EU Risk Management Plan for pomalidomide

RMP version to be assessed as part of this application:

RMP Version number: 0.4

Data lock point for this RMP: 24.5.2024

Date of final sign off: 24.5.2024

Rationale for submitting an updated RMP: Not applicable for initial marketing authorisation application submission.

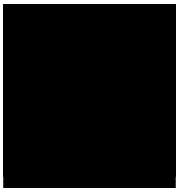
Summary of significant changes in this RMP: Not applicable.

Other RMP versions under evaluation: None

Details of the currently approved RMP: None

QPPV name: Irena Orel MD, MSc

QPPV signature:



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Part I: Product(s) Overview

Table Part I.1 – Product Overview

Active substance(s) **(INN or common name)**	pomalidomide
Pharmacotherapeutic group(s) (ATC Code)	Immunosuppressants, other immunosuppressants (L04AX06)
Marketing Authorisation Holder or Applicant	KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia and Krka's subsidiaries
Medicinal products to which this RMP refers	1
Invented name(s) in the European Economic Area (EEA)	Pomalidomide Krka
Marketing authorisation procedure	centralised
Brief description of the product	Chemical class Pomalidomide is an aromatic amine that is thalidomide substituted at position 4 on the isoindole ring system by an amino group.
	Summary of mode of action Pomalidomide has direct anti-myeloma tumoricidal activity, immunomodulatory activities and inhibits stromal cell support for multiple myeloma tumour cell growth. Specifically, pomalidomide inhibits proliferation and induces apoptosis of haematopoietic tumour cells. Additionally, pomalidomide inhibits the proliferation of lenalidomide-resistant multiple myeloma cell lines and synergises with dexamethasone in both lenalidomide-sensitive and lenalidomide-resistant cell lines to induce tumour cell apoptosis. Pomalidomide enhances T cell- and natural killer (NK) cell-mediated immunity and inhibits production of pro-inflammatory cytokines (e.g., TNF-α and IL-6) by monocytes. Pomalidomide also inhibits angiogenesis by blocking the migration and adhesion of endothelial cells.

<table>
<tr><td></td><td>Important information about its composition
None</td></tr>
<tr><td>Hyperlink to the Product Information</td><td>Please refer to module 1.3.1 of dossier</td></tr>
<tr><td rowspan="2">Indication(s) in the EEA</td><td>Current:
Pomalidomide Krka in combination with bortezomib and dexamethasone is indicated in the treatment of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide.

Pomalidomide Krka in combination with dexamethasone is indicated in the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.</td></tr>
<tr><td>Proposed (if applicable):
/</td></tr>
<tr><td>Dosage in the EEA</td><td>Current:
Treatment must be initiated and monitored under the supervision of physicians experienced in the management of multiple myeloma.

Dosing is continued or modified based upon clinical and laboratory findings (see section 4.4).

<u>Posology</u>
- Pomalidomide in combination with bortezomib and dexamethasone
The recommended starting dose of pomalidomide is 4 mg taken orally once daily on Days 1 to 14 of repeated 21-day cycles.

Pomalidomide is administered in combination with bortezomib and dexamethasone, as shown in Table 1.
The recommended starting dose of bortezomib is 1.3 mg/m^2 intravenous or subcutaneous once daily, on the days shown in Table 1. The recommended dose of dexamethasone is 20 mg taken orally once daily, on the days shown in Table 1.

Treatment with pomalidomide combined with bortezomib and dexamethasone should be given until disease progression or until unacceptable toxicity occurs.

Table 1. Recommended dosing scheme for pomalidomide in combination with bortezomib and dexamethasone

Cycle 1-8 | Day (of 21-day cycle)</td></tr>
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	<table><tr><td></td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td><td>10</td><td>11</td><td>12</td><td>13</td><td>14</td><td>15</td><td>16</td><td>17</td><td>18</td><td>19</td><td>20</td><td>21</td></tr><tr><td>Pomalidomide (4 mg)</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Bortezomib (1.3 mg/m^2)</td><td>•</td><td></td><td></td><td>•</td><td></td><td></td><td></td><td>•</td><td></td><td></td><td>•</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Dexamethasone (20 mg)*</td><td>•</td><td>•</td><td></td><td>•</td><td>•</td><td></td><td></td><td>•</td><td>•</td><td></td><td>•</td><td>•</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr></table> <table><tr><td>Cycle 9 onwards</td><td colspan="21">Day (of 21-day cycle)</td></tr><tr><td></td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td><td>10</td><td>11</td><td>12</td><td>13</td><td>14</td><td>15</td><td>16</td><td>17</td><td>18</td><td>19</td><td>20</td><td>21</td></tr><tr><td>Pomalidomide (4 mg)</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td>•</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Bortezomib (1.3 mg/m^2)</td><td>•</td><td></td><td></td><td></td><td></td><td></td><td></td><td>•</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr><tr><td>Dexamethasone (20 mg)*</td><td>•</td><td>•</td><td></td><td></td><td></td><td></td><td></td><td>•</td><td>•</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr></table> * For patients > 75 years of age, see Special populations. - *Pomalidomide in combination with dexamethasone* The recommended starting dose of pomalidomide is 4 mg taken orally once daily on Days 1 to 21 of each 28-day cycle. The recommended dose of dexamethasone is 40 mg taken orally once daily on Days 1, 8, 15 and 22 of each 28-day cycle. Treatment with pomalidomide combined with dexamethasone should be given until disease progression or until unacceptable toxicity occurs.
	Proposed (if applicable): /
Pharmaceutical form(s) and strengths	Current: hard capsules 1 mg hard capsules 2 mg hard capsules 3 mg hard capsules 4 mg
	Proposed (if applicable): /

Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Not applicable.

Part II: Module SII - Non-clinical part of the safety specification

Not applicable.

Part II: Module SIII - Clinical trial exposure

Not applicable.

Part II: Module SIV - Populations not studied in clinical trials

Not applicable.

Part II: Module SV - Post-authorisation experience

Not applicable.

Part II: Module SVI - Additional EU requirements for the safety specification

Not applicable.

Part II: Module SVII - Identified and potential risks

Not applicable. The list of safety concerns is published on EMA's website (Imnovid, MAH Bristol-Myers Squibb Pharma EEIG, version 17.0, sign off date 7.7.2023).

Part II: Module SVIII - Summary of the safety concerns

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	Teratogenicity
	Severe infection due to neutropenia and pancytopenia
	Thrombocytopenia and bleeding
	Cardiac failure
	Non-melanoma skin cancer
Important potential risks	Other second primary malignancies
	Cardiac arrhythmia
Missing information	None

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

Analysis of Adverse Drug Reactions of Special Interest within the required PSURs:

- Emerging potential safety signals can be detected by periodic and if appropriate, cumulative evaluation of the ADRs. The results are compiled in the PSUR with summaries and conclusions submitted to the health authorities.
- In addition, data regarding pregnancy exposure to pomalidomide are targeted for review and specifically discussed in the PSUR document. These data include all pregnancy case reports collected during the specified period together with cumulative data. Non-medically confirmed case reports of suspected foetal exposure are also provided, whenever applicable. Non-patient exposure in pregnant females (eg, a nurse opening the capsules, laboratory technician, or carer) is also provided with the corresponding outcome in each PSUR.

Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:

- <u>Expedited Reporting and Follow-up of Pregnancy</u>
  - The pregnancy capture and follow-up procedure are detailed below. The PPP aims to minimise the risks of teratogenicity by ensuring HCPs and patients are fully informed of and understand the risks of teratogenicity prior to starting their pomalidomide treatment. Like thalidomide and lenalidomide, pomalidomide is an immunomodulatory agent with expected teratogenic effects in humans. The PPP reflects advice, guidance and direction obtained from the Member States during the implementation process. The same principles on obtaining follow-up data on pregnancies are implemented in all territories where pomalidomide is marketed whilst taking into account the legal and healthcare differences in those territories worldwide.
  - The objectives of the system are:
    - To obtain information on all reported pregnancies of females exposed to pomalidomide.
    - To obtain information on all reported pregnancies of female partners of male patients exposed to pomalidomide.
    - To determine the root cause of all pregnancies and hence failures of the PPP.
  - The capture of reports of pregnancy is enhanced by Standard Initial Pregnancy Reporting Forms, which are included with each HCP Kit, additionally the Educational Materials in the Educational HCP's Kit make reference to the requirement to report all suspected pregnancies to the local office and where applicable to the NCA. The Patient Brochure also advises the patient to immediately seek medical advice if there is any risk or suspicion of possible pregnancy. Similar advice is also provided with reference to female partners of male patients.

- Database of Pregnancy Reports: All reports of pregnancies received are entered into Global Safety Database. This includes all Consumer reports in addition to HCP reports. Any abnormal pregnancy test result (eg, β-hCG elevated and positive urine pregnancy test) is immediately processed. EU Health Authorities are notified of these reports.
- Follow-up: All reports of pregnancies are followed up. Follow-up is via the physician/obstetrician/neonatologist/paediatrician as appropriate. In each representative office, any report of pregnancy is followed up by the Drug Safety staff. All reports of pregnancy are also immediately notified to the QPPV and QPPV deputy. All reports of abnormal pregnancy test results are followed up with the prescriber and follow-up information sent to Health Authorities.
- Frequency/Duration of Follow-up: Upon receipt of a notification of pregnancy, the HCP is asked to complete the Initial Pregnancy Report Form. The Initial Pregnancy Report Form includes a field for Estimated Date of Delivery. Upon receipt of this information by MAH, dates for further follow-up actions are tracked. The HCP/Obstetrician is also sent a Follow-Up and Outcome Form to be completed at the outcome of the Pregnancy. An Infant follow-up form is available for use in the event that a birth defect is detected as an outcome. Corresponding standard forms are available on request.
- Root Cause of Failure of Pregnancy Prevention Programme: The Pregnancy Background Form includes questions to determine why the PPP was unsuccessful for the case in question.
- Regulatory Reporting of Pregnancies: All initial pregnancy reports and follow-up information are reported on an expedited basis within 15 days.

