janssen
PHARMACEUTICAL COMPANIES
OF Johnson&Johnson

IMPORTANT DRUG WARNING
XARELTO® (rivaroxaban) film-coated oral tablets
Distribute this Information to Your Members

September, 2013

Dear Professional Organization:

Janssen Pharmaceuticals, Inc., would like to inform you of important safety information for XARELTO® (rivaroxaban). XARELTO® is an orally bioavailable reversible factor Xa inhibitor. XARELTO®, among other uses, is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (15 mg and 20 mg).

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS), which consists of a Communication Plan, is necessary to ensure that the benefits of XARELTO® outweigh the potential risks in patients with nonvalvular atrial fibrillation, including:

- Increased risk of thrombotic events if XARELTO® is discontinued without introducing an adequate alternative anticoagulant
- Potential decreased efficacy of XARELTO® (15 mg and 20 mg) if not taken with the evening meal

The XARELTO® labeling includes a **Boxed WARNING** to highlight the safety issue of increased risk of thrombotic events following discontinuation of XARELTO®.

WARNING: PREMATURE DISCONTINUATION OF XARELTO® INCREASES RISK OF THROMBOTIC EVENTS

Premature discontinuation of any anticoagulant, including XARELTO®, increases the risk of thrombotic events. If anticoagulation with XARELTO® is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

Discontinuing Administration of XARELTO® in Nonvalvular Atrial Fibrillation Patients

XARELTO® has a plasma half-life of 5 to 9 hours in healthy subjects (ages 20 to 45 years) and 11 to 13 hours in the elderly. Therefore, the anticoagulant effect of XARELTO® is only present when the drug is taken. Discontinuing any anticoagulant including XARELTO® places nonvalvular atrial fibrillation patients at an increased risk of thrombotic events. An increased rate of stroke was observed during the transition from XARELTO® to warfarin in clinical trials in atrial fibrillation patients. If XARELTO® must be discontinued for a reason other than pathological bleeding, consider coverage with another anticoagulant. Please read the recommendations in the US Prescribing Information for appropriate management of the switching or transition of XARELTO® to warfarin or another anticoagulant. Additionally, advise patients to take XARELTO® only as directed and not to discontinue XARELTO® without first speaking to you.

Take XARELTO® (15 and 20 mg) with the Evening Meal

The 20 mg tablet has an absolute bioavailability of approximately 66% under fasting conditions, which could result in a potential risk of inadequate anticoagulation with XARELTO® therapy. Coadministration of XARELTO® with food can approximately increase the mean AUC by 39% and C_{max} by 76% in both the 15 mg and 20 mg strengths. XARELTO® 15 mg and 20 mg tablets should be taken orally once daily with the evening meal to reduce the potential risk of decreased efficacy of therapy. Please inform your nonvalvular atrial fibrillation patients to take this medication as instructed.

Reporting Adverse Events

To report any adverse events potentially associated with the use of XARELTO®, contact:

- Janssen Pharmaceuticals, Inc., at 1-800-526-7736 and/or
- FDA's MedWatch Reporting System by phone at 1-800-FDA-1088 (1-800-332-1088) or online at www.fda.gov/medwatch/report.htm

This letter is not intended as a comprehensive description of the risks associated with the use of XARELTO®. Please read the enclosed US Prescribing Information and Medication Guide for a complete description of these risks.

If you have any questions about XARELTO® including any information found in this letter, the US Prescribing Information and Medication Guide for XARELTO®, please call our Medical Information Center at 1-800-526-7736.

Sincerely,

Paul Chang, MD
Vice President Medical Affairs
Internal Medicine

Enclosures:
US Prescribing Information