ZENBEXUS™ REMS

(Risk Evaluation and Mitigation Strategy)

Prescriber and Pharmacy Guide

Bristol Myers Squibb®

Table of Contents

Indication

ZENBEXUS™ (iberdomide) is indicated, in combination with daratumumab and hyaluronidase-fihj and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least 1 prior line of therapy including a proteasome inhibitor and an immunomodulatory agent.

ZENBEXUS is a cereblon-modulating protein degrader.

Risk of Embryo-Fetal Toxicity

ZENBEXUS is embryo-fetal toxic in animals and can cause birth defects or embryo-fetal death in humans. Advise all patients of the risk of embryo-fetal toxicity. Advise females who can become pregnant to use effective contraception. Advise males that ZENBEXUS may pass into human semen, to use a latex or synthetic condom, and for males to not donate sperm.

Using the **Patient Guide**, counsel

All Patients on:

- Following safe-use conditions
- Not sharing ZENBEXUS
- Not donating blood during treatment and for 4 weeks after treatment last dose
- Returning any unused ZENBEXUS to a drug take back location

Females who can become pregnant on:

- The risk of embryo-fetal toxicity
- Using effective methods of contraception for 4 weeks prior to treatment initiation, during treatment, and for 4 weeks following discontinuation of treatment
- Completing pregnancy tests every 2 or 4 weeks
- Completing a **Patient Survey** every 4 weeks
- Contacting you if the patient misses a menstrual period or if pregnancy is suspected
- Not donating eggs during treatment and 4 weeks after treatment

Males on:

- The risk of embryo-fetal toxicity
- Using a latex or synthetic condom
- The risks of donating sperm while on treatment
- Completing a **Patient Survey** every 4 weeks

Females who cannot become pregnant on:

- The risk of embryo-fetal toxicity after a change in reproductive status
- Contacting the prescriber right away if there is a change to their reproductive status

REMS Overview

ZENBEXUS™ REMS Goal and Objectives

Due to the risk of embryo-fetal toxicity, ZENBEXUS is available only through a restricted distribution program called ZENBEXUS REMS. The goal of ZENBEXUS REMS is to mitigate the risk of embryo-fetal toxicity associated with the use of ZENBEXUS by meeting the following objectives:

1. Patients' reproductive status is assessed to determine who can get pregnant.
2. Females who can become pregnant and males agree to use contraception or abstinence during treatment with ZENBEXUS.
3. Before treatment initiation, females who can become pregnant have two negative pregnancy tests.
4. During treatment, females who can become pregnant have a pregnancy test prior to each dispense.

Patient Risk Categories

Patients treated with ZENBEXUS™ (iberdomide) fall into 3 risk categories based on their reproductive potential status.

Females Who Can Become Pregnant

- Biologically female sex with a uterus and at least one ovary, who is at least Tanner Stage 3, or entered puberty and has not completed menopause*

Males

- Biologically male sex

Females Who Cannot Become Pregnant

- Biologically female sex who has undergone a hysterectomy or a bilateral oophorectomy, not gone through menarche, or reached Tanner Stage 3, or completed menopause

***Menopause:** Defined as 12 months of spontaneous amenorrhea or 6 months of spontaneous amenorrhea with serum FSH levels > 40 mIU/ml or 6 weeks postsurgical bilateral oophorectomy with or without hysterectomy.

Contraceptive Guidance for Females Who Can Become Pregnant

Females who can become pregnant need to use effective methods of contraception every time they have sex, at least 4 weeks prior to treatment initiation, while taking ZENBEXUS, and for at least 4 weeks after discontinuation of ZENBEXUS.

Refer to the chart on page 5 for effective methods of contraception.

Contraceptive Guidance for Males

Males need to use a latex or synthetic condom every time they have sex, while taking ZENBEXUS, and for at least 4 weeks after discontinuation of ZENBEXUS even if they had a successful vasectomy.

Effective Methods of Contraception Used at the Same Time

Unless patients completely abstain from sexual intercourse, they are required to use at least 1 highly effective birth control method **and** at least 1 additional effective birth control method at the same time.