- <u>Specific follow-up questionnaires:</u>

Specific adverse reaction follow-up questionnaires for the following safety concerns:	**Follow-up Form Title**
Teratogenicity	Event-Specific Questionnaire for HCP - Pregnancy Background (Patient or Partner of Patient) Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner - Pregnancy Background Event-Specific Questionnaire for HCP - Pregnancy Follow-up (Patient or Partner of Patient) Event-Specific Questionnaire for HCP - Pregnancy Outcome (Patient or Partner of Patient) Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner - Pregnancy Outcome Event-Specific Questionnaire for Primary Care Physician or Paediatrician - Infant Follow-up
Severe infection due to neutropenia and pancytopenia	Neutropenia
Thrombocytopenia and bleeding	Thrombocytopenia/Bleeding

Cardiac failure	Cardiac failure
Non-melanoma skin cancer, Other second primary malignancies	Second Primary Malignancies
Cardiac arrhythmia	Cardiac Arrhythmia and ECG Changes

III.2 Additional pharmacovigilance activities

Monitoring of Pregnancy Prevention Programme (PPP) implementation

Study short name and title: Monitoring of Pregnancy Prevention Programme implementation

Rationale and study objectives: Monitoring of implementation of PPP

Study design: The monitoring of the implementation of the PPP (category 3 study) will be agreed on a country-specific basis with the relevant National Competent Authority (NCA) in accordance with local legal framework. Methods are anticipated to be similar to the activities in place for the reference medicinal product. Moreover, data will be collected on a regular basis after product launch and the results will be reported in PSURs, in accordance with the PSUR schedule.

Study population: Patients in the EU receiving pomalidomide

Milestones: Routine PSURs in line with DLP of the latest EURD list

III.3 Summary Table of additional Pharmacovigilance activities

Pregnancy Prevention Programme Implementation

Study Status	**Summary of objectives**	**Safety concerns addressed**	**Milestones**	**Due dates**
Category 3 - Required additional pharmacovigilance activities				
Monitoring of Pregnancy prevention programme implementation (category 3 study) Status: Planned	Monitoring of implementation of PPP	*Teratogenicity*	Routine PSURs in line with DLP of the latest EURD list	Data will be reviewed on an on-going basis as a part of signal detection and reported within PSURs with in-line with EURD list

Part IV: Plans for post-authorisation efficacy studies

Not applicable.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

V.1. Routine Risk Minimisation Measures

Table Part V.1: Description of routine risk minimisation measures by safety concern

Safety concern	**Routine risk minimisation activities**
Important identified risks	
Teratogenicity	**Routine risk communication:** **SmPC** **Section 4.8.** **PL** **Section 4** **Routine risk minimisation activities recommending specific clinical measures to address the risk:** **SmPC** **Section 4.3., Section 4.4., Section 4.6., Section 5.3.** **PL** **Section 2** **Other routine risk minimisation measures beyond the Product Information:** Legal status: Pomalidomide is subject to restricted medical prescription.
Severe infection due to neutropenia and pancytopenia	Routine risk communication:

	<u>SmPC</u> **Section 4.8.** **<u>PL</u>** **Section 4** **Routine risk minimisation activities recommending specific clinical measures to address the risk:** **<u>SmPC</u>** **Section 4.2, Section 4.4** **<u>PL</u>** **<u>Section 2</u>** **Other routine risk minimisation measures beyond the Product Information:** Legal status: Pomalidomide is subject to restricted medical prescription.
Thrombocytopenia and bleeding	**Routine risk communication:** **<u>SmPC</u>** **Section 4.8.** **<u>PL</u>** **Section 4** **Routine risk minimisation activities recommending specific clinical measures to address the risk:** **<u>SmPC</u>** **Section 4.2, Section 4.4** **PL** **Section 2** **Other routine risk minimisation measures beyond the Product Information:** Legal status: Pomalidomide is subject to restricted medical prescription.
Cardiac failure	**Routine risk communication:**

	SmPC **Section 4.8** **PL** **Section 4** **Routine risk minimisation activities recommending specific clinical measures to address the risk:** **SmPC** **Section 4.4** **PL** **Section 2** **Other routine risk minimisation measures beyond the Product Information:** Legal status: Pomalidomide is subject to restricted medical prescription.
Non-melanoma skin cancer	**Routine risk communication:** **SmPC** **Section 4.8** **PL** **Section 4** **Routine risk minimisation activities recommending specific clinical measures to address the risk:** **SmPC** **Section 4.4** **PL** **Section 2** **Other routine risk minimisation measures beyond the Product Information:** Legal status: Pomalidomide is subject to restricted medical prescription.
Important potential risks	
Other second primary malignancies	**Routine risk communication:** None proposed. **Routine risk minimisation activities recommending specific clinical measures to address the risk:**

	<u>SmPC</u> **Section 4.4** **PL** **Section 2** **Other routine risk minimisation measures beyond the Product Information:** Legal status: Pomalidomide is subject to restricted medical prescription.
Cardiac arrhythmia	**Routine risk communication:** **<u>SmPC</u>** **Section 4.8** **<u>PL</u>** **Section 4** **Routine risk minimisation activities recommending specific clinical measures to address the risk:** None proposed. **Other routine risk minimisation measures beyond the Product Information:** Legal status: Pomalidomide is subject to restricted medical prescription.

V.2. Additional Risk Minimisation Measures

Pregnancy prevention programme (PPP)

Objectives:

The objective of the PPP is to minimise the risk of teratogenicity by:

- Ensuring that exposure of an unborn child to pomalidomide does not occur.
- Ensuring early alert to the physician of any pregnancies.
- Educating patients and HCPs on the safe use of pomalidomide
- Pregnancy testing and contraception requirements.
- A system to ensure that all appropriate measures have been performed prior to the drug being dispensed
- Managing and monitoring the distribution of pomalidomide
- Follow-up on the effectiveness of the PPP
- Compliance monitoring and assessment (examples include record of counselling patients prior to prescription, record of negative pregnancy test within 3 days of prescription and record of dispensing within 7 days of prescription date).

This controlled access is designed to minimise the risk of exposure to paediatric patients or non-target populations and provide education on the risk and the necessary steps to prevent foetal exposure.

Rationale for the additional risk minimisation activity: Since there is increased risk of teratogenicity due to pomalidomide, additional measures are needed to minimize the risk of teratogenicity and provide education on the risk and on the necessary steps to prevent foetal exposure.

Target audience and planned distribution path:

Targeted audience are the HCPs prescribing/dispensing this product and patients.

Proposed Actions

The key elements of the PPP are:

- Educational Programme:
    - Educational HCP's kit to include educational healthcare professional brochure, educational brochures for patients, patient card, risk awareness forms, and information on where to find latest SmPC.
- Therapy management
- Prescribing controls
- Dispensing controls
- Assessment

The Patient Card and/or an equivalent tool is used to manage the controlled access within the national territoryas agreed with the NCA.

Plans to evaluate the effectiveness of the interventions and criteria for success: The status of the implementation in each member states, any adaptations to the PPP, the results of any compliance measurements as process indicators undertaken in individual countries according to country specific agreements with NCAs, reports of pregnancy exposure will be reviewed on an ongoing basis and summarized at the time of the PSUR overall and by country, outcome of pregnancy, modifications and corrective action will be taken accordingly. Pregnancy root cause analysis in cases of pregnancy exposure will be performed. Criteria for success: Outcome indicator - pregnancy exposures.

Additional HCP Educational Materials

Educational health care professional brochure

Objectives: Raising awareness of healthcare professionals. To help healthcare professionals, who treat patients with pomalidomide, to understand the risk of thrombocytopenia and bleeding and cardiac failure associated with pomalidomide.

Rationale for the additional risk minimisation activity: HCPs to understand the risks specified above and the appropriate management of these risks.

Target audience and planned distribution path: Targeted audience are the physicians prescribing this product and pharmacists.

Plans to evaluate the effectiveness of the interventions and criteria for success: AE reports will be reviewed on an ongoing basis, AE will be summarized at the time of the PSUR and modifications and corrective action will be taken accordingly. Criteria for success will be no increase in frequency or severity of the events as stated in the product information.

Additional Patient Educational Materials

Educational brochure for patients

Objectives: Raising awareness of patients regarding the risk of thrombocytopenia and bleeding.

Rationale for the additional risk minimisation activity: A Pomalidomide Patient brochure is provided as additional educational material to advise patients that pomalidomide may cause thrombocytopenia and the need for regular blood tests.

Target audience and planned distribution path: Targeted audience are the patients who are prescribed pomalidomide.

Plans to evaluate the effectiveness of the interventions and criteria for success: AE reports will be reviewed on an ongoing basis, AE will be summarized at the time of the PSUR and modifications and corrective action will be taken accordingly. Criteria for success will be no increase in frequency or severity of the events as stated in the product information.

Further details regarding aforementioned additional risk minimization measures are provided in the Annex 6.

V.3. Summary of risk minimisation measures

Table Part V.3: Summary table of pharmacovigilance activities and risk minimisation activities by safety concern

Safety concern	Risk minimisation measures	Pharmacovigilance activities

Teratogenicity	**Routine risk minimisation measures:**
	SmPC
	Section 4.3., Section 4.4., Section 4.6, Section 4.8, Section 5.3
	PL
	Section 2 and 4.
	
	Legal status:
	Pomalidomide is subject to restricted medical prescription.
	
	Additional risk minimisation measures:
	Pomalidomide Pregnancy Prevention Programme (PPP)
	- Educational programme for healthcare professionals and patients:
	  ○ Educational HCP kit (Educational healthcare professional brochure, Educational brochures for patients, Patient card, Risk awareness forms, and information on where to find latest SmPC.),
	- Therapy management
	  • Criteria for determining WCBP, Contraceptive measures and pregnancy testing for WCBP
	  • Advice in SmPC and educational materials
		Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:
		Specific adverse reaction follow-up questionnaires for risk of "teratogenicity".
		
		Additional pharmacovigilance activities:
		Monitoring of the implementation of the PPP agreed on a country-specific basis with the relevant National Competent Authority (NCA) in accordance with local legal framework.

