' or B-cells;
- Follicular lymphoma, which is a slow growing cancer that affects B-lymphocytes.

In multiple myeloma, lenalidomide is used (see SmPC for the full indication):

- on its own, in adults who have had an autologous stem cell transplantation;
- in combination with dexamethasone, or bortezomib and dexamethasone, or melphalan and prednisone, for the treatment of adults with previously untreated multiple myeloma, who cannot have stem cell transplantation;
- in combination with dexamethasone, in adults whose disease has been treated at least once in the past.

In myelodysplastic syndromes, lenalidomide is used on its own only in adult patients whose disease has specific characteristics (see SmPC for the full indication).

In mantle cell lymphoma, lenalidomide is used on its own in adult patients with relapsed or refractory disease.

In follicular lymphoma, lenalidomide is used in combination with rituximab in adult patients with previously untreated disease.

The Applicant's Lenalidomide contains lenalidomide as the active substance and it is given as 2.5, 5, 7.5, 10, 15, 20 and 25 mg capsules.

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

Important risks of lenalidomide, together with measures to minimise such risks and the proposed studies for learning more about lenalidomide's risks, are outlined below.

Measures to minimise the risks identified for this medicinal product are:

- 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. Lenalidomide is subject to restricted medical prescription.

Together, these measures constitute *routine risk minimisation* measures.

In the case of lenalidomide, 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 is regularly analysed, including PSUR assessment, 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 lenalidomide 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 lenalidomide. 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).

Summary of safety concerns	
Important identified risks	Second primary malignancies Serious infection due to neutropenia Teratogenicity *Tumour lysis syndrome* Important identified risks related to indication/target population For mantle cell lymphoma and follicular lymphoma: Tumour flare reaction
Important potential risks	Cardiac arrhythmias *Cardiac failure* Ischaemic heart disease (including *Myocardial infarction*) *Off label use*
Missing information	None

II.B Summary of important risks

Important identified risks	
Second primary malignancies	
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.4 and 4.8. • PL section 4. • Lenalidomide is a prescription only medicine. Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Specific adverse reaction follow-up questionnaires for SPM. Additional risk minimisation measures: None proposed.
Serious infection due to neutropenia	
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.2, 4.4 and 4.8 • PL sections 2 and 4. • Lenalidomide is a prescription only medicine. Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Specific adverse reaction follow-up questionnaires for Serious infection due to *Neutropenia*. Additional risk minimisation measures: None proposed.

Teratogenicity	
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.3, 4.4, 4.6, 4.8 and 5.3. • PL section 2: Advice to patients concerning pregnancy, fertility and contraception methods. • Special warning on outer packaging carton. • Lenalidomide is a prescription only medicine. Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Specific adverse reaction follow-up questionnaires for Teratogenicity. Additional risk minimisation measures: PPP, HCP kit, patient brochures, patient card.
Additional pharmacovigilance activities	The effectiveness of PPP will be agreed on with the concerned national competent authorities.
Important identified risks related to indication/target population **For mantle cell lymphoma and follicular lymphoma: Tumour flare reaction**	
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.2, 4.4 and 4.8. • Lenalidomide is a prescription only medicine. Additional risk minimisation measures: None proposed.
Important potential risks	
Cardiac arrhythmias	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.8. • PL section 4. • Lenalidomide is a prescription only medicine. Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Specific adverse reaction follow-up questionnaires for *Cardiac failure* and cardiac arrhythmias. Additional risk minimisation measures: None proposed.
Cardiac failure	
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.8. • PL sections 2 and 4. • Lenalidomide is a prescription only medicine.

	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Specific adverse reaction follow-up questionnaires for *Cardiac failure* and cardiac arrhythmias. Additional risk minimisation measures: None proposed.
Ischaemic heart disease (including *Myocardial infarction*)	
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.4 and 4.8. • PL section 4. • Lenalidomide is a prescription only medicine. Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Specific adverse reaction follow-up questionnaires for ischaemic heart disease (including *Myocardial infarction*). Additional risk minimisation measures: None proposed.
Off label use	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.4. • Lenalidomide is a prescription only medicine. Additional risk minimisation measures: None proposed.
Additional pharmacovigilance activities	*Off label use* will be tracked as part of evaluation of the effectiveness of PPP.

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 Lenalidomide.

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

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