Important Safety Information ZENBEXUS (IBERDOMIDE) GUIDE FOR RISK MINIMIZATION FOR HEALTHCARE PROFESSIONALS

This Guide for Risk Minimization for Healthcare Professionals is not a substitute for the prescribing information. Please consult the Saudi *label* for full safety and prescribing information.

This educational material is provided to remind HCPs and inform them on the required risk minimization measures to prevent embryo-fetal exposure to iberdomide.

It is advised to be read carefully before prescribing/dispensing/ administering the product

This document has been reviewed and approved by the Saudi Food and Drug Authority (SFDA)

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Bristol Myers Squibb®

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1 INTRODUCTION

The goal of the Guide for Risk Minimization for Healthcare Professionals is to help mitigate the risk of embryo-fetal toxicity associated with iberdomide by ensuring that healthcare professionals (HCPs) are aware of the risk of embryo-fetal toxicity associated with iberdomide and the need to ensure that the safe-use conditions are met to prevent potential fetal exposure during pregnancy.

A full list of all side effects, further information, and recommended precautions can be found in the Saudi label.

2 EDUCATIONAL MATERIALS

The educational materials include the following:

- Guide for Risk Minimization for Healthcare Professionals
  - Contains information for HCPs, providing an overview of the pregnancy prevention safety requirements.
- Risk Awareness Dialogue Form
  - Contains information for HCPs to counsel patients who can become pregnant and to confirm that the patient has been fully informed of the risk of embryo-fetal toxicity associated with iberdomide and the intended actions for risk minimization.
- Guide for Risk Minimization for Patients
  - This guide should be given to all patients who can become pregnant. It reinforces the safety messages about the risk of embryo-fetal toxicity associated with iberdomide and the intended actions for risk minimization.
- Patient Card
  - This card should be given to all patients who can become pregnant to remind them of the key safety information and intended actions necessary for effective risk minimization.

3 RISK OF EMBRYO-FETAL TOXICITY (EFT)

Based on data from non-clinical studies, iberdomide causes embryo-fetal toxicity in animals and therefore has the potential to cause embryo-fetal harm in humans.

During iberdomide clinical trials, no pregnancy cases due to iberdomide were reported and there's no data on the use of iberdomide in pregnant patients.

Iberdomide is therefore contraindicated in pregnancy and requires safety measures for patients who can become pregnant (at-risk population). This contraindication is independent of product formulation and route of administration.

Moreover, It is not known whether iberdomide is excreted in breast milk. Therefore, breast-feeding should be discontinued during therapy with iberdomide.

4 OVERVIEW OF RISK MINIMIZATION REQUIREMENTS

To prevent any potential embryo-fetal exposure during pregnancy, safety requirements have been established for iberdomide. These measures are designed to educate HCPs and patients about the risk of embryo-fetal toxicity and the intended actions for risk minimization. Before prescribing iberdomide, HCPs must have access to the:

- Guide for Risk Minimization for HCPs
- Risk Awareness Dialogue Form
- Guide for Risk Minimization for Patients
- Patient Card

The following are the key safety requirements:

1. Iberdomide is contraindicated in pregnancy and in patients who can become pregnant unless all of the conditions of pregnancy prevention, as described in this guide, are met.
2. All HCPs must ensure that they have read and understood this guide before prescribing or dispensing iberdomide.
3. At treatment initiation, all patients who can become pregnant must undergo counseling about the need to avoid fetal exposure during pregnancy.
4. HCPs should refer to the Risk Awareness Dialogue Form for counseling patients who can become pregnant to ensure awareness of the intended actions for risk minimization and the pregnancy prevention safety requirements.
5. Patients should be capable of complying with the requirements for the safe use of iberdomide.

