i-SECURE

Imnovid® (Pomalidomide)

PREGNANCY PREVENTION PROGRAM

HEALTHCARE PROFESSIONAL BROCHURE FOR IMMUNOMODULATORY AGENTS

Table of Contents

1. RISKS OF IMMUNOMODULATORY AGENTS

The following section contains advice to Healthcare Professionals about how to minimize the main risks associated with the use of **Pomalidomide**.

Thrombocytopenia

With **Pomalidomide**, thrombocytopenia is one of the major dose-limiting toxicities of treatment. It is therefore encouraged to monitor complete blood counts, including platelet count, weekly for the first 8 weeks and monthly thereafter. Patients may require use of blood product support and /or growth factors.

Thrombocytopenia can be managed with dose modifications and/or interruptions.

Recommended dose modifications during treatment and restart of treatment with **Pomalidomide** are outlined in the local product label and listed in the below tables.

Pomalidomide dose modification instructions

Toxicity	Dose modification
Neutropenia ANC < 0.5 x 10^9/1or febrile neutropenia (fever ≥ 38.5°C and ANC < 1 x 10^9/1)	Interrupt pomalidomide treatment for remainder of cycle. Follow CBC weekly.
ANC return to ≥ 1 x 10^9/1	Resume pomalidomide treatment at one dose level lower than previous dose.
For each subsequent drop < 0.5 x 10^9/1	Interrupt pomalidomide treatment.
ANC return to ≥ 1 x 10^9/1	Resume pomalidomide treatment at one dose level lower than the previous dose.
Thrombocytopenia Platelet count < 25 x 10^9/1	Interrupt pomalidomide treatment for remainder of cycle. Follow CBC weekly.
Platelet count return ≥ 50 x 10^9/1	Resume pomalidomide treatment at one dose level lower than previous dose.
For each subsequent drop < 25 x 10^9/1	Interrupt pomalidomide treatment.
Platelet count return ≥ 50 x 10^9/1	Resume pomalidomide treatment at one dose level lower than the previous dose.
Rash Rash = Grade 2-3	Consider dose interruption or discontinuation of pomalidomide treatment.
Rash = Grade 4 or blistering (including angioedema, anaphylactic reaction, exfoliative or bullous rash or if Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is suspected)	Permanently discontinue treatment
Other Other ≥ Grade 3 pomalidomide-related adverse events	Interrupt pomalidomide treatment for remainder of cycle. Resume at one dose level lower than previous dose at next cycle (adverse event must be resolved or improved to ≤ Grade 2 before restarting dosing

Dose modification instructions in this table are applicable to pomalidomide in combination with bortezomib and dexamethasone and to pomalidomide in combination with dexamethasone.

In case of neutropenia, the physician should consider the use of growth factors.

ANC – Absolute Neutrophil Count;
CBC – Complete Blood Count

Pomalidomide dose reduction

Dose level	Oral pomalidomide dose
Starting dose	4 mg
Dose level -1	3 mg
Dose level -2	2 mg
Dose level -3	1 mg

Dose reduction in this table is applicable to pomalidomide in combination with bortezomib and dexamethasone and to pomalidomide in combination with dexamethasone.

Cardiac Failure

With **Pomalidomide**, the risk of cardiac failure may occur during the treatment. Please refer to the **Pomalidomide** local product information for further information about adverse reactions and recommended precautions.

Off-label use

For the currently approved indication for **Pomalidomide**,please refer to the local approved label.

2. THE PREGNANCY PREVENTION PROGRAM AT A GLANCE

This brochure contains safety information for prescribing and dispensing the immunomodulatory agents, pomalidomide, with regard to the Pregnancy Prevention Program (PPP), to ensure safe use and handling of the product. This brochure addresses the teratogenic risk and pregnancy prevention requirements, as well as adverse reactions for immunomodulatory agents. Please refer to the ***local label*** for the full safety and prescribing information, available on request from:
Email: medinfo@biologixpharma.com

Healthcare professionals must:

1) Communicate the benefits and risks of treatment with immunomodulatory agents to their patients.
2) Provide pregnancy prevention counseling per patient risk categorization at treatment initiation.
3) Perform a pregnancy test (if applicable) prior to each prescription every 4 weeks.
4) Prescribe a maximum treatment duration of 4 weeks for women of childbearing potential, according to the approved indications dosing regimens, for all other patients, the prescription can be for a maximum duration of 12 weeks.
5) Issue patient educational materials to patients, as described below.
6) Remind patients of the safe use of immunomodulatory agents at each consultation and each time a prescription is dispensed.