Safety concern	Risk minimisation measures	Pharmacovigilance activities
	- System to ensure appropriate measures have been completed • Patient card or equivalent tool to document childbearing status, counselling and pregnancy testing.	
Severe infection due to neutropenia and pancytopenia	**Routine risk minimisation measures:** SmPC Section 4.2., Section 4.4., Section 4.8. PL Section 2 and 4 Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures:** No risk minimisation measures.	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** Specific adverse reaction follow-up questionnaires for risk of "serious infection due to neutropenia and pancytopenia" **Additional pharmacovigilance activities:** None
Thrombocytopenia and bleeding	**Routine risk minimisation measures:** SmPC Section 4.2., Section 4.4., Section 4.8. PL Section 2 and 4 Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures:** - Educational HCP brochure	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** Specific adverse reaction follow-up questionnaires for risk of "thrombocytopenia and bleeding" **Additional pharmacovigilance activities:** None

Safety concern	Risk minimisation measures	Pharmacovigilance activities
	- Educational brochure for patients	
Cardiac failure	**Routine risk minimisation measures:** SmPC Section 4.4., Section 4.8. PL Section 2 and 4 Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures:** Educational HCP brochure	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** Specific adverse reaction follow-up questionnaires for risk of "cardiac failure" **Additional pharmacovigilance activities:** None
Non-melanoma skin cancer	**Routine risk minimisation measures:** SmPC Section 4.4., Section 4.8. PL Section 2 and 4. Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures:** No risk minimisation measures	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** Specific adverse reaction follow-up questionnaires for risk of "second primary malignancies" **Additional pharmacovigilance activities:** None
Other second primary malignancies	**Routine risk minimisation measures:** SmPC Section 4.4. PL Section 2 Legal status: Pomalidomide is subject to restricted medical prescription.	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** Specific adverse reaction follow-up questionnaires for risk of "second primary malignancies" **Additional pharmacovigilance activities:** None

Safety concern	Risk minimisation measures	Pharmacovigilance activities
	Additional risk minimisation measures: No risk minimisation measures	
Cardiac arrhythmia	**Routine risk minimisation measures:** SmPC Section 4.8. PL Section 4 Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures:** No risk minimisation measures	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** Specific adverse reaction follow-up questionnaires for risk of "cardiac arrhythmias and ECG changes" **Additional pharmacovigilance activities:** None

Part VI: Summary of the risk management plan

Summary of risk management plan for Pomalidomide Krka (pomalidomide)

This is a summary of the risk management plan (RMP) for Pomalidomide Krka. The RMP details important risks of Pomalidomide Krka, how these risks can be minimised, and how more information will be obtained about Pomalidomide Krka's risks and uncertainties (missing information).
Pomalidomide Krka's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Pomalidomide Krka should be used.

This summary of the RMP for Pomalidomide Krka 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 Pomalidomide Krka's RMP.

I. The medicine and what it is used for

Pomalidomide Krka is authorised for treatment of multiple myeloma (see SmPC for the full indication). It contains pomalidomide as the active substance and it is given orally.
Further information about the evaluation of Pomalidomide Krka’s benefits can be found in Pomalidomide Krka’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage < link to the EPAR summary landing page. >

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

Important risks of Pomalidomide Krka, together with measures to minimise such risks and the proposed studies for learning more about Pomalidomide Krka'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 Pomalidomide Krka, 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 as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of important risks and missing information

Important risks of Pomalidomide Krka 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 Pomalidomide Krka. 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
	Severe infection due to neutropenia and pancytopenia
	Thrombocytopenia and bleeding
	Cardiac failure
	Non-melanoma skin cancer
Important potential risks	Other second primary malignancies
	Cardiac arrhythmia
Missing information	None

II.B Summary of important risks

Important identified risk: Teratogenicity	
Risk minimisation measures	**Routine risk minimisation measures** SmPC SmPC section 4.3, 4.4, 4.6, 4.8, 5.3

Important identified risk: Teratogenicity	

	PL
	Section 2 and 4
	
	Legal status:
	Pomalidomide is subject to restricted medical prescription.
	
	Additional risk minimisation measures
	- Pomalidomide Pregnancy Prevention Programme
	- Educational programme for healthcare professionals and patients:
	  ○ HCP kit,
	  ○ Treatment algorithm, pregnancy reporting form, patient card, patient guide and checklists
	- Therapy management
	  • Criteria for determining WCBP, Contraceptive measures and pregnancy testing for WCBP
	  • Advice in SmPC and educational materials
	- System to ensure appropriate measures have been completed
	  • Patient card to document childbearing status, counselling and pregnancy testing

Additional pharmacovigilance activities	Additional pharmacovigilance activities: Monitoring of the implementation of the PPP agreed on a country-specific basis with the relevant National Competent Authority (NCA) in accordance with local legal framework.

Important identified risk: Severe infection due to neutropenia and pancytopenia	
Risk minimisation measures	**Routine risk minimisation measures** SmPC SmPC section 4.2, 4.4, 4.8. PL Section 2 and 4. Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures** No risk minimisation measures.

Important identified risk: Thrombocytopenia and bleeding	
Risk minimisation measures	**Routine risk minimisation measures** SmPC SmPC section 4.2, 4.4, 4.8. PL Section 2 and 4 Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures** Educational information for healthcare professionals Patient brochure

Important identified risk: Cardiac failure	
Risk minimisation measures	**Routine risk minimisation measures** SmPC SmPC section 4.4. 4.8. PL Section 2 and 4. Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures** Educational information for healthcare professionals

Important identified risk: Non-melanoma skin cancer	
Risk minimisation measures	**Routine risk minimisation measures** SmPC SmPC section 4.4, 4.8. PL Section 2 and 4. Legal status:

Important identified risk: Non-melanoma skin cancer	
	Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures** No risk minimisation measures

Important potential risk: Other second primary malignancies	
Risk minimisation measures	**Routine risk minimisation measures** SmPC SmPC section 4.4. PL Section 2. Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures** No risk minimisation measures

Important potential risk: Cardiac arrhythmia	
Risk minimisation measures	**Routine risk minimisation measures** SmPC SmPC section 4.8. PL Section 4. Legal status: Pomalidomide is subject to restricted medical prescription. **Additional risk minimisation measures** No risk minimisation measures

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 Pomalidomide Krka.

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

Monitoring of Pregnancy Prevention Programme implementation

Purpose of the study: Monitoring of implementation of the PPP.

Part VII: Annexes

Annex 1 – EudraVigilance Interface

Not applicable.

Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme

Not applicable.

Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan

Study	Summary of objectives	Safety concerns addressed	Protocol link Milestones
Monitoring of Pregnancy Prevention Programme implementation (Category 3 study) Status: Planned	Monitoring of implementation of PPP	Teratogenicity	Routine PSURs in line with DLP of latest EURD list

Annex 4 - Specific adverse drug reaction follow-up forms

Specific adverse reaction follow-up questionnaires for the following safety concerns:	**Follow-up Form Title**
Teratogenicity	Event-Specific Questionnaire for HCP - Pregnancy Background (Patient or Partner of Patient) Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner - Pregnancy Background Event-Specific Questionnaire for HCP - Pregnancy Follow-up (Patient or Partner of Patient) Event-Specific Questionnaire for HCP - Pregnancy Outcome (Patient or Partner of Patient) Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner - Pregnancy Outcome Event-Specific Questionnaire for Primary Care Physician or Paediatrician - Infant Follow-up
Severe infection due to neutropenia and pancytopenia	Neutropenia
Thrombocytopenia and bleeding	Thrombocytopenia/Bleeding
Cardiac failure	Cardiac failure
Non-melanoma skin cancer, Other second primary malignancies	Second Primary Malignancies
Cardiac arrhythmia	Cardiac Arrhythmia and ECG Changes

Pregnancy follow-up questionnaires

Event-Specific Questionnaire for HCP- Pregnancy Background

(Patient or Partner of Patient)

Telephone: _____

Fax: _____

Email: _____

Reporter Information			
REPORTER NAME:			
ADDRESS:		CITY, STATE, ZIP , COUNTRY:	
PHONE NO.:		FAX NO.:	
Obstetrician Information (Please provide)			
OBSTETRICIAN NAME:			
ADDRESS:		CITY, STATE, ZIP, COUNTRY:	
PHONE NO.:		FAX NO.:	
Patient Information			
PATIENT ID :	DATE OF BIRTH	ETHNICITY: ☐ WHITE ☐ AFRICAN-AMERICAN ☐ ASIAN ☐ OTHER, SPECIFY:	
Partner of Patient Information ☐ Not applicable			
DATE OF BIRTH:	ETHNICITY: ☐ WHITE ☐ AFRICAN-AMERICAN ☐ ASIAN ☐ OTHER, SPECIFY:		
Patient Treatment Information:			
LOT NO.:	EXPIRY DATE:	DOSE:	FREQUENCY:
ROUTE:	START DATE:	STOP DATE:	
INDICATI0N FOR USE:			
CYTOGENETIC ABNORMALITIES: ☐ NO ☐ YES If Yes, specify:			

Current Pregnancy			
Date of Last Menstrual Period:		Estimated Delivery Date:	
PREGNANCY TEST	DATE	REFERENCE RANGE	RESULT
Urine qualitative			
Serum quantitative			

Prenatal Tests		
	DATE	RESULT
Ultrasound		
Ultrasound		
Ultrasound		
Amniocentesis		
Maternal serum AFP		

Pregnancy History		
No. of previous pregnancies: Date of last pregnancy:	No. of full term deliveries:	No. of pre-term births:
No. of fetal deaths:	No. of living children:	No. of abortions: Elective_____ Spontaneous _____

Type of delivery: ☐ Vaginal ☐ C-section

Did birth defect occur in any previous pregnancy? ☐ No ☐ Yes ☐ Unknown

If Yes, specify:

Did a stillbirth or spontaneous abortion occur in any previous pregnancy? ☐ No ☐ Yes ☐ Unknown

If yes, in what week of pregnancy did the stillbirth or spontaneous abortion occur? Week:

Was there any birth defect noted? ? ☐ No ☐ Yes, if Yes please specify:

Relevant Medical History

☐ No ☐ Yes, if Yes please specify:

MEDICAL HISTORY	DATE OF DIAGNOSIS	MEDICAL HISTORY	DATE OF DIAGNOSIS

Social History	
ALCOHOL ☐ NO ☐ YES, IF YES, AMOUNT/UNIT CONSUMED PER DAY:	
TOBACCO ☐ NO ☐ YES	IV OR RECREATIONAL DRUG USE ☐ NO ☐ YES, if Yes SPECIFY:

Family History: CONGENITAL ABNORMALITIES ☐ NO ☐ YES, if yes SPECIFY:

If there is a family history of congenital abnormalities, was there a consultation with a Geneticist?