Highly effective birth control methods		Additional effective birth control methods
• Intrauterine device (IUD) • Hormonal methods (birth control pills, hormonal patches, injections, vaginal rings, or implants) • Tubal ligation (having your tubes tied) • Partner's vasectomy (tying of the tubes to prevent the passing of sperm)	+	• Male latex or synthetic condom • Diaphragm • Cervical cap

Remind patients that not having sexual intercourse is the only method of birth control that is 100% effective.

Roles of Prescribers

Prescriber Certification

To prescribe ZENBEXUS™ (iberdomide), healthcare professionals must become certified in ZENBEXUS™ REMS by completing the following steps:

- Review the **Prescribing Information** and this **Prescriber and Pharmacy Guide**
- Complete and submit the **Prescriber Enrollment Form** online at www.BMSREMSPatientSafety.com, email to REMSContactCenter@bms.com, or fax to 1-877-296-1932

Patient Enrollment and Counseling

For Females Who Can Become Pregnant

Before treatment:

- Assess the patient's reproductive status referring to the patient risk categories on page 4 in this **Prescriber and Pharmacy Guide.** Document and submit using the **Patient Enrollment Form**
- Counsel patients using the **Patient Guide** on:
  - The risk of embryo-fetal toxicity
  - Using effective methods of contraception at least 4 weeks prior to treatment initiation, during treatment, and for at least 4 weeks following discontinuation of treatment
  - Completing pregnancy tests every 4 weeks
  - Completing a **Patient Survey** every 4 weeks
  - Contacting their prescriber right away if the patient misses a menstrual period or if pregnancy is suspected
  - Not donating blood or eggs during treatment and for 4 weeks after treatment last dose
  - Not sharing ZENBEXUS
  - Returning unused ZENBEXUS to a drug take back program
- Assess the patient's pregnancy status by reviewing 2 pregnancy test results completed in a medical setting (e.g., prescriber's office, clinic, or laboratory)
  - Conduct the first pregnancy test 10 to 14 days before treatment initiation and then conduct a second pregnancy test within 24 hours before treatment initiation
  - Document using the **Patient Enrollment Form**
- Enroll the patient by completing a **Patient Enrollment Form** and submitting to ZENBEXUS REMS
- Provide a copy of the **Patient Guide** to the patient
- Enroll the patient by completing and submitting the **Patient Enrollment Form**
- If patient does not receive ZENBEXUS within 7 days of their pregnancy test and have not started ZENBEXUS, repeat a confirmatory pregnancy test. Document and submit result to the REMS

Roles of Prescribers (cont'd)

For Females Who Can Become Pregnant (cont'd)

During treatment, every 4 weeks:

- Counsel patients on:
  - The risk of embryo-fetal toxicity
  - Pregnancy prevention requirements
  - Performing required pregnancy testing every 4 weeks
  - Completing a **Patient Survey** every 4 weeks
  - Contacting their prescriber right away if they miss a menstrual period or if pregnancy is suspected
  - Not donating blood during treatment and for 4 weeks after treatment last dose
  - Not sharing ZENBEXUS™ (iberdomide)
  - Returning unused ZENBEXUS to a drug take back program
- **For females who can become pregnant with regular menstrual cycles:** Every 4 weeks: Assess the patient's pregnancy status reviewing a pregnancy test and confirming a negative result. Document and submit the result to the REMS
- **For females who can become pregnant with irregular menstrual cycles:** Every 2 weeks: Assess the patient's pregnancy status by reviewing a pregnancy test and confirming a negative result
- Complete **Prescriber Survey** to verify patient's reproductive status, pregnancy prevention methods, negative pregnancy test result, and completion of counseling. Obtain authorization for each prescription
- Prescribe no more than a 28-day supply (21 days of treatment followed by a 7-day treatment-free period), with no refills
- Send the prescription to a certified pharmacy

After treatment discontinuation, 4 weeks after the last dose:

- Assess the patient's pregnancy status by reviewing a pregnancy test and confirming a negative result

At all times:

- Report any pregnancies or suspected pregnancies of patients to ZENBEXUS™ REMS at 1-888-423-5436
- If you allow patients to complete pregnancy tests outside of a medical setting (for illness or emergency), obtain the pregnancy test results from the patient. Develop processes and procedures to minimize misinterpretation and falsification of pregnancy test results
- Within 10 business days of awareness, report a change or misclassification in a patient's reproductive potential status to ZENBEXUS REMS using the **Change in Reproductive Potential Status Form**
- For patients with a lapse of treatment of 12 months or longer who will restart treatment with ZENBEXUS: re-enroll the patient

