

Initial Shared System REMS approval: 04/2019

Mifepristone Tablets, 200 mg

Progestin Antagonist

**RISK EVALUATION AND MITIGATION STRATEGY (REMS)
SINGLE SHARED SYSTEM FOR MIFEPRISTONE 200MG**

I. GOAL

The goal of the REMS for mifepristone is to mitigate the risk of serious complications associated with mifepristone by:

- a) Requiring healthcare providers who prescribe mifepristone to be certified in the Mifepristone REMS Program.
- b) Ensuring that mifepristone is only dispensed in certain healthcare settings by or under the supervision of a certified prescriber.
- c) Informing patients about the risk of serious complications associated with mifepristone.

II. REMS ELEMENTS

A. Elements to Assure Safe Use

1. Healthcare providers who prescribe mifepristone must be specially certified.
 - a. To become specially certified to prescribe mifepristone, healthcare providers must:
 - i. Review the Prescribing Information for mifepristone.
 - ii. Complete a *Prescriber Agreement Form*. By signing a *Prescriber Agreement Form*, prescribers agree that:
 - 1) They have the following qualifications:
 - a) Ability to assess the duration of pregnancy accurately
 - b) Ability to diagnose ectopic pregnancies
 - c) Ability to provide surgical intervention in cases of incomplete abortion or severe bleeding, or to have made plans to provide such care through others, and ability to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary.
 - 2) They will follow the guidelines for use of mifepristone (see b.i-v below).
 - b. As a condition of certification, healthcare providers must follow the guidelines for use of mifepristone described below:
 - i. Review the *Patient Agreement Form* with the patient and fully explain the risks of the mifepristone treatment regimen. Answer any questions the patient may have prior to receiving mifepristone.

- ii. Sign the *Patient Agreement Form* and obtain the Patient's signature on the *Form*
 - iii. Provide the patient with a copy of the *Patient Agreement Form* and Medication Guide.
 - iv. Place the signed *Patient Agreement Form* in the patient's medical record.
 - v. Record the serial number from each package of mifepristone in each patient's record.
 - vi. Report any deaths to the Mifepristone Sponsor that provided the mifepristone, identifying the patient by a non-identifiable reference and the serial number from each package of mifepristone.
- c. Mifepristone Sponsors must:
- i. Ensure that healthcare providers who prescribe their mifepristone are specially certified in accordance with the requirements described above and de-certify healthcare providers who do not maintain compliance with certification requirements
 - ii. Provide the Prescribing Information and their *Prescriber Agreement Form* to healthcare providers who inquire about how to become certified.

The following materials are part of the REMS and are appended:

- *Prescriber Agreement Form for Danco Laboratories, LLC*
 - *Prescriber Agreement Form for GenBioPro, Inc.*
 - *Patient Agreement Form*
2. Mifepristone must be dispensed to patients only in certain healthcare settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber.
 - a. Mifepristone Sponsors must:
 - i. Ensure that their mifepristone is available to be dispensed to patients only in clinics, medical offices and hospitals by or under the supervision of a certified prescriber.
 - ii. Ensure that their mifepristone is not distributed to or dispensed through retail pharmacies or other settings not described above.
 3. Mifepristone must be dispensed to patients with evidence or other documentation of safe use conditions.
 - a. The patient must sign a *Patient Agreement Form* indicating that she has:
 - i. Received, read and been provided a copy of the *Patient Agreement Form*.
 - ii. Received counseling from the prescriber regarding the risk of serious complications associated with mifepristone.

B. Implementation System

1. Mifepristone Sponsors must ensure that their mifepristone is only distributed to clinics, medical offices and hospitals by or under the supervision of a certified prescriber by:
 - a. Ensuring that distributors who distribute their mifepristone comply with the program requirements for distributors. The distributors must:

- i. Put processes and procedures in place to:
 - a. Complete the healthcare provider certification process upon receipt of a Prescriber Agreement Form.
 - b. Notify healthcare providers when they have been certified by the Mifepristone REMS Program.
 - c. Ship mifepristone only to clinics, medical offices, and hospitals identified by certified prescribers in their signed *Prescriber Agreement Form*.
 - d. Not ship mifepristone to prescribers who become de-certified from the Mifepristone REMS Program.
 - e. Provide the Prescribing Information and their Prescriber Agreement Form to healthcare providers who (1) attempt to order mifepristone and are not yet certified, or (2) inquire about how to become certified.
 - ii. Put processes and procedures in place to maintain a distribution system that is secure, confidential and follows all processes and procedures, including those for storage, handling, shipping, tracking package serial numbers, proof of delivery and controlled returns of mifepristone.
 - iii. Train all relevant staff on the Mifepristone REMS Program requirements.
 - iv. Comply with audits by Mifepristone Sponsors, FDA or a third party acting on behalf of Mifepristone Sponsors or FDA to ensure that all processes and procedures are in place and are being followed for the Mifepristone REMS Program. In addition, distributors must maintain appropriate documentation and make it available for audits.
 - b. Ensuring that distributors maintain secure and confidential distribution records of all shipments of mifepristone.
2. Mifepristone Sponsors must monitor their distribution data to ensure compliance with the REMS Program.
 3. Mifepristone Sponsors must audit their new distributors within 90 calendar days after the distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the Mifepristone REMS Program. Mifepristone Sponsors will take steps to address their distributor compliance if noncompliance is identified.
 4. Mifepristone Sponsors must take reasonable steps to improve implementation of and compliance with the requirements of the Mifepristone REMS Program based on monitoring and assessment of the Mifepristone REMS Program.
 5. Mifepristone Sponsors must report to FDA any death associated with mifepristone whether or not considered drug-related, as soon as possible but no later than 15 calendar days from the initial receipt of the information by the applicant. This requirement does not affect the applicants other reporting and follow-up requirements under FDA regulations.

C. Timetable for Submission of Assessments

The NDA Sponsor must submit REMS assessments to FDA one year from the date of the initial approval of the REMS (04/11/2019) and every three years thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. The NDA Sponsor must submit each assessment so that it will be received by the FDA on or before the due date.