☐ NO ☐ YES, if yes SPECIFY:

Environmental Exposure (e.g. RADIATION, CHEMICAL EXPOSURE) ☐ NO ☐ YES, if yes SPECIFY:

Medications/Treatments (including herbal, alternative and over-the-counter medicines and dietary supplements) During Pregnancy

MEDICATION/TREATMENT	START DATE	STOP DATE/ ONGOING	INDICATION

Adverse Event(s) During Pregnancy

EVENT(S)	SERIOUS		ONSET DATE	STOP DATE/ ONGOING	CAUSAL RELATIONSHIP TO POMALIDOMIDE	
	YES/NO	SERIOUS CRITERIA[1]			YES/NO	IF NO, WHAT MEDICATIONS, DISEASE STATES, etc, PLAYED A ROLE IN THE EVENT?

[1] Serious Criteria: 1) death, 2) life-threatening, 3) required inpatient hospitalization or prolongation of existing hospitalization, 4) a persistent or significant disability/incapacity, 5) a congenital anomaly/birth defect, 6) medically significant

Root cause of Pregnancy

1. What forms of birth control was your patient using while on [Drug Name] before becoming pregnant or impregnating their partner? Please check all that apply.

Tubal ligation	□ YES	□ NO
IUD	□ YES	□ NO
Hormonal birth control	□ YES	□ NO
Partner's vasectomy	□ YES	□ NO
Male latex or synthetic condom	□ YES	□ NO
Diaphragm	□ YES	□ NO
Cervical cap or shield	□ YES	□ NO
Spermicide or sponge	□ YES	□ NO
Withdrawal	□ YES	□ NO
Abstinence	□ YES	□ NO

2. Was your patient or their partner without contraception for even one day at any time during use of [DRUG NAME]?

□ No, please proceed to Question 5

□ Yes, please answer Question 3, Question 4, Question 5, and Question 6

3. If applicable per Question 2, how often did your patient have unprotected sexual intercourse?

□ Multiple times □ Once a week □ Once every 2 weeks □ Once a month □ Not at all □ Other, specify
4. If applicable per Question 2, why did your patient and/or their partner interrupt or stop using contraception? □ Wanted a child ¨ Partner disapproved □ Side effects □ Health concerns □ Inconvenient to use □ Other, specify
5. Please ask your patient if they received the [Drug Name] Patient Information (e.g. Medication Guide or patient leaflet). □ No, please proceed to Question 5.3 □ Yes, please answer Question 5.1
5.1 Please ask your patient if they read the [Drug Name] Patient Information (e.g. Medication Guide or patient leaflet). □ No, please proceed to Question 5.3 □ Yes, please answer Question 5.2
5.2 Please ask your patient if they understood the information in the [Drug Name] Patient Information (e.g. Medication Guide or patient leaflet). □ No, please proceed to Question 5.3 □ Yes, please proceed to Question 5.3
5.3 Please ask your patient where most of their knowledge about contraception during [Drug Name] use came from. □ Physician who prescribed [Drug Name □ Patient Guide to the [Drug Name] □ [Drug Name] Patient Information (e.g. Medication Guide or patient leaflet) □ Other, specify:
6. Please ask your patient if they felt that they and their partner had a good understanding of the risk of pregnancy during [Drug Name] use. □ No □ Yes □ Don’t know

SIGNATURE OF PERSON COMPLETING THIS FORM _____ DATE _____

Event-Specific Questionnaire for HCP- Pregnancy Follow-up

(Patient or Partner of Patient)

Telephone: _____

Fax: _____

Email: _____

Date:	**Period Covered**:_____(Date) to _____(Date)

Reporter Information	
REPORTER NAME:	
ADDRESS:	CITY, STATE, ZIP, COUNTRY:
PHONE NO.:	FAX NO.:
Name of Patient or Pregnant Partner of Male Patient:	
Current Pregnancy	

Prenatal Tests (If any additional medical records relating to these prenatal tests are available, please attach along with this form)

TEST	DATE	RESULT
Ultrasound		
Ultrasound		
Ultrasound		
Amniocentesis		
Maternal Serum AFP		
Other Tests, Specify:		

Pregnancy Type

☐ SINGLETON ☐ TWIN ☐ TRIPLET ☐ OTHER, SPECIFY:

Medications/Treatments (including herbal, alternative and over-the-counter medicines and dietary supplements) During Pregnancy

MEDICATION/TREATMENT	START DATE	STOP DATE/ CONTINUING	INDICATION

Adverse Event(s) During Pregnancy						
EVENT(S)	ONSET DATE	STOP DATE/ ONGOING	SERIOUS		CAUSAL RELATIONSHIP TO POMALIDOMIDE	
			YES/ NO	SERIOUS CRITERIA[1]	YES/ NO	IF NO, WHAT MEDICATIONS, DISEASE STATES, etc, PLAYED A ROLE IN THE EVENT?

[1] Serious Criteria: 1) death, 2) life-threatening, 3) required inpatient hospitalization or prolongation of existing hospitalization, 4) a persistent or significant disability/incapacity, 5) a congenital anomaly/birth defect, 6) medically significant

SIGNATURE OF PERSON COMPLETING THIS FORM _____ DATE _____

Event-Specific Questionnaire for HCP - Pregnancy Outcome

(Patient or Partner of Patient)

Telephone: _____

Fax: _____

Email: _____

Reporter Information			
REPORTER NAME:			
ADDRESS:		CITY, STATE, ZIP, COUNTRY:	
PHONE NO.:		FAX NO.:	
Patient Information			
PATIENT ID:	DATE OF BIRTH:	ETHNICITY: ☐WHITE ☐BLACK ☐ASIAN ☐OTHER, SPECIFY:	
Partner of Patient Information ☐ Not applicable			
DATE OF BIRTH:	ETHNICITY: ☐WHITE ☐BLACK ☐ASIAN ☐OTHER, SPECIFY:		

Pregnancy Type

□ SINGLETON □ TWIN □ TRIPLET □ OTHER, SPECIFY:

Pregnancy Outcome			
DATE OF DELIVERY :			GESTATION AGE AT DELIVERY:
DELIVERY DETAILS	NO	YES	ADDITIONAL COMMENTS
Normal	☐	☐	
C-section	☐	☐	
Induced	☐	☐	
Assisted (e.g., forceps)	☐	☐	
Elective termination	☐	☐	Date:
Spontaneous abortion (≤ 20 weeks)	☐	☐	Weeks from LMP:
Fetal death/Stillbirth (> 20 weeks)	☐	☐	
Were the products of conception examined?	☐	☐	If yes, was the fetus normal? ☐Yes ☐No ☐Unknown If no, describe: _____

Obstetrics Information			
	NO	YES	
Complications During Pregnancy	☐	☐	If Yes, specify: _____

Complications During Labor/Delivery	☐	☐	If Yes, specify: _____
Post-partum Maternal Complications	☐	☐	If Yes, specify: _____
Fetal Outcome			
	NO	YES	
Live Normal Infant	☐	☐	
Fetal Distress	☐	☐	
Intra-uterine Growth Retardation	☐	☐	
Neonatal Complications*	☐	☐	If Yes, please specify: _____
Birth Defect Noted?	☐	☐	If Yes, please specify: _____

Sex: ☐Male ☐Female **Birth Weight**:_____lbs_____oz or _____kg

Length:_____inches or _____cm

Apgar Score:	Unknown:	1 min	5 mins:	10 mins:

*PLEASE PROVIDE A BRIEF SUMMARY OF THE MANAGEMENT OF THE COMPLICATIONS

SIGNATURE OF PERSON COMPLETING THIS FORM _____ DATE _____

Event-Specific Questionnaire for Primary Care Physician or Pediatrician

Infant Follow-up

Telephone: _____

Fax: _____

Email: _____

Date of assessment:_____

Age in months:

Weight (at the time of this assessment): lbs oz or kg_

Length:_____inches or _____cm

Name of Patient on pomalidomide:

Name of infant (if known):

Plese provide the period from (Date) to (Date)

Birth Defects/Anomalies

New birth defects or anomalies noted since previous report? □ Yes □ No

If Yes, please list the birth defects/anomalies below:

BIRTH DEFECT/ANOMALY	WAS THE DEFECT/ ANOMALY ATTRIBUTED TO pomalidomide THERAPY? (Y/N/UNKNOWN)	FACTORS THAT MAY HAVE CONTRIBUTED TO THIS OUTCOME: (e.g., FAMILY HISTORY, MATERNAL AGE, OBESITY, ALCOHOL CONSUMPTION DURING PREGNANCY, etc.)	DEFECT/ ANOMALY NOTED PRIOR TO BIRTH? (Y/N)	INFANT AGE WHEN DEFECT/ ANOMALY WAS NOTED (SPECIFY WEEKS OR MONTHS)

Development Assessment:

Is the child developing normally for his/her age? ☐ Yes □ No

If No, please define your concerns regarding any developmental issues or abnormalities:

_____

_____

Diagnosis date of any developmental issues: _____

Infant illnesses, hospitalizations, Drug therapies:

Infant Illnesses	Hospitalized?	Drug Therapies
	□Yes □ No	
	□Yes □ No	
	□Yes □ No	
	□Yes □ No	
	□Yes □ No	

SIGNATURE OF PERSON COMPLETING THIS FORM _____ DATE _____

Adverse Event Report Questionnaire

CARDIAC ARRHYTYMIA & ECG CHANGES

INFORMATION PREVIOUSLY PROVIDED DOES NOT NEED TO BE REPEATED ON THIS FORM:

Patient Demographics:

Patient's date of birth (DD-MMM-YYYY): Gender: ☐Male ☐ Female

Age:_____

Race/Ethnicity: □ Aborginal □ African American □Asian □ American Indian or Alaskan Native □ Native Hawaiian or other Pacific Islander □ Torres strait Islander ☐ White □ Black □ Non Hispanic

Age group:_____

Note: Please provide Age Group if Patient's Date of Birth or Age is not available.