3. PREGNANCY PREVENTION PROGRAM (i-SECURE)

The PPP was developed to help healthcare professionals (HCPs) and patients understand the risks of immunomodulatory agents and pregnancy. These materials provide a comprehensive overview of how the PPP prevents birth defects and fetus exposure to pomalidomide.
1) Thalidomide is a powerful human teratogen and, if taken during pregnancy, can cause severe birth defects or death to a developing fetus. In the 1950s and 1960s, thalidomide was prescribed to pregnant women as a sedative and to relieve morning sickness. Consequently, approximately 12,000 children were born with severe birth defects caused by thalidomide. Lenalidomide and pomalidomide are structurally related to thalidomide. Pomalidomide was found to be teratogenic in both rats and rabbits whenadministered during the period of major organogenesis. If Pomalidomide is given during pregnancy, a teratogenic effect in humans cannot be ruled out.
2) Immunomodulatory agents are contraindicated in pregnancy and in female patients of childbearing potential unless all of the conditions of the PPP, as described in this brochure, are met.

3) Immunomodulatory agents can pass into seminal fluid. Male patients must also follow the necessary requirements of the PPP to prevent exposure to a female partner.
4) It is a requirement of the PPP that all HCPs ensure that they have read and understood this brochure before prescribing or dispensing immunomodulatory agents to their patients.
5) At treatment initiation, all male patients and all female patients of childbearing potential should undergo counseling about the need to avoid pregnancy. A Risk Awareness Form for Counseling Patients Receiving Immunomodulatory Agents is appended to this document to guide HCPs through the fulfillment of the PPP requirements. Please use the Patient Agreement Form for Immunomodulatory Agents to document patient understanding.
6) Healthcare professionals are advised to refer to the Risk Awareness Form for Counseling Patients Receiving Immunomodulatory Agents for more information about ensuring that patients receiving treatment with immunomodulatory agents are aware of the requirements of the PPP and the steps required for compliance.
7) Patients should be capable of complying with the requirements for safe use of immunomodulatory agents.
Prior to treatment initiation, the HCPs must fill in the Risk Awareness Form for Immunomodulatory Agents, and must provide the patients with the patient educational materials (Patient Agreement Form and Patient Card for Immunomodulatory Agent)
8) The description of the PPP and the categorization of patients based on gender and childbearing potential is described in the algorithm (attached).

For more information about prescribing and dispensing immunomodulatory agents, including the recommended dosing schedule and duration, consult the ***local label***.

3.1 Guidance for All Patients

Patients must be informed not to donate blood during treatment and for at least 7 days after cessation of treatment with immunomodulatory agents. Any unused medication at the end of treatment must be disposed of as per local regulations.

Patients must understand that their treatment is only for them and it:
1) Must not be shared with anyone else, even if they have similar symptoms.
2) Must be stored away safely so that no-one else can take the medicine by accident.
3) Must be kept out of reach of children.

Patients must also understand that they should not open, crush, or overly handle the capsules. For more information on safe handling of immunomodulatory agents, please refer to the Product Handling Instructions for Immunomodulatory Agents.

3.2 Determining Childbearing Potential

Prior to treatment, female patients of childbearing potential must be informed about the risks and precautions associated with immunomodulatory agents, including potential risk of birth defects and the need for pregnancy prevention during and following discontinuation of treatment. Please refer to the Risk Awareness Form for Counseling Patients Receiving Immunomodulatory Agents for additional guidance.

To determine if a female patient is not of childbearing potential, please refer to the below guidelines and refer the patient for a gynecological opinion if you are uncertain.

1. Females ≥50 years old and naturally amenorrhoeic for ≥ 1 year
   - Amenorrhoea following cancer therapy does not rule out childbearing potential
2. Females that have premature ovarian failure confirmed by a gynecologist
3. Females with bilateral salpingo-oophorectomy or hysterectomy
4. Females with XY genotype, Turner's syndrome or uterine agenesis

A female patient must never take immunomodulatory agents if she is pregnant.

3.3 PPP Guidance for Female Patients of Childbearing Potential

Female patients of childbearing potential are required to have a negative pregnancy test and at least 4 weeks of effective contraceptive use or commit to absolute and continuous abstinence from heterosexual intercourse prior to beginning treatment.

A female patient must never take immunomodulatory agents if they are able to become pregnant, even if not planning to become pregnant, unless all of the conditions of the PPP are met.

In view of the teratogenic risk associated with immunomodulatory agents, fetal exposure should be avoided.

Female patients of childbearing potential (even if they have amenorrhea or irregular menstrual periods) must:

1) use at least one effective method of contraception for at least 4 weeks before, during, and until at least 4 weeks after cessation of treatment with immunomodulatory agents, and even in case of dose interruption or

2) commit to absolute and continuous abstinence from heterosexual intercourse during the entire period of risk associated with immunomodulatory agents. The reliability of sexual abstinence needs to be evaluated by the HCP in relation to the duration of use of treatment with immunomodulatory agents and the preferred and usual lifestyle of the patient and be confirmed on a monthly basis. The HCP should document this each month in the patient's medical records.