6. Before treatment initiation, patients who can become pregnant must receive the Guide for Risk Minimization for Patients and the Patient Card. These educational materials will provide the relevant information to patients who can become pregnant receiving treatment with iberdomide.
7. The categorization of patients who can or cannot become pregnant are described in the algorithm (see Section 8).
8. Prescriptions for patients who can become pregnant can be for a maximum duration of 4 weeks at a time according to the approved indication's dosing regimens. *Dispensing of iberdomide should occur within a maximum of 7 days of the prescription, and the date of the last negative pregnancy test must be within 3 days prior to the date of the prescription.*

For more information about prescribing and dispensing iberdomide, including the recommended dosing schedule and duration, consult the Saudi label.

4.1 Patients Who Can Become Pregnant

Before treatment, patients who can become pregnant must be counseled about the risks and the intended actions for risk minimization. This includes the need to prevent embryo-fetal exposure before treatment initiation, throughout treatment (including any dose interruptions), and after treatment discontinuation. For additional guidance, please refer to the Risk Awareness Dialogue Form for counseling patients who can become pregnant receiving iberdomide.

To determine if a patient can become pregnant, please refer to the guidelines below and refer the patient for a gynecological opinion if you are uncertain.

Patients who can become pregnant are patients who have achieved menarche and do not fulfill any of the below criteria:

- Assigned male at birth.
- Age ≥ 50 years and naturally amenorrheic for ≥ 1 year (amenorrhea following cancer therapy or during breastfeeding does not rule out being able to become pregnant).
- Previous hysterectomy, bilateral salpingectomy, or bilateral oophorectomy.

4.2 Requirements for Patients Who Can Become Pregnant

Due to the risk of embryo-fetal toxicity associated with iberdomide, patients who can become pregnant (including those with amenorrhea or irregular menstrual cycles) must not take iberdomide, even if pregnancy is not planned, unless all pregnancy prevention safety requirements listed below are met.

Patients who can become pregnant (even if they have amenorrhea or irregular menstrual cycles) must:

1. never take iberdomide if they are pregnant.
2. use effective contraception (refer to Section 5) for at least 4 weeks before, during, and until at least 4 weeks after treatment discontinuation, and even in case of dose interruption, **OR**
3. commit to absolute and continuous abstinence from heterosexual intercourse during the entire period of treatment, including dose interruptions and until at least 4 weeks after treatment discontinuation. This requirement needs to be confirmed by the HCP every 4 weeks before each prescription and should be documented in the patient's medical records.
4. have at least one medically supervised negative pregnancy test (with a minimum sensitivity of 25 mIU/mL) before treatment initiation.
   - if you have regular or no menstrual cycles, pregnancy tests must be performed weekly for the first 4 weeks and then every 4 weeks while taking iberdomide and for at least 4 weeks following the last dose of iberdomide.
   - if you have irregular menstrual cycles, pregnancy tests must be performed weekly for the first 4 weeks and then every 2 weeks while taking iberdomide and every 2 weeks for at least 4 weeks following the last dose of iberdomide.
   - this requirement also applies to patients who confirm absolute and continuous abstinence from heterosexual intercourse during the **entire period of treatment with iberdomide.**
5. be advised to inform the HCP prescribing their contraception about their treatment with iberdomide.
6. be advised to inform the HCP prescribing iberdomide if a change in their method of contraception is needed.

Patients should be capable of complying with the requirements for safe use of iberdomide. If a pregnancy does occur while receiving treatment with iberdomide, treatment must be discontinued immediately, and the HCP informed immediately. Refer the patient to an HCP specialized or experienced in teratology for evaluation and advice.

5 CONTRACEPTION OPTIONS FOR PATIENTS WHO CAN BECOME PREGNANT

Prescribers must ensure that the patient is established on effective contraception and has received contraceptive advice and counseling about medical options in the event of unprotected heterosexual intercourse or known or suspected contraceptive failure from an appropriately trained HCP.