Age Group Definition: Neonate: 0 - 27 days, Infant: 28 days to 23 months, Child: 2 years to 11years, Adolescent: 12 years to 18 years, Adult: More than 18 years and less than or equal to 65 years and Elderly: equal or greater than 66 years)

Suspect Products: Please provide suspect product(s) information [those product(s) that are suspected to be associated with one or more adverse events]:

	Suspect Product #1	Suspect Product #2	Suspect Product #3
Product name			
Daily dose and regimen			
Route of administration			
Indication			
Start date or treatment duration (DD/MM/YYYY)			
Stop date (DD/MM/YYYY)			
Lot/Batch number(s)			
Expiration date(s)			
Action Taken with the suspect product			

(Choose from one of the following for action Taken with Suspect Product: Drug withdrawn, Dose reduced, Dose increased, Dose not changed, Unknown)

Adverse Event (AE) Description: Please provide diagnosis or symptoms/signs if diagnosis is unavailable.

Add diagnosis here→	Adverse event #1	Adverse event #2	Adverse event #3	Adverse event #4
Start date (DD/MM/YYYY)				
Stop date (DD/MM/YYYY)				
Time lag if AE occurred after cessation of treatment with the suspect product(s):				
Required Hospitalization (Yes/No)				
Life-Threatening (Yes/No)				
Persistent or significant disability (Yes/No)				
Congenital abnormality (Yes/No)				
Cause of Death (Yes/No)				
Treatment of Adverse Event				
Outcome (recovery and sequelae, if any)				
Did the event(s) abate after suspect Product was stopped or dose reduced? (Yes/No)				
Did the event recur after reintroducing (Yes/No)				

Please summarize course of reported events including signs and symptoms in chronological order:

_____
_____
_____
_____

Diagnostic tests (use additional pages if needed): Please indicate test unit where applicable.

Date	Test name	Pre-treatment value	AE onset value	AE resolution value	Normal low	Normal high
	CPK					
	CPK-MB					
	Troponin					
	RBC					
	Hemoglobin					
	Metabolic Panel (specify)					
	Serum potassium					
	Serum magnesium					
	Phosphorus					
	Calcium					
	Uric acid					
	Creatinine					
	BUN					

Please provide causal relationship assessment between the suspect product(s) and adverse event(s):

_____
_____

Concomitant Medications (use additional pages if needed):

Did the Patient take any concomitant medication? □ Yes (please complete below) □ No □ Unknown

Please include any antiemetics.

Medication name	Daily dose and regimen	Route of administration	Indication	Start date (DD/MM/YYYY)	Stop date (DD/MM/YYYY)

Other Etiological Factors: □ Yes (please complete below) □ None □ Unknown

□ Relevant medical and/or drug history (please specify), including start date or duration:

_____

_____

□ Family history (please specify):

□ Drug/alcohol/tobacco abuse:

□ Other (please specify):

Additional questions: Please provide a brief description of the cardiac arrhythmia, or ECG change, including the type and the clinical signs/symptoms observed, including start and stop dates:

Please specify the type of arrhythmia/ECG change.

Clinical signs and symptoms, if present (if none please state)

Start date Stop date

Does this patient have a relevant cardiac history? If yes, please specify in box below. If no, please state.

Does this patient have a history of cardiac risk factors (e.g. hypertension, hyperlipidemia, hypercholesterolemia, diabetes, sepsis, obesity, smoking, renal disease, cardio respiratory problems)? If yes, please specify in the box below. If no, please state

Please provide the available results of the diagnostic workup (include dates of baseline, event onset, and resolution results)

Test Name	Pre-treatment results	AE onset results	AE resolution results
EKG findings			
Echocardiogram			
Chest x-ray			
Holter, Stress Test			

Please describe specific treatments and interventions of the arrhythmia

Health Practitioner Name (Print)

Health Practitioner Name (Signature)

Additional information regarding this Adverse Event Report:

Description of event: [narrative]

Adverse Event Report Questionnaire

CARDIAC FAILURE

INFORMATION PREVIOUSLY PROVIDED DOES NOT NEED TO BE REPEATED ON THIS FORM:

Patient Demographics:

Patient's date of birth (DD-MMM-YYYY): Gender: □Male □ Female

Age:_____

Race/Ethnicity: □ Aborginal □ African American □Asian □ American Indian or Alaskan Native □ Native Hawaiian or other Pacific Islander □ Torres strait Islander □ White □ Black □ Non Hispanic

Age group:_____

Note: Please provide Age Group if Patient's Date of Birth or Age is not available.

Age Group Definition: Neonate: 0 - 27 days, Infant: 28 days to 23 months, Child: 2 years to 11years, Adolescent: 12 years to 18 years, Adult: More than 18 years and less than or equal to 65 years and Elderly: equal or greater than 66 years)

Suspect Products: Please provide suspect product(s) information [those product(s) that are suspected to be associated with one or more adverse events]:

	Suspect Product #1	Suspect Product #2	Suspect Product #3
Product name			
Daily dose and regimen			
Route of administration			
Indication			
Start date or treatment duration (dd/MM/YYYY)			
Stop date (dd/MM/YYYY)			
Lot/Batch number(s)			
Expiration date(s)			
Action Taken with the suspect product			

(Choose from one of the following for action Taken with Suspect Product: Drug withdrawn, Dose reduced, Dose increased, Dose not changed, Unknown)

Adverse Event (AE) Description: Please provide diagnosis or symptoms/signs if diagnosis is unavailable.

Add diagnosis here→	Adverse event #1	Adverse event #2	Adverse event #3	Adverse event #4
Start date (DD/MM/YYYY)				
Stop date (DD/MM/YYYY)				
Time lag if AE occurred after cessation of treatment with the suspect product(s):				
Required Hospitalization (Yes/No)				
Life-Threatening (Yes/No)				
Persistent or significant disability (Yes/No)				
Congenital abnormality (Yes/No)				
Cause of Death (Yes/No)				
Treatment of Adverse Event				
Outcome (recovery and sequelae, if any)				
Did the event(s) abate after suspect Product was stopped or dose reduced? (Yes/No)				
Did the event recur after reintroducing (Yes/No)				

Please summarize course of reported events including signs and symptoms in chronological order:

_____
_____
_____
_____

Diagnostic tests (use additional pages if needed): Please indicate test unit where applicable.

Date	Test name	Pre-treatment value	AE onset value	AE resolution value	Normal low	Normal high
	Calcium					
	Magnesium					
	Total CPK					
	CK-MB					
	Troponins					
	BNP					
	WBC					
	RBC					
	Platelets					
	Hemoglobin					
	Hematocrit					

Please provide causal relationship assessment between the suspect product(s) and adverse event(s):

_____
_____

Concomitant Medications (use additional pages if needed): Did the Patient take any concomitant medication? □ Yes (please complete below) □ No □ Unknown

Medication name	Daily dose and regimen	Route of administration	Indication	Start date (DD/MM/YYYY)	Stop date (DD/MM/YYYY)

Other Etiological Factors: □ Yes (please complete below) □ None □ Unknown

□ Relevant medical and/or drug history (please specify), including start date or duration:

_____

_____

□ Family history (please specify):

□ Drug/alcohol/tobacco abuse:

□ Other (please specify):

Additional questions:

1.) Did the cardiac failure occur prior to therapy? □ Yes □ No

a. It the cardiac failure occurred prior to therapy, would you consider it an exacerbation? □ Yes □ No

b. Please provide the date the exacerbation was diagnosed: _____

2) Please circle classification of cardiac failure:

a) Class I (mild) Patients with cardiac disease but without limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or angina pain

b) Class II (mild) Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or angina pain.

c) Class III (moderate) Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or angina pain.

d) Class IV (severe) Patients with cardiac disease resulting in the inability to carry on any physical activity without discomfort. Symptoms of heart failure or the angina syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased

Please provide results for EKG, echocardiogram, angiogram, CT scan, MRI and ejection fraction.

3) Did the patient receive any recent blood transfusions or IV infusions? □ Yes □ No
It yes, please specify what was transfused and provide the amount transfused with dates.

4) Does the patient have other cardiac history including congenital heart disease, coronary artery disease, cardiac stents, myocardial infarction, valvular heart disease, cardiomyopathy, endocarditis, or myocarditis?

5) Please provide any associated risk factors including history of hyperlipidemia, obesity, hypertension COPD, renal disease, diabetes, sepsis, substance abuse, and family history of heart disease.

6) Any exposure to other chemotherapeutic agents (previous and/or ongoing)? Please specify

7) Are there any concurrent events that contributed or led up to the cardiac failure? Please specify.

8) What treatments/interventions were provided to the patient tor the cardiac failure?

Health Practitioner Name (Print)

Health Practitioner Name (Signature)

Additional information regarding this Adverse Event Report:

Description of event: [narrative]

Adverse Event Report Questionnaire

NEUTROPENIA

INFORMATION PREVIOUSLY PROVIDED DOES NOT NEED TO BE REPEATED ON THIS FORM:

Patient Demographics:

Patient's date of birth (DD-MMM-YYYY): Gender: □Male □ Female

Age:_____

Race/Ethnicity: □ Aborginal □ African American □Asian □ American Indian or Alaskan Native □ Native Hawaiian or other Pacific Islander □ Torres strait Islander □ White □ Black □ Non Hispanic

Age group:_____

Note: Please provide Age Group if Patient's Date of Birth or Age is not available.

