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Approval Package for:

APPLICATION NUMBER:

202155Orig1s002

Trade Name:	Eliquis 2.5 and 5 mg Tablets
Generic Name:	apixaban
Sponsor:	Bristol-Myers Squibb
Approval Date:	January 30, 2014
Indications:	ELIQUIS is a factor Xa inhibitor anticoagulant indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

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APPROVAL LETTER

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202155/S-002

SUPPLEMENT APPROVAL

Bristol-Myers Squibb
ATTENTION: Linda Gambone, Ph.D.
Associate Director, Global Regulatory Sciences
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Gambone:

Please refer to your Supplemental New Drug Application (sNDA) dated April 29, 2013, received April 29, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Eliquis (apixaban) 2.5 and 5 mg Tablets.

This Prior Approval supplemental new drug application provides verbiage to better differentiate temporary interruption vs. discontinuation, new information and dosing recommendations for patient with end stage renal disease, and to include data from a drug-drug interaction study with prasugrel. The agreed upon changes to the Full Prescribing Information (FPI) language are as follows:

- The title of subsection 2.3 was changed to "**Temporary Interruption for Surgery and Other Interventions**"

- The subsection of **DOSAGE AND ADMINISTRATION**, 2.7 **Renal Impairment,** was changed from:

  "The dosing adjustment for moderate renal impairment is described above *[see Dosage and Administration (2.2)]*. No data inform use in patients with creatinine clearance <15 mL/min or on dialysis."

  To

  "The dosing adjustment for moderate renal impairment is described above *[see Dosage and Administration (2.2)]*.The recommended dose for patients with end-stage renal disease (ESRD) maintained on hemodialysis is 5 mg twice daily. Reduce dose to 2.5 mg twice daily if one of the following patient characteristics (age ≥80 years or body weight ≤60 kg) is present *[see Use in Specific Population (8.6) and Clinical Pharmacology (12.3)]*."

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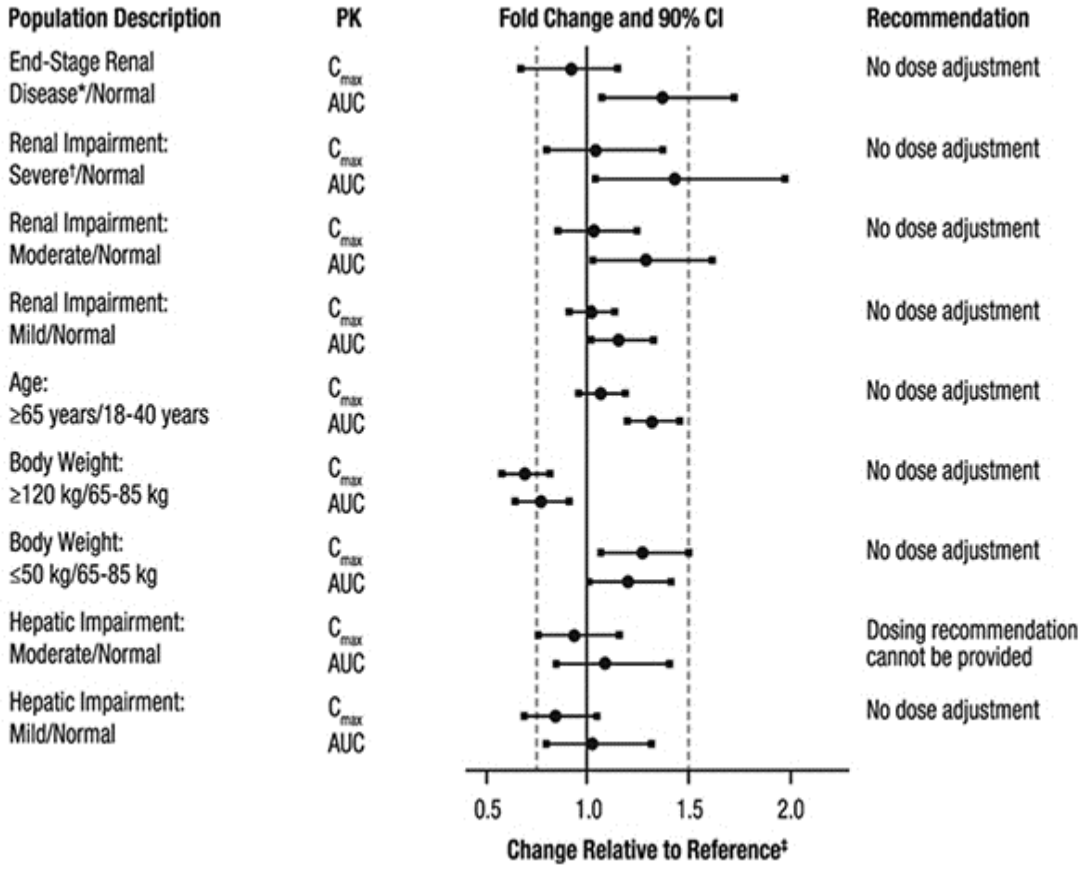
- A new subsection within **USE IN SPECIFIC POPULATIONS** was added. This new subsection, 8.6 **End-Stage Renal Disease Patients Maintained with Hemodialysis**, reads:

  "Patients with ESRD with or without hemodialysis were not studied in clinical efficacy and safety studies with ELIQUIS; therefore, the dosing recommendation is based on pharmacokinetic and pharmacodynamic (anti-Factor Xa activity) data in subjects with ESRD maintained on dialysis. The recommended dose for ESRD patients maintained with hemodialysis is 5 mg orally twice daily. For ESRD patients maintained with hemodialysis with one of the following patient characteristics, age ≥80 years or body weight ≤60 kg, reduce dose to 2.5 mg twice daily *[see Dosage and Administration (2.7), Clinical Pharmacology (12.2, 12.3)]*."

- In subsection 12.3, **Pharmacokinetics**, Figure 3, "Effect of Specific Populations on the Pharmacokinetics of Apixaban" was replaced with the below:



* ESRD subjects maintained with chronic and stable hemodialysis; Reported PK findings are following single dose of apixaban post hemodialysis.
† Creatinine clearance 15 to 29 mL/min.
‡ Dashed vertical lines illustrate pharmacokinetic changes that were used to inform dosing recommendations.

- There were also a few minor editorial and formatting changes made to throughout the FPI.

- The HIGHLIGHTS and Table of Contents were amended to reflect these changes to the FPI.

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