AND

3) have a medically supervised negative pregnancy test (with a minimum sensitivity of [25] mIU/mL) once contraception has been established for at least 4 weeks prior to treatment initiation, at least every 4 weeks during treatment (this includes dose interruptions) and at least 4 weeks after the end of treatment (unless confirmed tubal sterilization). This includes female patients of childbearing potential who confirm absolute and continuous abstinence from heterosexual intercourse during the entire period of risk associated with immunomodulatory agents.

4) Patients should be advised to inform the HCP prescribing her contraception about the immunomodulatory agent.
5) Patients should be advised to inform the HCP prescribing her immunomodulatory agent if a change or cessation in method of contraception is needed.

A patient not established on effective contraception must be referred to an appropriately trained HCP for contraceptive advice in order that contraception can be initiated.

The following methods are examples of effective contraception:
implant, levonorgestrel-releasing intrauterine system, medroxyprogesterone acetate depot, tubal sterilization, sexual intercourse with a vasectomized male partner only (vasectomy must be confirmed by two negative semen analyses), and ovulation inhibitory progesterone-only pills (ie, desogestrel),
Because of the increased risk of venous thromboembolism in patients with multiple myeloma, combined oral contraceptive pills are not recommended. If a patient is currently using combined oral contraception, the patient should switch to one of the effective methods listed above. The risk of venous thromboembolism continues for 4 to 6 weeks after discontinuing combined oral contraception.

Patients should be advised to inform their HCP of a missed menstrual period, any unusual menstrual bleeding, or if she believes that she may be pregnant. If a pregnancy does occur while receiving treatment with immunomodulatory agents, treatment must be discontinued, and the HCP informed immediately. Refer the patient to an HCP specialized in teratology for evaluation and advice.

3.4 Requirements in the Event of a Suspected Pregnancy in Female Patient
1) If female patient, stop treatment immediately and inform the HCP immediately.
2) Refer female patient to an HCP specialized or experienced in teratology for evaluation and advice.
3) Notify SFDA or Biologix of all such occurrences: - The National Pharmacovigilance Centre (NPC), SFDA:
SFDA Call Center: 19999
E-mail: **npc.drug@sfda.gov.sa**
Website: https://ade.sfda.gov.sa

-LOCAL REPRESENTATIVE OF THE MARKETING AUTHORISATION HOLDER IN KSA:
Biologix FZCO, Hibatullah Al Ghaffari Street-Suliemaniah
Kingdom of Saudi Arabia P.O.Box 991, Riyadh 11421 Biologix Pharmacovigilance Department:
E-mail: **Pharmacovigilance-ksa@biologixpharma.com**
Tel + 966 11 4646 955 Ext 286
Mobile: +966559994037

BMS will wish to follow up with you regarding the progress of all suspected pregnancies in female patients

3.5 PPP Guidance for Male Patients

1) In view of the teratogenic risk associated with immunomodulatory agents, fetal exposure should be avoided.
2) Prior to treatment, male patients must be informed about the risks and precautions associated with immunomodulatory agents, including potential risk of birth defects and the need for pregnancy prevention during and following discontinuation of treatment. Please refer to the Risk Awareness Form for Counseling Patients Receiving Immunomodulatory Agents for additional guidance.
3) Pomalidomide have been detected in seminal fluid. Therefore, all male patients should use condoms throughout treatment duration, during dose interruptions, and for at least 7 days after cessation of treatment if his partner is pregnant or of childbearing potential and is not using effective contraception (even if the male patient has undergone vasectomy).
4) Inform patients which effective contraceptive methods his female partner can use.
5) Instruct patients that if his partner becomes pregnant while he is on treatment with immunomodulatory agents or within 7 days after medication has been discontinued, the HCP should be informed immediately. His partner should inform her HCP immediately. It is recommended that she be referred to an HCP specialized in teratology for evaluation and advice.
6) Notify BMS of all such occurrences and BMS will wish to follow up with you regarding the progress of all suspected pregnancies in female partners of male patients.
7) Male patients should not donate semen or sperm during treatment, including during dose interruptions and for at least 7 days following discontinuation of treatment as immunomodulatory agents can pass into seminal fluid.

4. REPORTING OF ADVERSE REACTIONS

The safe use of immunomodulatory agents is of paramount importance. As part of our ongoing safety monitoring, BMS wishes to be informed of adverse reactions that have occurred during the use of these medicines. Please report any adverse reactions to:

The National Pharmacovigilance Centre (NPC), SFDA:
SFDA Call Center: 19999
E-mail: **npc.drug@sfda.gov.sa**
Website: https://ade.sfda.gov.sa

or

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Biologix FZCO, Hibatullah Al Ghaffari Street-Suliemaniah Kingdom of Saudi Arabia P.O.Box 991, Riyadh 11421 Biologix Pharmacovigilance Department:
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5. CONTACT DETAILS

For information and questions on the risk management of BMS's products and the PPP, contact Biologix:
Email: **medinfo@biologixpharma.com**

5.1 Patient Risk Categorization, Pregnancy Test and Contraception Requirements Algorithm