Age Group Definition: Neonate: 0 - 27 days, Infant: 28 days to 23 months, Child: 2 years to 11years, Adolescent: 12 years to 18 years, Adult: More than 18 years and less than or equal to 65 years and Elderly: equal or greater than 66 years)

Suspect Products: Please provide suspect product(s) information [those product(s) that are suspected to be associated with one or more adverse events]:

	Suspect Product #1	Suspect Product #2	Suspect Product #3
Product name			
Daily dose and regimen			
Route of administration			
Indication			
Start date or treatment duration (dd/MM/YYYY)			
Stop date (dd/MM/YYYY)			
Lot/Batch number(s)			
Expiration date(s)			
Action Taken with the suspect product			

(Choose from one of the following for action Taken with Suspect Product: Drug withdrawn, Dose reduced, Dose increased, Dose not changed, Unknown)

Adverse Event (AE) Description: Please provide diagnosis or symptoms/signs if diagnosis is unavailable.

Add diagnosis here→	Adverse event #1	Adverse event #2	Adverse event #3	Adverse event #4
Start date (DD/MM/YYYY)				
Stop date (DD/MM/YYYY)				
Time lag if AE occurred after cessation of treatment with the suspect product(s):				
Required Hospitalization (Yes/No)				
Life-Threatening (Yes/No)				
Persistent or significant disability (Yes/No)				
Congenital abnormality (Yes/No)				
Cause of Death (Yes/No)				
Treatment of Adverse Event				
Outcome (recovery and sequelae, if any)				
Did the event(s) abate after suspect Product was stopped or dose reduced? (Yes/No)				
Did the event recur after reintroducing (Yes/No)				

Please summarize course of reported events including signs and symptoms in chronological order:

_____
_____
_____
_____

Diagnostic tests (use additional pages if needed): Please indicate test unit where applicable.

Date	Test name	Pre-treatment value	AE onset value	AE resolution value	Normal low	Normal high
	WBC					
	ANC					

Please provide causal relationship assessment between the suspect product(s) and adverse event(s):

_____
_____

Concomitant Medications (use additional pages if needed): Did the Patient take any concomitant medication? □ Yes (please complete below) □ No □ Unknown

Medication name	Daily dose and regimen	Route of administration	Indication	Start date (DD/MM/YYYY)	Stop date (DD/MM/YYYY)

Other Etiological Factors: □ Yes (please complete below) □ None □ Unknown

□ Relevant medical and/or drug history (please specify), including start date or duration:

_____

_____

□ Family history (please specify):

□ Drug/alcohol/tobacco abuse:

□ Other (please specify):

Additional questions:

1. What treatment were given for the neutropenia? Please include dates. Did the patient receive G-CSF? GM-CSF? Please provide details.

2. Did your patient experience an infection in association with the neutropenia?
   ☐Yes ☐ No
   If yes, please provide location of the infection

3. Does the patient have a history of recurrent infection?
   ☐Yes ☐ No
   If yes, please explain.

4. Please provide the stage/classification of the patient's disease (specify) at the time of the infection.

5. Does your patient have a medical history of autoimmune disease, abnormal disease of spleen, bone marrow disease, etc.?

6. Has your patient received prior radiation therapy? If so, please provide treatment details including dates.

7. Does your patient have a medical history of cancer effecting bone marrow?

8. Please include culture / serology / bone marrow studies / x-ray for the event of infection.

Health Practitioner Name (Print)

Health Practitioner Name (Signature)

Additional information regarding this Adverse Event Report:

Description of event: [narrative]

Adverse Event Report Questionnaire

SECOND PRIMARY MALIGNANCIES (SPM)

INFORMATION PREVIOUSLY PROVIDED DOES NOT NEED TO BE REPEATED ON THIS FORM:

Patient Demographics:

Patient's date of birth (DD-MMM-YYYY): Gender: □Male □ Female

Age:_____

Race/Ethnicity: □ Aborginal □ African American □Asian □ American Indian or Alaskan Native □ Native Hawaiian or other Pacific Islander □ Torres strait Islander □ White □ Black □ Non Hispanic

Age group:_____

Note: Please provide Age Group if Patient's Date of Birth or Age is not available.

Age Group Definition: Neonate: 0 - 27 days, Infant: 28 days to 23 months, Child: 2 years to 11years, Adolescent: 12 years to 18 years, Adult: More than 18 years and less than or equal to 65 years and Elderly: equal or greater than 66 years)

Suspect Products: Please provide suspect product(s) information [those product(s) that are suspected to be associated with one or more adverse events]:

	Suspect Product #1	Suspect Product #2	Suspect Product #3
Product name			
Daily dose and regimen			
Route of administration			
Indication			
Start date or treatment duration (dd/MM/YYYY)			
Stop date (dd/MM/YYYY)			
Lot/Batch number(s)			
Expiration date(s)			
Action Taken with the suspect product			

(Choose from one of the following for action Taken with Suspect Product: Drug withdrawn, Dose reduced, Dose increased, Dose not changed, Unknown)

Adverse Event (AE) Description: Please provide diagnosis or symptoms/signs if diagnosis is unavailable.

Add diagnosis here→	Adverse event #1	Adverse event #2	Adverse event #3	Adverse event #4
Start date (DD/MM/YYYY)				
Stop date (DD/MM/YYYY)				
Time lag if AE occurred after cessation of treatment with the suspect product(s):				
Required Hospitalization (Yes/No)				
Life-Threatening (Yes/No)				
Persistent or significant disability (Yes/No)				
Congenital abnormality (Yes/No)				
Cause of Death (Yes/No)				
Treatment of Adverse Event				
Outcome (recovery and sequelae, if any)				
Did the event(s) abate after suspect Product was stopped or dose reduced? (Yes/No)				
Did the event recur after reintroducing (Yes/No)				

Please summarize course of reported events including signs and symptoms in chronological order:

_____
_____
_____
_____

Diagnostic tests (use additional pages if needed): Please indicate test unit where applicable.

Date	Test name	Pre-treatment value	AE onset value	AE resolution value	Normal low	Normal high
	Calcium					
	Phosphate					
	Uric acid					
	Creatinine					
	Potassium					
	LDH					
	Albumin					
	Protein					

Please provide causal relationship assessment between the suspect product(s) and adverse event(s):

_____
_____

Concomitant Medications (use additional pages if needed): Did the Patient take any concomitant medication? □ Yes (please complete below) □ No □ Unknown

Please include drugs that are potentially nephrotoxic (NSAIDS, antibiotics) including over the counter drugs.

Medication name	Daily dose and regimen	Route of administration	Indication	Start date (DD/MM/YYYY)	Stop date (DD/MM/YYYY)

Other Etiological Factors: □ Yes (please complete below) □ None □ Unknown

□ Relevant medical and/or drug history (please specify), including start date or duration:

_____

_____

□ Family history (please specify):

□ Drug/alcohol/tobacco abuse:

□ Other (please specify):

Additional questions:

When querying about SPMs, specify the malignancy or diagnosis. Do not use the term SPM when diagnosis is known.

Core Questions tor Follow-up of SPMs:

1. Dates of the underlying disease's diagnosis.
2. Date of first clinical symptoms of SPM.
3. Stage of the underlying disease treated with pomalidomide at baseline, the end of treatment if applicable, and at the time of the event with supportive documentation if available.
4. Medical history of bone marrow transplant including dates, type, donor details, source, and conditioning regimens such as treatment with alkylating agents (i.e. Cyclophosphamide, Melphalan, etc.).
5. Environmental exposure e.g. atmospheric pollutants/toxic chemicals (pesticides, herbicides, benzene, solvents); occupation/hobbies.
6. Full SPM (specify malignancy or diagnosis if known) biopsy reports. If not available please provide the detailed results.

In addition to the Core Questions specific information should be requested based on the risk factors for individual types of cancer, including:

Hematologic Malignancies (including Lymphoma and B-cell malignancy):

☐ Previous chemotherapy rounds (dates, type) and /or radiotherapy (zone, duration, cumulative dose) or subsequent ones if SPM (specify malignancy or diagnosis) detected after product discontinuation ☐ Medical conditions that compromise the immune system – HIV/AIDS, autoimmune diseases, diseases requiring immune suppressive therapy-organ transplant

☐ For lymphoma: Infection with HIV, Epstein-Barr virus+++, Helicobacter pylori, hepatitis B or C, human T-lymphotrophic virus type I, Burkitt's lymphoma

☐ Concurrent or medical/family history of inherited syndromes with genetic changes that raise the risk of acute lymphocytic leukemia (ALL) including: Down syndrome, Klinefelter syndrome, Fanconi anemia, Bloom syndrome, Ataxia-telangiectasia, Neurofibromatosis.

☐ Exposure to benzene (solvent used in the rubber industry, oil refineries, chemical plants, shoe manufacturing, and gasoline-related industries, and is also present in cigarette smoke, as well as some glues, cleaning products, detergents, art supplies, and paint strippers).

☐ Smoking history – Product smoked (i.e. cigars, cigarettes, etc.) and depth of inhalation, length of time, number of cigarettes/days or pack-years, age at starting

☐ Exposure to high levels of radiation ◇ Medical history of treated hematologic malignancies or concurrent leukemias or lymphomas including: Chronic Lymphocytic Leukemia (CLL), Richter transformation, and Diffuse Large B-cell lymphoma (DLBCL) such as Hodgkin's disease and plasmablastic lymphoma.

