1 GOAL

The goal of the ELIQUIS REMS is to inform healthcare providers (HCPs) about:

- the increased risk of thrombotic events in patients with nonvalvular atrial fibrillation when discontinuing ELIQUIS without introducing an adequate alternative anticoagulant
- the importance of following the recommendations in the US Prescribing Information (USPI) on how to convert patients with nonvalvular atrial fibrillation from ELIQUIS to warfarin or other anticoagulants.

2 REMS ELEMENTS

2.1 Communication Plan

Bristol-Myers Squibb will implement a communication plan to HCPs to support implementation of this REMS.

1. Dear Healthcare Professional Letter
A Dear Healthcare Professional (DHCP) Letter will be distributed by direct mail or electronic delivery to HCPs including: cardiologists, neurologists, emergency medicine physicians, internal medicine physicians, primary care physicians, nurse practitioners, physician assistants, and pharmacists. The letter will be distributed within 60 days of approval of ELIQUIS. Annual letters will be sent within 60 days of the anniversary date of approval for ELIQUIS every year for two additional years and within 60 days of FDA approval of any substantial safety update. The DHCP Letter will also be provided to FDA MedWatch at these times. A copy of the USPI and Medication Guide will accompany the DHCP Letter.

In addition, the DHCP Letter, USPI and Medication Guide will also be available on the ELIQUIS REMS website and upon request.

1. The DHCP letter is part of the REMS and is appended.
   2. ELIQUIS REMS Website

2. Within 30 days of REMS approval, Bristol-Myers Squibb will post information for HCPs and patients on the ELIQUIS REMS website (http://www.ELIQUISREMS.com). This information will remain on the website for a period of 2 years.

3. The content of the print or web-based material will include the following:
   - Goal of the REMS
   - Information about the risk
   - US Prescribing Information for ELIQUIS
   - Medication Guide for ELIQUIS
   - DHCP Letter (for a period of 2 years)

The ELIQUIS REMS website is part of the REMS and is appended.

3. Letters to Professional Organizations

A Professional Organization Letter will be distributed by direct mail or electronic delivery within 60 days of the REMS approval date. This communication to professional organizations will include the same information as that contained in the DHCP Letter. Bristol-Myers Squibb will request that these organizations disseminate this information to their members. Bristol-Myers Squibb will communicate the letter to the leadership of the following professional organizations:
The USPI and the Medication Guide will be provided in conjunction with the letter.
The Professional Organization Letter is part of the REMS and is appended.

2.2 Timetable for Submission of Assessments

Bristol-Myers Squibb will submit REMS Assessments to the FDA at 18 months, 3 years, and 7 years from the date of the REMS approval. 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 for that assessment. Bristol-Myers Squibb will submit each assessment so that it will be received by the FDA on or before the due date.
The assessment plan must include, but is not limited to, the following components:

1) A report on the distribution of DHCP letters and Professional Organization Letters

2) An evaluation of healthcare providers’ awareness and understanding of the serious risks associated with ELIQUIS (for example, through surveys of healthcare providers).

3) With respect to the REMS goals, an assessment of the extent to which the REMS is meeting its goals or whether the goals or other elements should be modified.

4) Information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.