Roles of Prescribers (cont'd)

For Males

Before treatment:

- Counsel patients using the **Patient Guide** on:
  - The risk of embryo-fetal toxicity and to remind the patient to use a latex or synthetic condom during treatment, and for 4 weeks following treatment last dose
  - Not donating sperm during treatment and for 4 weeks after treatment last dose
  - Completing a **Patient Survey** every 4 weeks
  - Contacting their prescriber right away if pregnancy is suspected in their sexual partner
  - Not donating blood during treatment and for 4 weeks after treatment last dose
  - Not sharing ZENBEXUS™ (iberdomide)
  - Returning unused ZENBEXUS to a drug take back program
- Provide a copy of the **Patient Guide** to the patient
- Enroll the patient by completing and submitting the **Patient Enrollment Form**

During treatment, every 4 weeks:

- Counsel patients on:
  - The risk of embryo-fetal toxicity and to remind the patient to use a latex or synthetic condom during treatment, and for 4 weeks following treatment last dose and not to donate sperm
  - Completing a **Patient Survey** every 4 weeks
  - Contacting their prescriber right away if pregnancy is suspected in their sexual partner
- Obtain authorization by contacting the REMS to complete the **Prescriber Survey** to verify the use of latex or synthetic condom, the patient has not donated sperm, and completion of counseling
- Prescribe no more than a 28-day supply (21 days of treatment followed by a 7-day treatment-free period), with no refills

At all times:

- Report any pregnancies of female partners of male patients immediately to ZENBEXUS™ REMS at 1-888-423-5436
- For patients with a lapse of treatment of 12 months or longer who will restart treatment with ZENBEXUS: re-enroll the patient

Roles of Prescribers (cont'd)

For Females Who Cannot Become Pregnant

Before treatment:

- Enroll patients in ZENBEXUS™ REMS by completing the **Patient Enrollment Form**
- Counsel patients using the **Patient Guide** on:
  - The risk of embryo-fetal toxicity and to report a change in reproductive status
  - Not sharing ZENBEXUS™ (iberdomide)
  - Not donating blood during treatment and for 4 weeks after treatment last dose
  - Returning unused ZENBEXUS to a drug take back program

During treatment, every 6 months:

- Counsel the patient on:
  - The risk of embryo-fetal toxicity
  - Not sharing ZENBEXUS
  - Not donating blood during treatment and for 4 weeks after treatment last dose
  - Returning unused ZENBEXUS to a drug take back program

At all times:

- Within 10 business days of awareness, report a change or misclassification in a patient's reproductive potential status to ZENBEXUS REMS using the **Change in Reproductive Potential Status Form**
- For patients with a lapse of treatment of 12 months or longer who will restart treatment with ZENBEXUS: re-enroll the patient

Report a Change in Reproductive Potential Status

Based on the patient risk categories shown on page 4, report a change in a female's reproductive potential status using the **Change in Reproductive Potential Status Form** within 10 business days of awareness.

This includes reproductive potential status changes such as a:

- **Female Who CAN Become Pregnant** to a **Female Who CANNOT Become Pregnant**
  - Reasons for change in status:
    - Menopause
    - Medical/surgical (specify)
    - Previous misclassification
    - Other (specify)
- **Female Who CANNOT Become Pregnant** to a **Female Who CAN Become Pregnant**
  - Reasons for change in status:
    - Reached Tanner Stage 3 or entered puberty
    - Previous misclassification
    - Other (specify)

Roles of Pharmacies

Pharmacy Certification

- Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS requirements on behalf of the pharmacy
- Have the Authorized Representative review the ZENBEXUS™ (iberdomide) **Prescribing Information** and this **Prescriber and Pharmacy Guide**
- Enroll in REMS by completing the **Pharmacy Enrollment Form** and submitting it to ZENBEXUS™ REMS
- Train all relevant pharmacy staff involved in counseling and dispensing ZENBEXUS using this **Prescriber and Pharmacy Guide**
- Establish processes and procedures:
  - **For females who can become pregnant and males:** To complete the **Pharmacy Counseling Checklist** and submit it to the REMS
  - **For females who can become pregnant:** Establish processes and procedures to dispense when there are 7 days or less remaining on the patient's existing prescription and to dispense no more than a 28-day supply
  - **For males:** Dispense no more than a 28-day supply

