

Most recent modification: May 2017

Initial REMS Approval: 04/2011

NDA 22-405 CAPRELSA[®] (vandetanib)

Kinase inhibitor

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RISK EVALUATION AND MITIGATION STRATEGY

I. GOALS

The goals of the CAPRELSA REMS Program are to mitigate the serious risks of QT prolongation, Torsades de pointes, and sudden death associated with use of CAPRELSA by:

- Educating prescribers on the following:
 - Serious risks of QT prolongation, Torsades de pointes, and sudden death associated with use of CAPRELSA.
 - The need to monitor for QT prolongation and electrolyte abnormalities.
 - Appropriate management of QT prolongation to minimize the occurrence of Torsades de pointes and sudden death associated with use of CAPRELSA.
- Informing patients on the following:
 - Serious risks of QT prolongation, Torsades de pointes, and sudden death associated with use of CAPRELSA.

II. ELEMENTS

A. Elements to Assure Safe Use

1. Healthcare providers who prescribe CAPRELSA are specially certified.

- a. Genzyme Corporation (Genzyme) must ensure that healthcare providers who prescribe CAPRELSA are specially certified.
- b. To become certified to prescribe CAPRELSA, healthcare providers must:

- 1) Review the *CAPRELSA REMS Prescriber Training Pamphlet* or *CAPRELSA REMS Prescriber Training Slide Deck* and the Prescribing Information.
- 2) Complete the *CAPRELSA REMS Prescriber Training Questions* and submit the responses to these questions online or by telephone to the CAPRELSA REMS Program at 1-800-817-2722.
- 3) Enroll in the CAPRELSA REMS Program by completing the *CAPRELSA REMS Prescriber Enrollment Form* online or by telephone.
- 4) Agree to review the *CAPRELSA Patient Brochure* with the patient or caregiver.

Genzyme must:

- 1) Ensure that prescriber enrollment can successfully be completed via the CAPRELSA REMS website, or by telephone via the CAPRELSA Program Coordinating Call Center at 1-800-817-2722. The CAPRELSA REMS website (www.caprelsarems.com) is part of the CAPRELSA REMS Program and is appended.
- 2) Ensure that, as part of the enrollment process, prescribers receive or have access to the following materials that are part of the CAPRELSA REMS Program and are appended:

CAPRELSA REMS Prescriber Training Pamphlet
CAPRELSA REMS Prescriber Training Slide Deck
CAPRELSA REMS Prescriber Training Questions
CAPRELSA REMS Prescriber Enrollment Form
CAPRELSA Patient Brochure

- 3) Ensure that prescribers have completed the training and ensure that the enrollment form is complete before activating a prescriber's enrollment in the CAPRELSA REMS Program.
- 4) Ensure that prescribers are notified when they are successfully enrolled in the CAPRELSA REMS Program, and therefore, are certified to prescribe CAPRELSA.

2. CAPRELSA must only be dispensed by pharmacies that are specially certified.

- a. Genzyme must ensure that CAPRELSA will only be dispensed by certified pharmacies. To become certified to dispense CAPRELSA, each pharmacy must be enrolled in the CAPRELSA REMS Program.
- b. To become certified, the authorized pharmacist on behalf of the pharmacy must agree to the following:
 - 1) I understand that only prescribers enrolled in the CAPRELSA REMS Program can prescribe CAPRELSA.

- 2) The pharmacy must have a system in place to verify that the prescriber is enrolled in the CAPRELSA REMS Program each time CAPRELSA is dispensed. If the prescriber is not enrolled, CAPRELSA cannot be dispensed.
- 3) All pharmacy staff and critical employees involved in the dispensing of CAPRELSA will be educated on the requirements of the CAPRELSA REMS Program.
- 4) The pharmacy will maintain a system, records, and documentation that can be audited to document compliance with the CAPRELSA REMS Program, including prescriber certification each time CAPRELSA is dispensed.
- 5) Complete the *CAPRELSA REMS Pharmacy Enrollment Form* and submit it to the CAPRELSA REMS Program.

The *CAPRELSA REMS Pharmacy Enrollment Form* is part of the CAPRELSA REMS Program and is appended.

B. Implementation System

1. Genzyme must ensure that pharmacies (including pharmacy distributors) dispensing CAPRELSA are specially certified using the criteria described above.
2. Genzyme must ensure that distributors who distribute CAPRELSA are specially certified. Specially certified distributors must agree to:
 - a. Distribute CAPRELSA only to pharmacies certified in the CAPRELSA REMS Program.
 - b. Put processes and procedures in place to ensure that the requirements of the CAPRELSA REMS Program are followed.
 - c. Agree to be audited to ensure that CAPRELSA is distributed according to the CAPRELSA REMS Program.
3. Genzyme must maintain a secure, validated, interactive, web-based database of all enrolled entities (prescribers, pharmacies, and distributors). Prescribers will be able to enroll in the program by completing the enrollment requirements online or by calling the CAPRELSA Program Coordinating Call Center at 1-800-817-2722. Certified pharmacies can access the database to verify prescriber enrollment status as required by the REMS.
4. Genzyme must monitor distribution and prescription data to ensure that only enrolled distributors are distributing, enrolled pharmacies are dispensing, and enrolled prescribers are prescribing CAPRELSA. Corrective action must be initiated by Genzyme for prescribers, pharmacies, or distributors who are found not to be complying with the CAPRELSA REMS Program.
 - a. Inpatients in acute care settings will be shipped drug per patient if the prescriber is enrolled in the CAPRELSA REMS Program.

- b. Patients in long-term care facilities will be shipped drug per patient if the prescriber is enrolled in the CAPRELSA REMS Program.
- 5. Genzyme must monitor and audit the online enrollment database, distribution, and dispensing systems to check that all processes and procedures are in place and functioning to support the requirements of the CAPRELSA REMS Program.
- 6. Genzyme must maintain a Program Coordinating Center with a Call Center to support prescribers, pharmacies, and distributors in interfacing with the CAPRELSA REMS Program and CAPRELSA REMS Program website (www.caprelsarems.com) that must continue for the duration of the REMS. Genzyme must ensure that all materials listed in or appended to the CAPRELSA REMS Program will be available through the CAPRELSA REMS website (www.caprelsarems.com) and by calling the CAPRELSA Program Coordinating Call Center at 1-800-817-2722.
- 7. Genzyme must ensure that within 60 calendar days of REMS modification the REMS materials listed in or appended to the CAPRELSA REMS document are available through the CAPRELSA REMS Program Website and by calling the CAPRELSA REMS Program Call Center.
- 8. Based on monitoring and evaluation of these elements to assure safe use, Genzyme must take reasonable steps to improve implementation of these elements and to maintain compliance with the CAPRELSA REMS Program requirements, as applicable.
- 9. Genzyme must train appropriate personnel, and develop and follow written procedures and scripts to implement the CAPRELSA REMS Program. Genzyme will modify them as required based on the results of assessments.

III. TIMETABLE FOR SUBMISSION OF ASSESSMENTS

Genzyme must submit assessments to the FDA annually On the date of the initial approval of the CAPRELSA REMS (April 6, 2011). 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 of the assessment. Genzyme must submit each assessment so that it will be received by the FDA on or before the due date.