Part VI: Summary of the risk management plan

Summary of risk management plan for Lenalidomide Basics 2.5 mg, 5 mg, 7.5 mg 10 mg, 15 mg, 20 mg and 25 mg hard capsules

(lenalidomide)

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

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

I. The medicine and what it is used for

Lenalidomide BASICS as monotherapy is authorised for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.

Lenalidomide BASICS as combination therapy with dexamethasone, or bortezomib and dexamethasone, or melphalan and prednisone (see section 4.2 of the SmPC) is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

Lenalidomide BASICS in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

Follicular lymphoma
Lenalidomide in combination with rituximab (anti-CD20 antibody) is indicated for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 – 3a).

It contains lenalidomide 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 Lenalidomide BASICS , together with measures to minimise such risks and the proposed studies for learning more about Lenalidomide BASICS '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 the case of Lenalidomide BASICS, 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, including PSUR assessment 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 Lenalidomide BASICS is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Lenalidomide BASICS 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 Lenalidomide BASICS. 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	• **Teratogenicity** • **Serious Infection due to Neutropenia** • **Second primary malignancies (SPM)** **Important Identified Risk Related to Indication/Target Population** • **For follicular lymphoma (FL): tumour flare reaction (TFR)**
Important potential risks	• **Cardiac failure** • **Cardiac arrhythmias** • **Ischaemic heart disease (including myocardial infarction)** • **Off-label use**
Missing information	• **None**

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product Revlimid.

Table SVI-Summary of important risks

Important identified risk: Teratogenicity	
Risk minimization measures	**Routine Risk minimisation measures:** • SPC 4.3, 4.4, 4.6, 4.8 and 5.3 *the potential teratogenic effects of lenalidomide are highlighted.* *Section 4.3 of SmPC: contraindicated in pregnant women and in FCBP unless all the conditions of the lenalidomide PPP are met.* *Section 4.4 of SmPC: warnings and precautions for use* *– Criteria for women of non-childbearing potential* *– Counselling* *– Contraception* *– Pregnancy testing* *– Precautions for men* *– Additional precautions* *– Reference to educational materials, prescribing and dispensing restrictions.* *Section 4.6 of SmPC: fertility, pregnancy and lactation.* *Sections 4.8 and 5.3 of SmPC: the potential teratogenic effects of* *lenalidomide are highlighted.* • **PL section 2** • Subject to restricted medical prescription • **Pack size:** *The pack is based on a maximum 4-week supply of capsules to ensure that* *FCBP are required to obtain a new monthly prescription with a medically* *supervised pregnancy test* **Additional risk minimisation measures:** • **Pregnancy Prevention programme (PPP)** • **Educational Programme for healthcare professionals and patients**: ○ HCP kit to include booklet ○ Treatment algorithm, pregnancy reporting form, patient card, patient guide and checklists. - <u>Therapy management</u> • Criteria for determining FCBP, Contraceptive measures and pregnancy testing for FCBP • Advice in SmPC, and educational materials - <u>System to ensure appropriate measures have been completed.</u> <u>- Patient card to document childbearing status, counselling and pregnancy testing</u>.
Additional pharmacovigilance activities	Additional pharmacovigilance activities:

	Monitoring of implementation of PPP on a country specific basis in accordance with local legal framework and with agreement of the relevant NCA
Important identified risk: Second primary malignancies (SPM)	
Risk minimization measures	**Routine Risk minimisation measures:** • **SPC section 4.4 and 4.8** - *Section 4.4 of SmPC warning of SPM and advice for cancer screening.* - *Listed as ADRs in Section 4.8 of SmPC.* • **Advice to patients provided in PL section 4** **Additional risk minimisation measures:** - **HCP Kit: HCP Guide.**
Important identified risk: Tumour Flare Reaction	
Risk minimization measures	**Routine Risk minimisation measures:** • **SPC sections 4.2, 4.4 and 4.8** – *Section 4.2 of SmPC: dose interruption advice for TFR.* – *Section 4.4 of SmPC warning.* – *Listed as an ADR in Section 4.8 of SmPC.* • **Additional risk minimisation measures:** - **HCP Kit: HCP Guide.**
Important identified risk: Serious infection due to neutropenia	
Risk minimization measures	Routine risk minimisation measures: Section 4.2, 4.4 4.8 and 5.3 of Lenalidomide SmPC and corresponding section of PIL has information on this safety concern. Advice to patients in PL, including that the doctor is advised to check if the patient has ever had hepatitis B infection prior to starting lenalidomide treatment Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: None
Pharmacovigilance activity:	Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in pharmacovigilance system master file. Specific follow-up questionnaires have been proposed for neutroprenia and infection Additional pharmacovigilance activity: None
Important Potential Risk: Cardiac failure	
Risk minimisation measures:	Routine risk minimisation measures: Section 4.8 of Lenalidomide SmPC and corresponding section

	of PIL has information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: None
Pharmacovigilance activity:	Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in pharmacovigilance system master file. Specific follow-up questionnaires have been proposed for cardiac failure Additional pharmacovigilance activity: None
Important Potential Risk: Cardiac arrhythmias	
Risk minimisation measures:	Routine risk minimisation measures: Section 4.8 of Lenalidomide SmPC and corresponding section of PIL has information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: None
Pharmacovigilance activity:	Routine pharmacovigilance activity: Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in pharmacovigilance system master file. Specific follow-up questionnaires have been proposed for cardiac arrhythmias Additional pharmacovigilance activity: None
Important Potential Risk: Ischaemic heart disease (including myocardial infarction)	
Risk minimisation measures:	Routine risk minimisation measures: Section 4.4 and 4.8 of Lenalidomide SmPC and corresponding section of PIL has information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product. Additional risk minimisation measures: None
Pharmacovigilance activity:	Routine pharmacovigilance activity: Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in pharmacovigilance system master file. Specific follow-up questionnaires have been proposed for Ischaemic heart disease (including myocardial infarction) Additional pharmacovigilance activity: None
Important Potential Risk: Off label use	
Risk minimisation measures:	Routine risk minimisation measures: Section 4.4 of Lenalidomide SmPC has information on this safety concern. Other routine risk minimisation measures include the prescription only status of the product.

	Additional risk minimisation measures: None
Pharmacovigilance activity:	Routine pharmacovigilance activity: Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in pharmacovigilance system master file. Additional pharmacovigilance activity: None

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 Lenalidomide BASICS.

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

There are no studies required for Lenalidomide BASICS.