Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for LENALIDOMIDE TEVA (lenalidomide)

This is a summary of the risk management plan (RMP) for LENALIDOMIDE TEVA, LENALIDOMIDE RATIOPHARM (hereinafter referred to as 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.

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

Lenalidomide is authorised:

- as monotherapy for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation
- as combination therapy with dexamethasone, or bortezomib and dexamethasone, or melphalan and prednisone for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.
- in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.
- as monotherapy for the treatment of adult patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate.
- as monotherapy for the treatment of adult patients with relapsed or refractory mantle cell lymphoma
- in combination with rituximab for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 – 3a) (see SmPC for the full indication).

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, 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 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, 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*.

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).

List of important risks and missing information	
Important identified risks	• Teratogenicity • Serious infection due to neutropenia • Second primary malignancies • Cardiac failure • Cardiac arrhythmias • Ischaemic heart disease (including myocardial infarction)
Important potential risks	• Off-label use
Missing information	• None

II.B Summary of Important Risks

Table 12: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important identified risk: Teratogenicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.6, 4.8 and 5.3. Section 4.4 of the SmPC where specific guidance is given. PL section 2. Pack size. Legal status. Additional risk minimisation measures: Pregnancy prevention programme Educational Programme (Educational Healthcare Professional brochure, Educational brochures for patients, Patient card, Risk awareness forms, Information on where to find latest SmPC) Therapy management (Criteria for determining WOCBP, Contraceptive measures and pregnancy testing for WOCBP)
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Additional monitoring of implementation of Teva PPP on a country specific basis in accordance with local legal network framework and with agreement of the relevant NCA (ie, monitoring of patient card completion, monitoring by external agency and surveys.
Important identified risk: Serious infection due to neutropenia	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. PL sections 2 and 4. Legal status. SmPC section 4.2 where dose reduction advice for neutropenia is given. SmPC section 4.4 where advice for blood testing is provided. Additional risk minimisation measures: None.
Important identified risk: Second primary malignancies	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. SmPC section 4.4 where advice for cancer screening is provided. Additional risk minimisation measures: The Educational Healthcare Professional's brochure.
Important identified risk: Cardiac failure	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. PL section 4. Legal status.

	Additional risk minimisation measures: None.
Important identified risk: Cardiac arrhythmias	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. PL section 4. Legal status. Additional risk minimisation measures: None.
Important identified risk: Ischaemic heart disease (including myocardial infarction)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section4.8. SmPC section 4.4 advises monitoring of patients with known risk factors. PL section 4. Legal status. Additional risk minimisation measures: None
Important potential risk: Off-label use	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4. Legal status. Additional risk minimisation measures: None.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorisation

Table 13: Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Activity	Rationale and objectives	Milestones
Monitoring of the implementation of Teva's Pregnancy Prevention Programme	A pregnancy prevention programme (PPP) for Lenalidomide shall be implemented and monitored as Category 3 study to investigate teratogenicity as an important identified risk and to evaluate the effectiveness of PPP as risk minimisation measure.	In line with the PSUR (as required per EURD list).

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Lenalidomide.

Summary of Risk Management Plan for LENALIDOMIDE RATIOPHARM (lenalidomide)

This is a summary of the risk management plan (RMP) for LENALIDOMIDE RATIOPHARM (hereinafter referred to as 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.

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

Lenalidomide is authorised:

- as monotherapy for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation
- as combination therapy with dexamethasone, or bortezomib and dexamethasone, or melphalan and prednisone for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.
- in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.
- as monotherapy for the treatment of adult patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate.
- as monotherapy for the treatment of adult patients with relapsed or refractory mantle cell lymphoma
- in combination with rituximab for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 – 3a) (see SmPC for the full indication).

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, 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 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, 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*.

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).

List of important risks and missing information	
Important identified risks	• Teratogenicity • Serious infection due to neutropenia • Second primary malignancies • Cardiac failure • Cardiac arrhythmias • Ischaemic heart disease (including myocardial infarction)
Important potential risks	• Off-label use
Missing information	• None

II.B Summary of Important Risks

Table 14: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important identified risk: Teratogenicity	
Risk minimisation measures	Routine risk minimisation measures:

	SmPC sections 4.6, 4.8 and 5.3. Section 4.4 of the SmPC where specific guidance is given. PL section 2. Pack size. Legal status. Additional risk minimisation measures: Pregnancy prevention programme Educational Programme (Educational Healthcare Professional brochure, Educational brochures for patients, Patient card, Risk awareness forms, Information on where to find latest SmPC) Therapy management (Criteria for determining WOCBP, Contraceptive measures and pregnancy testing for WOCBP)
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Additional monitoring of implementation of Teva PPP on a country specific basis in accordance with local legal network framework and with agreement of the relevant NCA (ie, monitoring of patient card completion, monitoring by external agency and surveys.
Important identified risk: Serious infection due to neutropenia	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. PL sections 2 and 4. Legal status. SmPC section 4.2 where dose reduction advice for neutropenia is given. SmPC section 4.4 where advice for blood testing is provided. Additional risk minimisation measures: None.
Important identified risk: Second primary malignancies	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. SmPC section 4.4 where advice for cancer screening is provided. Additional risk minimisation measures: The Educational Healthcare Professional's brochure.
Important identified risk: Cardiac failure	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. PL section 4. Legal status. Additional risk minimisation measures: None.
Important identified risk: Cardiac arrhythmias	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8. PL section 4.

	Legal status. Additional risk minimisation measures: None.
Important identified risk: Ischaemic heart disease (including myocardial infarction)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section4.8. SmPC section 4.4 advises monitoring of patients with known risk factors. PL section 4. Legal status. Additional risk minimisation measures: None
Important potential risk: Off-label use	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4. Legal status. Additional risk minimisation measures: None.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorisation

Table 15: Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Activity	Rationale and objectives	Milestones
Monitoring of the implementation of Teva's Pregnancy Prevention Programme	A pregnancy prevention programme (PPP) for Lenalidomide shall be implemented and monitored as Category 3 study to investigate teratogenicity as an important identified risk and to evaluate the effectiveness of PPP as risk minimisation measure.	In line with the PSUR (as required per EURD list).

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Lenalidomide.