Pharmacy Counseling

Before dispensing ZENBEXUS:

For all patients

- Obtain confirmation to dispense each prescription by contacting the REMS to verify prescriber is certified; the patient is enrolled, not pregnant, and authorized to receive ZENBEXUS
- Document the confirmation number

For Females Who Can Become Pregnant

- Using the **Pharmacy Counseling Checklist**, counsel patients on:
  - The risk of embryo-fetal toxicity
  - Using effective methods of contraception every time they have sex, beginning at least 4 weeks before taking ZENBEXUS, while taking ZENBEXUS, and for at least 4 weeks after stopping ZENBEXUS
  - Completing monthly pregnancy tests
  - Completing a **Patient Survey** every 4 weeks
  - Contacting their prescriber right away and stop treatment if the patient misses a menstrual period or if pregnancy is suspected
  - Not donating blood or eggs during treatment and for 4 weeks after treatment last dose
  - Not sharing ZENBEXUS
  - Returning unused ZENBEXUS to a drug take back location
- Submit a completed **Pharmacy Counseling Checklist** to ZENBEXUS REMS

For Males

- Using the **Pharmacy Counseling Checklist**, counsel patients on:
  - The risk of embryo-fetal toxicity
  - Using a latex or synthetic condom
  - Not donating blood or sperm while on treatment and for 4 weeks after treatment last dose

Roles of Pharmacies (cont'd)

Before dispensing ZENBEXUS: (cont'd)

For Males (cont'd)

- Completing a **Patient Survey** every 4 weeks
- Following safe-use conditions
- Not sharing ZENBEXUS™ (iberdomide)
- Returning unused ZENBEXUS to a drug take back location

- Submit a completed **Pharmacy Counseling Checklist** to ZENBEXUS™ REMS

At all times:

For Females Who Can Become Pregnant

- Obtain confirmation to dispense through ZENBEXUS REMS
- Dispense within 7 days of the date of the last pregnancy test
- Dispense only if there are 7 days or less remaining on the patient's existing prescription
- Dispense no more than a 28-day supply (21 days of treatment followed by a 7-day treatment-free period) with no refills
- Ship medication the same day the confirmation number is obtained or have it picked up within 24 hours of obtaining the confirmation number
- Ensure shipment method (e.g., overnight, ground) avoids delays or interruption in therapy
- Report any suspected pregnancy to ZENBEXUS REMS at 1-888-423-5436

For Males

- Dispense no more than a 28-day supply (21 days of treatment followed by a 7-day treatment-free period) with no refills
- Ship medication within 24 hours of receiving the confirmation number or have it picked up within 24 hours of obtaining the confirmation number

For Females Who Cannot Become Pregnant And Males

- Obtain confirmation to dispense through ZENBEXUS REMS
- Ship medication within 24 hours of receiving the confirmation number or have it picked up within 24 hours of obtaining the confirmation number
- Ensure shipment method (e.g., overnight, ground) avoids delays or interruption in therapy

Additional requirements:

- Report any suspected pregnancy to ZENBEXUS REMS at 1-888-423-5436
- Only distribute, transfer, loan, or sell ZENBEXUS as authorized by ZENBEXUS REMS
- Notify Bristol Myers Squibb (BMS) immediately of any dispense changes or cancellations after a dispense has been confirmed with ZENBEXUS REMS
- Maintain records of dispensing information including the confirmation number and the date it was obtained
- Maintain records of completion of ZENBEXUS REMS training by relevant staff, and that all processes and procedures are being followed
- Comply with audits conducted by BMS or a third party acting on behalf of BMS to ensure that all processes and procedures are in place and being followed
- Have a new Authorized Representative enroll by completing and submitting a **Pharmacy Enrollment Form** if the Authorized Representative changes

Contact Us

Suspected pregnancies	1-888-423-5436 (REMS Call Center)
Suspected adverse events or product quality complaints associated with ZENBEXUS™ (iberdomide)	1-888-423-5436 (REMS Call Center) 1-800-FDA-1088 www.fda.gov/medwatch
For more information about ZENBEXUS™ REMS	www.ZENBEXUSREMS.com 1-888-423-5436 (REMS Call Center)

Bristol Myers Squibb®