Patients who can become pregnant must use at least one effective method of contraception. The following are examples of effective methods of contraception. listed as below:

- **For Women:**
  1. Implant
  2. Levonorgestrel-releasing intrauterine system (IUS)
  3. Medroxyprogesterone acetate depot
  4. Tubal sterilization
  5. Sexual intercourse with a vasectomized male partner only; vasectomy must be confirmed by two negative semen analyses
  6. Ovulation inhibitory progesterone-only pills (i.e. desogestrel)

- **For Men:**

  Iberdomide passes into human semen.

If your partner is pregnant or able to become pregnant and is not using birth control, you must use condoms for the entire duration of treatment and for at least 3 days after the end of treatment.

If the patient who can become pregnant is not established on effective contraception prior to treatment initiation, the patient must be referred to an appropriately trained healthcare professional for contraception advice to ensure appropriate contraception can be initiated.

6 REQUIREMENTS IN THE EVENT OF A SUSPECTED PREGNANCY

1. Inform the patient to stop treatment with iberdomide immediately in the event of a suspected pregnancy and inform the prescribing physician immediately.
2. Refer the patient to an HCP specialized or experienced in teratology for evaluation.
3. Notify Bristol-Myers Squibb Company (BMS) of all such occurrences immediately upon awareness of the suspected pregnancy.

Bristol Myers Squibb, Saudi Arabia :
At via email: medinfo.SaudiArabia@bms.com
or call: 800 844 7710

4. BMS will follow up with you regarding the progress of all suspected pregnancies in patients.
5. To Report Saudi Food and Drug Authority (SFDA):
   The National Pharmacovigilance Centre (NPC)
   Saudi Food and Drug Authority (SFDA):
   SFDA call center: 19999
   E-mail: npc.drug@sfda.gov.sa
   Website: https://ade.sfda.gov.sa

7 REPORTING ADVERSE EVENTS AND PREGNANCIES

As part of our ongoing safety monitoring, BMS wishes to be informed of adverse reactions that have occurred while using these medicines. Please report any pregnancies or adverse reactions to: Bristol Myers Squibb, Saudi Arabia :
At via email: medinfo.SaudiArabia@bms.com
or call: 800 844 7710

8 PATIENT RISK CATEGORIZATION, PREGNANCY TEST, AND CONTRACEPTION REQUIREMENTS ALGORITHM

Evaluate each patient at each prescription/dispense

Patient who cannot become pregnant

At least one criterion must be fulfilled:

The following patients are considered not able to become pregnant:

- Age ≥ 50 years and naturally amenorrheic for ≥ 1 year.*
- Previous bilateral salpingo-oophorectomy, or hysterectomy.
- Assigned male at birth.

Please note: Patients who have achieved menarche and do not fulfill any of the above criteria are considered patients who can become pregnant.

Start iberdomide. Contraception and pregnancy testing are not required.†

*Amenorrhea following cancer therapy or during breastfeeding does not rule out being able to become pregnant.

†For patients assigned male at birth, contraception use remains a recommendation.

Patient who can become pregnant

If not already using effective contraception, start effective contraception at least 4 weeks prior to initiation of treatment, unless practicing absolute and continuous abstinence from heterosexual intercourse.

<The following are examples of suitable methods of contraception:

Implant, Levonorgestrel-releasing intrauterine system (IUS), Medroxyprogesterone acetate depot, Tubal sterilization, Sexual intercourse with a vasectomized male partner only; vasectomy must be confirmed by 2 negative semen analyses, Ovulation inhibitory progesterone-only pills (ie, desogestrel).

Contraception continues during treatment, including dose interruptions, and for at least 4 weeks after treatment discontinuation.>

Test for pregnancy after at least 4 weeks of effective contraception (even if sexually abstinent). Test for pregnancy before initiating therapy.

Negative

Start iberdomide. Test for pregnancy (refer to Section 4).

Positive

DO NOT START TREATMENT.

For reporting any suspected adverse reactions via the national reporting system :
Bristol Myers Squibb, Saudi Arabia :
At: medinfo.SaudiArabia@bms.com
or call: 800 844 7710

The National Pharmacovigilance Centre (NPC)
Saudi Food and Drug Authority (SFDA):
SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa

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