☐ Relevant diagnostic test results (if available), including: biopsy, immunohistochemistry, flow cytometry, cytogenetics, reverse transcriptase polymerase chain reaction, Fluorescence in situ hybridization (FISH), and next generation sequencing

Lung Cancer:

☐ Smoking history – length of time, number of cigarettes/day, age at starting, gender, Product smoked and depth of inhalation

☐ Pre-existing pulmonary disease

☐ Family history of lung cancer

Thyroid Cancer:

☐ Personal or family history of thyroid and/or autoimmune diseases - hypo or hyperthyroidism, goiter, benign thyroid nodules, Hashimoto's disease, Graves disease

☐ Family history of familial medullary thyroid cancer, multiple endocrine neoplasia and familial adenomatous polyposis

☐ Living in iodine deficient area

☐ History of radiation exposure

Breast Cancer:

☐ Receptor status of the tumor – ER, PR, Her2/neu

☐ Age at onset of menses and age of menopause

☐ Number of pregnancies and age at first birth

☐ History of breastfeeding children

☐ Use of oral contraceptives or hormone replacement therapy

☐ Obesity

☐ Economic status and dietary iodine deficiency

Ovarian Cancer:

☐ Number of pregnancies and childbearing status

☐ History of hormone replacement therapy

☐ History of breast cancer

Uterine Cancer:

☐ Age at onset of menses and age of menopause

☐ Number of pregnancies

☐ Use of oral contraceptives
☐ Obesity

Colon Cancer:

☐ Family or personal history of adenomatous polyposis (FAP), Lynch syndrome (Hereditary nonpolyposis colorectal cancer)
☐ Diet high in red meat and animal fat, refined carbohydrates, low-fiber diet, and low overall intake of fruits and vegetables
☐ Obesity, and sedentary habits
☐ Any history of inflammatory conditions of digestive tract - Chronic ulcerative colitis, Crohn's disease longer duration, greater extent of colon involvement

Anorectal Cancer:

☐ History of infection with human papillomavirus, HIV, chronic fistulas, irradiated anal skin, leukoplakia, lymphogranulomatoma venereum, condyloma acuminatum

Gastric Cancer:

☐ Diet rich in pickled vegetables, salted fish, salt, and smoked meats
☐ Helicobacter pylori infection
☐ Obesity
☐ Previous gastric surgery
☐ Pernicious anemia, adenomatous polyps, gastric ulcer
☐ Chronic atrophic gastritis
☐ Radiation exposure
☐ History of alcohol use/smoking

Oesophageal Cancer:

☐ Genetic causes – tylosis (hyperkeratosis palmaris et plantaris)
☐ History of alcohol use/smoking
☐ History of chronic or acute inflammation (e.g. GERD, Barrett's esophagus, caustic ingestion), Achalasia (esophageal motility disorder)
☐ Human papilloma virus
☐ Sclerotherapy
☐ Plummer-Vinson syndrome (dysphagia, associated with iron deficiency anemia)

Liver cancer:

☐ History of cirrhosis (including alcoholic, biliary cirrhosis), other chronic liver dysfunction
☐ History of alcohol use/smoking
☐ Hepatitis B, C
☐ Hemochromatosis
☐ Indigestion of food contaminated with fungal aflatoxins (in subtropical regions)

Pancreatic Cancer:

☐ History of alcohol use/smoking
☐ Obesity
☐ Diet (red meat)
☐ History of chronic pancreatitis or long-standing diabetes mellitus (primarily in women).
☐ Inherited predisposition (hereditary pancreatitis, familial adenomatous poliposis)

Renal Cancer (renal cell carcinoma):

☐ Smoking history - Product smoked (i.e. cigars, cigarettes, etc.) and depth of inhalation, length of time, number of cigarettes/days or pack-years, age at starting

☐ Obesity

☐ Hypertension

☐ Phenacetin-containing analgesics taken in large amounts

☐ History of renal transplantation.

☐ Exposure to radiopaque dyes, asbestos, cadmium, and leather tanning and petroleum products

☐ Inherited von Hippel-Lindau disease (VHL) disease, Adult polycystic kidney disease, Tuberous sclerosis

Bladder Cancer:

☐ Smoking history – Product smoked (i.e. cigars, cigarettes, etc.) and depth of inhalation, length of time, number of cigarettes/days or pack-years, age at starting

☐ Industrial exposure to aromatic amines in dyes, paints, solvents, leather dust, inks, combustion products, rubber, and textiles

☐ Occupation - painting, driving trucks, and working with metal

☐ Prior spinal cord injuries with long-term indwelling catheters

Prostate Cancer:

☐ Smoking history – Product smoked (i.e. cigars, cigarettes, etc.) and depth of inhalation, length of time, number of cigarettes/days or pack-years, age at starting

☐ History of high-grade prostatic intraepithelial neoplasia (PIN)

☐ Genome changes-deletion of chromosome 3 and fusion of TMPRSS2 and ERG genes

☐ Testosterone level

☐ History of sexually transmitted diseases

☐ History of vasectomy

☐ History of exposure to cadmium

☐ History of genitor-urinary infections

Head and Neck Cancer:

☐ History of alcohol use/smoking

☐ Exposure to Human papilloma virus (HPV) or Epstein-Barr virus (EBV)

☐ History of poor oral hygiene and/or poor nutrition

☐ Exposure to asbestos, wood dust, paint fumes or chemicals

☐ History of Gastroesophageal reflux disease (GERD) or laryngopharyngeal reflux disease (LPRD)

Brain tumors (gliomas and meningiomas):

☐ Exposure to radiation

☐ Exposure to vinyl chloride, Pesticides

☐ Immune system disorders

☐ Hormone replacement therapy

Larynx Cancer:

☐ History of alcohol use/smoking

☐ Asbestos exposure

☐ Any activity requiring loud speech, exposure to sudden and frequent temperature changes

☐ Frequent hoarseness, frequent and persistent cough
☐ Persistently swollen neck glands
☐ Tonsillectomy and laryngeal surgery

Nasal and Paranasal Sinus Cancer:

☐ Woodworking, any dust/flour chronic exposure
☐ History of Infection with human papillomavirus (HPV)
☐ Smoking history – Product smoked (i.e. cigars, cigarettes, etc.) and depth of inhalation, length of time, number of cigarettes/days or pack-years, age at starting g

Mouth and Oropharyngeal Cancer:

☐ History of alcohol use/smoking
☐ History of poor oral hygiene
☐ Chronic mucosal/gum irritation / ill-filling dentures
☐ Betel-Nut Chewing (Indian populations)
☐ History of syphilis or viral infections
☐ Impaired immunity – AIDS, transplant with anti-rejection drugs
☐ Precancerous mouth plaques – Leukoplakia or erythroplasia
☐ History of cancer of the aero-digestive tract

Melanoma, basal cell carcinoma, squamous cell carcinoma of skin:

☐ History of prolonged sun exposure (UV radiation) – severe blistering sunburns, frequent tanning, use of sunlamps and tanning booths
☐ History of living close to equator or at high elevation
☐ History of skin conditions – Dysplastic nevus, Xeroderma pigmentosum, nevoid basal cell carcinoma syndromes
☐ Skin type – fair (pale) skin – burns easily, freckles
☐ Eye color – blue, green or gray, Hair color – blond or red
☐ Use of medication causing sensitivity to sun - antibiotics, hormones, antidepressants,
☐ Immune system depression – AIDS, leukemias,
☐ Exposure to arsenic, coal tar or creosote
☐ For eye localization: history of oculodermal melanocytosis or Dysplastic nevus syndrome

Health Practitioner Name (Print)

Health Practitioner Name (Signature)

Additional information regarding this Adverse Event Report:

Description of event: [narrative]

Adverse Event Report Questionnaire

THROMBOCYTOPENIA – BLEEDING

INFORMATION PREVIOUSLY PROVIDED DOES NOT NEED TO BE REPEATED ON THIS FORM:

Patient Demographics:

Patient's date of birth (DD-MMM-YYYY): Gender: □Male □ Female

Age:_____

Race/Ethnicity: □ Aborginal □ African American □Asian □ American Indian or Alaskan Native □ Native Hawaiian or other Pacific Islander □ Torres strait Islander □ White □ Black □ Non Hispanic

Age group:_____

Note: Please provide Age Group if Patient's Date of Birth or Age is not available.

Age Group Definition: Neonate: 0 - 27 days, Infant: 28 days to 23 months, Child: 2 years to 11years, Adolescent: 12 years to 18 years, Adult: More than 18 years and less than or equal to 65 years and Elderly: equal or greater than 66 years)

Suspect Products: Please provide suspect product(s) information [those product(s) that are suspected to be associated with one or more adverse events]:

	Suspect Product #1	Suspect Product #2	Suspect Product #3
Product name			
Daily dose and regimen			
Route of administration			
Indication			
Start date or treatment duration (dd/MM/YYYY)			
Stop date (dd/MM/YYYY)			
Lot/Batch number(s)			
Expiration date(s)			
Action Taken with the suspect product			

(Choose from one of the following for action Taken with Suspect Product: Drug withdrawn, Dose reduced, Dose increased, Dose not changed, Unknown)

Adverse Event (AE) Description: Please provide diagnosis or symptoms/signs if diagnosis is unavailable.

Add diagnosis here→	Adverse event #1	Adverse event #2	Adverse event #3	Adverse event #4
Start date (DD/MM/YYYY)				
Stop date (DD/MM/YYYY)				
Time lag if AE occurred after cessation of treatment with the suspect product(s):				
Required Hospitalization (Yes/No)				
Life-Threatening (Yes/No)				
Persistent or significant disability (Yes/No)				
Congenital abnormality (Yes/No)				
Cause of Death (Yes/No)				
Treatment of Adverse Event				
Outcome (recovery and sequelae, if any)				
Did the event(s) abate after suspect Product was stopped or dose reduced? (Yes/No)				

Did the event recur after reintroducing (Yes/No)				

Please summarize course of reported events including signs and symptoms in chronological order:

_____
_____
_____
_____

Diagnostic tests (use additional pages if needed): Please indicate test unit where applicable.

Date	Test name	Pre-treatment value	AE onset value	AE resolution value	Normal low	Normal high
	Platelets					
	PT					
	aPTT					
	INR					
	ESR					
	LFTs					
	Factor VIII Factor IX					

Please provide causal relationship assessment between the suspect product(s) and adverse event(s):

_____
_____

Concomitant Medications (use additional pages if needed): Did the Patient take any concomitant medication? □ Yes (please complete below; Please provide relevant concomitant medications, including

thromboprophylaxis (type/dose/dates as well as corresponding lab monitoring values if applicable), and possible platelet transfusion need to prevent hemorrhagic event])

□ No □ Unknown

Medication name	Daily dose and regimen	Route of administration	Indication	Start date (DD/MM/YYYY)	Stop date (DD/MM/YYYY)

Other Etiological Factors: □ Yes (please complete below) □ None □ Unknown

□ Relevant medical and/or drug history (please specify), including start date or duration:

_____

_____

□ Family history (please specify):

□ Drug/alcohol/tobacco abuse:

□ Other (please specify):

Additional questions:

1. Please provide location of the bleeding / haemorrhage.

2. Relevant medical history:
   Does the patient have:
   a. History of anaemia?

      Was patient transfusion dependent? If yes, since when and how frequent?

b. Episodes of hypotension? Hypertension? Gingivorrhagia or epistaxis? Headaches? Pallor? Dyspnoea? Weakness? Please describe.

c. History of bleeding/hemorrhage? Coagulation disorder? Please describe.

