I. GOALS

The goals of the CAPRELSA REMS are:

1. to educate prescribers about the risk, appropriate monitoring, and management of QT prolongation to help minimize the occurrence of Torsades de pointes and sudden death associated with CAPRELSA.

2. to inform patients about the serious risks associated with CAPRELSA.

II. REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each CAPRELSA prescription in accordance with 21 CFR 208.24.

The Medication Guide is part of the CAPRELSA REMS Program and is appended.

B. Communication Plan

AstraZeneca will implement a communication plan to healthcare providers to support implementation of this REMS.

If AstraZeneca has a presence at the following conferences where commercial CAPRELSA product information is displayed, AstraZeneca will display the CAPRELSA REMS Convention Panel outlining details of the CAPRELSA REMS Program.
American Society of Clinical Oncology (ASCO)
American Thyroid Association (ATA)
National Comprehensive Cancer Network (NCCN)
Oncology Nursing Society (ONS)

The CAPRELSA REMS Convention Panel is part of the CAPRELSA REMS Program and is appended.

C. Elements to Assure Safe Use

1. Healthcare providers who prescribe CAPRELSA are specially certified.

   a. AstraZeneca will ensure that healthcare providers who prescribe CAPRELSA are specially certified.

   b. To become certified to prescribe CAPRELSA, prescribers will be required to enroll in the CAPRELSA REMS Program and must:

      1) Review the CAPRELSA REMS HCP Education Pamphlet or Slide Set and the Full Prescribing Information which includes the Medication Guide.

      2) Complete the Prescriber Training.

      3) Complete and sign the CAPRELSA Prescriber Enrollment Form and submit it to the CAPRELSA REMS Program.

      4) Agree to review the Medication Guide with the patient or caregiver.

   c. Prescribers are required to be re-trained following substantive changes to the CAPRELSA REMS. Substantive changes are defined as 1) significant changes to the operation of the CAPRELSA REMS Program; 2) changes to the Prescribing Information and Medication Guide that affect the risk benefit profile of Caprelsa® (vandetanib).

   d. AstraZeneca will:

      1) Ensure that prescriber enrollment can successfully be completed via the CAPRELSA REMS website, or by phone via the call center.

         The CAPRELSA REMS Web Site (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:

- *HCP Education Pamphlet*
- *HCP Education slides set*
- *Prescriber Training Program*
- *Prescriber Enrollment form*
- *Medication Guide*

These materials will be sent promptly to any uncertified prescriber who attempts to prescribe CAPRELSA.

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 will only be dispensed by pharmacies that are specially certified.**

   a. AstraZeneca will 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® (vandetanib).

      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 risks and requirements of the CAPRELSA REMS Program.

      4) The pharmacy will provide the Medication Guide each time CAPRELSA is dispensed.

      5) The pharmacy will ensure that it has adequate processes and procedures in place and that those processes and procedures are being followed for the CAPRELSA REMS Program.
6) 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.

7) Complete and sign the CAPRELSA Pharmacy Enrollment Form and submit it to the CAPRELSA REMS Program.

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

D Implementation System

1. AstraZeneca will ensure that pharmacies (including pharmacy distributors) dispensing CAPRELSA are specially certified using the criteria described above.

2. AstraZeneca will ensure that distributors who distribute CAPRELSA are specially certified. Specially certified distributors will agree to:
   a. Distribute CAPRELSA only to pharmacies certified in the CAPRELSA REMS.
   b. Put processes and procedures in place to ensure that the requirements of the CAPRELSA REMS are followed.
   c. Agree to be audited to ensure that CAPRELSA is distributed according to the REMS.

3. AstraZeneca will 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. Certified pharmacies can access the database to verify prescriber enrollment status as required by the REMS.

4. AstraZeneca will monitor distribution and prescription data to ensure that only enrolled distributors are distributing, enrolled pharmacies are dispensing, and enrolled prescribers are prescribing Caprelsa® (vandetanib). Corrective action will be initiated by AstraZeneca for prescribers, pharmacies, or distributors who are found not to be complying with the REMS.
   a. Inpatients in acute care settings will be shipped drug per patient if the prescriber is enrolled in the REMS
   b. Patients in long-term care facilities will be shipped drug per patient if the prescriber is enrolled in the REMS
   c. All shipments of CAPRELSA will be accompanied by a Medication Guide.
5. AstraZeneca will 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. AstraZeneca will maintain a Program Coordinating Center with a Call Center to support patients, prescribers, pharmacies, and distributors in interfacing with the REMS. AstraZeneca will ensure that all materials listed in or appended to the CAPRELSA REMS Program will be available through the REMS website (www.caprelsarems.com) or by calling the Call Center at 1-800-236-9933.

7. If there are substantive changes to the CAPRELSA REMS Program, AstraZeneca will update all affected materials and notify pharmacies, prescribers, and distributors, as applicable. Substantive changes are defined as:
   a. Significant changes to the operation of the CAPRELSA REMS Program
   b. Changes to the Prescribing Information and Medication Guide that affect the risk-benefit profile of CAPRELSA.

8. Based on monitoring and evaluation of these elements to assure safe use, AstraZeneca will take reasonable steps to improve implementation of these elements and to maintain compliance with the CAPRELSA REMS Program requirements, as applicable.

9. AstraZeneca will develop, train appropriate personnel, and follow written procedures and scripts to implement the REMS program. AstraZeneca will modify them as required based on the results of assessments.

III. TIMETABLE FOR SUBMISSION OF ASSESSMENTS

AstraZeneca will submit assessments of the Caprelsa® (vandetanib) REMS Program to the FDA every 6 months for the first year following the approval of the CAPRELSA REMS, and annually 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 days before the submission date of the assessment. AstraZeneca will submit each assessment so that it will be received by the FDA on or before the due date.