3. Please provide date of diagnosis of underlying disease, stage at the time of diagnosis and stage of the patient's disease at the time of the event.

4. Please include bone marrow studies / x-ray / CT scan results for the event of thrombocytopenia / bleeding / haemorrhage.

5. What treatment were given for the thrombocytopenia / bleeding / haemorrhage? Please include dates / dose.

Health Practitioner Name (Print)

Health Practitioner Name (Signature)

Additional information regarding this Adverse Event Report:

Description of event: [narrative]

Annex 5 - Protocols for proposed and on-going studies in RMP part IV

Not applicable.

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

1. The MAH shall agree the details of a controlled access programme with the National Competent Authorities and must implement such programme nationally to ensure that:

- Prior to prescribing (where appropriate, and in agreement with the National Competent Authority, dispensing) all healthcare professionals who intend to prescribe (and dispense) pomalidomide are provided with an Educational Healthcare Professional's Kit containing the following:
    - o Educational Health Care Professional brochure
    - o Educational brochures for patients
    - o Patient cards
    - o Risk awareness form
    - o Information on where to find the latest Summary of Product Characteristics (SmPC).

2. The MAH shall implement a pregnancy prevention programme (PPP) in each Member State. Details of the PPP should be agreed with the National Competent Authorities in each Member State and put in place prior to the marketing of the product.

3. The MAH should agree the final text of the contents of the Educational Healthcare Professional's Kit with the National Competent Authority in each Member State prior to launch of the medicinal product and ensure that the materials contain the key elements as described below.

4. The MAH should agree on the implementation of the controlled access programme in each Member State.

Key elements to be included

The Educational Healthcare Professional's Kit

The Educational Health Care Professional's Kit shall contain the following elements:

Educational Healthcare Professional brochure

- Brief background on pomalidomide
- Maximum duration of treatment prescribed
    - o 4 weeks for women with childbearing potential
    - o 12 weeks for men and women without childbearing potential
- The need to avoid foetal exposure due to teratogenicity of pomalidomide in animals and the

expected teratogenic effect of pomalidomide in humans

• Guidance on handling the blister or capsule of Pomalidomide Krka for healthcare professionals and caregivers

• Obligations of the health care professional in relation to the prescribing of pomalidomide

o Need to provide comprehensive advice and counselling to patients

o That patients should be capable of complying with the requirements for the safe use of pomalidomide

o Need to provide patients with appropriate patient educational brochure, patient card and/or equivalent tool

• Safety advice relevant to all patients

o Description and management of thrombocytopenia including incidence rates from clinical studies

o Description and management of cardiac failure

o Local country specific arrangements for a prescription for pomalidomide to be dispensed

o That any unused capsules should be returned to the pharmacist at the end of the treatment

o That the patient should not donate blood during treatment (including during dose interruptions) and for at least 7 days following discontinuation of pomalidomide

• Description of the PPP and categorisation of patients based on sex and childbearing potential

o Algorithm for implementation of PPP

o Definition of women of childbearing potential (WCBP) and actions the prescriber should take if unsure

• Safety advice for women of childbearing potential

o The need to avoid foetal exposure

o Description of the PPP

o Need for effective contraception (even if woman has amenorrhoea) and definition of effective contraception

o That if she needs to change or stop using her method of contraception she should inform:

▪ The physician prescribing her contraception that she is on pomalidomide

▪ The physician prescribing pomalidomide that she has stopped or changed her method of contraception

o Pregnancy test regime

- Advice on suitable tests
- Before commencing treatment
- During treatment based on method of contraception
- After finishing treatment

o Need to stop pomalidomide immediately upon suspicion of pregnancy

o Need to tell treating doctor immediately upon suspicion of pregnancy

• Safety advice for men

o The need to avoid foetal exposure

o The need to use condoms if sexual partner is pregnant or a WCBP not using effective contraception (even if man has had a vasectomy)

- During pomalidomide treatment
- For at least seven days following final dose

o That he should not donate semen or sperm during treatment (including during dose interruptions) and for at least 7 days following discontinuation of pomalidomide treatment

o That if his partner becomes pregnant whilst he is taking pomalidomide or shortly after he has stopped taking pomalidomide he should inform his treating doctor immediately

• Requirements in the event of pregnancy

o Instructions to stop pomalidomide immediately upon suspicion of pregnancy if female patients

o Need to refer to physician specialised or experienced in dealing with teratology and its diagnosis for evaluation and advice

o Local contact details for reporting of any suspected pregnancy immediately

o Pregnancy reporting form

• Local contact details for reporting adverse reactions

Educational Brochures for patients

The Educational brochures for patients should be of 3 types:

- Brochure for women patients of childbearing potential and their partner
- Brochure for women patients who are not of childbearing potential
- Brochure for male patients

All educational brochures for patients should contain the following elements:

• That pomalidomide is teratogenic in animals and is expected to be teratogenic in humans

• That pomalidomide may cause thrombocytopenia and the need for regular blood tests

• Description of the patient card and its necessity

• Guidance on handling pomalidomide for patients, caregivers and family members

• National or other applicable specific arrangements for a prescription for pomalidomide to be dispensed

• That the patient must not give pomalidomide to any other person

• That the patient should not donate blood during treatment (including during dose interruptions) and for at least 7 days after discontinuation of pomalidomide treatment

• That the patient should tell their doctor about any adverse events

• That any unused capsules should be returned to the pharmacist at the end of the treatment

The following information should also be provided in the appropriate brochure:

Brochure for women patients with childbearing potential

• The need to avoid foetal exposure

- Description of the PPP
- Need for effective contraception and definition of effective contraception
- That if she needs to change or stop using her method of contraception she should inform:
    - o The physician prescribing her contraception that she is on pomalidomide
    - o The physician prescribing pomalidomide that she has stopped or changed her method of contraception
- Pregnancy test regime
    - o Before commencing treatment
    - o During treatment (including dose interruptions), at least every 4 weeks except in case of confirmed tubal sterilisation
    - o After finishing treatment
- The need to stop pomalidomide immediately upon suspicion of pregnancy
- The need to contact their doctor immediately upon suspicion of pregnancy

Brochure for male patients

- The need to avoid fetal exposure
- The need to use condoms if sexual partner is pregnant or a WCBP and not using effective contraception (even if man has had vasectomy)
    - o During pomalidomide treatment (including dose interruptions)
    - o For 7 days following final dose
- That if his partner becomes pregnant he should inform his treating doctor immediately
- That he should not donate semen or sperm during treatment (including during dose interruptions) and for at least 7 days after discontinuation of pomalidomide treatment

Patient Card **or equivalent tool**

The patient card shall contain the following elements:

- Verification that appropriate counselling has taken place
- Documentation of childbearing potential status
- Check box (or similar) which physician ticks to confirm that patient is using effective contraception (if woman of childbearing potential)
- Pregnancy test dates and results

Risk Awareness Forms

There should be 3 types of risk awareness forms:

- Women of childbearing potential
- Women of non-childbearing potential
- Male patient

All risk awareness forms should contain the following elements:

- teratogenicity warning-patients receive the appropriate counselling prior to treatment initiation
- affirmation of patient understanding regarding the risk of pomalidomide and the PPP measures
- date of counselling

- patient details, signature and date
- prescriber name, signature and date
- aim of this document i.e. as stated in the PPP: "The aim of the risk awareness form is to protect patients and any possible foetuses by ensuring that patients are fully informed of and understand the risk of teratogenicity and other adverse reactions associated with the use of pomalidomide. It is not a contract and does not absolve anybody from his/her responsibilities with regard to the safe use of the product and prevention of foetal exposure."

Risk awareness forms for women of childbearing potential should also include:

- Confirmation that the physician has discussed the following:
  - the need to avoid foetal exposure
  - that if she is pregnant or plans to be, she must not take pomalidomide
  - that she understands the need to avoid pomalidomide during pregnancy and to apply effective contraceptive measures without interruption, at least 4weeks before starting treatment, throughout the entire duration of treatment, and at least 4weeks after the end of treatment
  - that if she needs to change or stop using her method of contraception she should inform:
    - the physician prescribing her contraception that she is taking pomalidomide
    - the physician prescribing pomalidomide that she has stopped or changed her method of contraception
  - of the need for pregnancy tests i.e. before treatment, at least every 4 weeks during treatment and after treatment
  - of the need to stop pomalidomide immediately upon suspicion of pregnancy
  - of the need to contact their doctor immediately upon suspicion of pregnancy
  - that she should not share the medicinal product with any other person
  - that she should not donate blood during treatment (including during dose interruptions) and for at least 7 days following discontinuation of pomalidomide
  - that she should return the unused capsules to the pharmacist at the end of treatment

Risk awareness forms for women with no childbearing potential should also include:

- Confirmation that the physician has discussed the following:
  - that she should not share the medicinal product with any other person
  - that she should not donate blood during treatment (including during dose interruptions) and for at least 7 days following discontinuation of pomalidomide
  - that she should return the unused capsules to the pharmacist at the end of treatment

Risk awareness forms for male patients should also include:

- Confirmation that the physician has discussed the following:
  - the need to avoid foetal exposure
  - that pomalidomide is found in semen and the need to use condoms if sexual partner is pregnant or is a WCBP not on effective contraception (even if the man has had a vasectomy)
  - that if his partner becomes pregnant, he should inform his treating doctor immediately and always use a condom
  - that he should not share the medicinal product with any other person

- that he should not donate blood or semen during treatment (including during dose interruptions) and for at least 7 days following discontinuation of pomalidomide
- that he should return the unused capsules to the pharmacist at the end of treatment

Annex 7 - Other supporting data (including referenced material)

Not applicable.

Annex 8 – Summary of changes to the risk management plan over time

Not applicable.