



June 21, 2012

FDA Issues Complete Response Letter for XARELTO® (rivaroxaban) for the Reduction of Secondary Cardiovascular Events in Patients with Acute Coronary Syndrome

RARITAN, N.J., June 21, 2012 - Janssen Research & Development, LLC (Janssen R&D) announced today the U.S. Food and Drug Administration (FDA) issued a complete response letter regarding a supplemental New Drug Application (sNDA) for XARELTO® (rivaroxaban) for the reduction of the risk of secondary cardiovascular events in patients with acute coronary syndrome (ACS). Janssen is evaluating the complete response letter and will respond to the agency's questions.

"We are confident in the robust study results of the ATLAS ACS 2 TIMI 51 trial and the positive benefit-risk profile of rivaroxaban in patients with ACS. We will continue to work with the FDA to fully address their questions as quickly as possible," said Paul Burton, M.D., Ph.D., Vice President, Cardiovascular Franchise Medical Leader at Janssen R&D.

XARELTO® is approved for three clinical uses in the U.S.: to reduce the risk of blood clots in the legs and lungs of people who have just had knee replacement surgery, to reduce this risk in people who have just had hip replacement surgery, and to reduce the risk of both hemorrhagic and thrombotic strokes as well as other blood clots in people with atrial fibrillation not caused by a heart valve problem.

ACS is a complication of coronary heart disease, which is the leading cause of death in the U.S. and one of the most prevalent non-communicable diseases in the world. ACS occurs when a blood clot blocks a coronary artery, reducing blood supply to the heart. This disruption of blood flow can cause a heart attack, or unstable angina, a condition signifying that a heart attack may soon occur. Each year, an estimated 1.2 million patients in the U.S. are discharged from the hospital with a diagnosis of ACS.

Janssen R&D [submitted this sNDA](#) on December 29, 2011 and [received a priority review](#) designation from FDA on February 27, 2012. On [May 23, 2012](#), the FDA's Cardiovascular and Renal Drugs Advisory Committee narrowly voted against recommending approval of XARELTO® in this indication.

The sNDA includes results from the pivotal Phase 3 ATLAS ACS 2 TIMI 51 (**Anti-Xa Therapy to Lower cardiovascular events in Addition to aspirin with/without thienopyridine therapy in Subjects with Acute Coronary Syndrome**) clinical trial of XARELTO® which were presented at the American Heart Association (AHA) annual Scientific Sessions in November 2011 and simultaneously published by [New England Journal of Medicine](#).

About XARELTO® (rivaroxaban)

XARELTO® belongs to a group of medicines called anticoagulants, and works by blocking the blood clotting Factor Xa, thereby reducing the tendency to form clots. XARELTO® is approved for three uses: to reduce the risk of blood clots in the legs and lungs of people who have just had knee replacement surgery, to reduce this risk in people who have just had hip replacement surgery, and to reduce the risk of both hemorrhagic and thrombotic strokes as well as other blood clots in people with atrial fibrillation not caused by a heart valve problem. There is limited information on how XARELTO® compares to a medicine called warfarin in reducing the risk of stroke when the blood levels of warfarin are well-controlled. The blood levels of warfarin often vary in patients.

XARELTO® has the broadest profile of any of the newer oral anticoagulants either in market today or coming to the U.S. market in the foreseeable future, and is broadly available for more than 90% of commercial and Medicare health plan members. To date, more than 1.5 million patients have received XARELTO® worldwide and nearly 350,000 prescriptions have been written for XARELTO® in the U.S. alone.

The extensive program of clinical trials evaluating rivaroxaban makes the compound the most studied oral, Factor Xa inhibitor in the world today. There are five filings currently under review at the FDA. Rivaroxaban is being developed jointly by Janssen R&D and Bayer HealthCare. U.S. marketing rights for XARELTO® are held by Janssen Pharmaceuticals, Inc.

About Janssen

At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Driven by

our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Janssen Research & Development, LLC and Janssen Pharmaceuticals, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Please visit <http://www.janssenrnd.com> for more information.

Important Safety Information

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT XARELTO®?

For people taking XARELTO® for atrial fibrillation:

People with atrial fibrillation (an irregular heart beat) are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. XARELTO® lowers your chance of having a stroke by helping to prevent clots from forming. If you stop taking XARELTO®, you may have an increased risk of forming a clot in your blood.

- **Do not stop taking XARELTO® without talking to the doctor who prescribes it for you. Stopping XARELTO® increases your risk of having a stroke or forming blood clots in other parts of your body.**

If you have to stop taking XARELTO®, your doctor may prescribe another blood thinner medicine to prevent a blood clot from forming.

For all people taking XARELTO®:

- XARELTO® can cause bleeding which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner that reduces blood clotting. While you take XARELTO® you are likely to bruise more easily and it may take longer for bleeding to stop.

You may have a higher risk of bleeding if you take XARELTO® and other medicines that increase your risk of bleeding including:

- aspirin or aspirin containing products,
- non-steroidal anti-inflammatory drugs (NSAIDs)
- warfarin sodium (Coumadin®, Jantoven®)
- any medicine that contains heparin
- clopidogrel (Plavix®)
- prasugrel (Effient®)
- ticagrelor (Brilinta®)

Tell your doctor if you take any of these medicines. Ask your doctor or pharmacist if you are not sure if your medicine is one listed above.

Call your doctor or get medical help right away if you develop any of these signs or symptoms of bleeding:

- tingling, numbness or muscle weakness, especially in your legs. This is particularly important if you had a procedure called spinal or epidural puncture as part of your anesthesia during surgery.
- any unexpected bleeding, or bleeding that lasts a long time (such as nose bleeds that happen often, unusual bleeding from gums, or menstrual bleeding that is heavier than normal or vaginal bleeding)
- bleeding that is severe or that you cannot control
- red, pink or brown urine
- bright red or black stools (look like tar)
- cough up blood or blood clots
- vomit blood or your vomit looks like "coffee grounds"
- headaches, feeling dizzy or weak
- pain, swelling, or new drainage at wound sites

WHO SHOULD NOT TAKE XARELTO®?

Do not take XARELTO® if you:

- currently have abnormal or unusual bleeding
- are allergic to rivaroxaban or any of the ingredients of XARELTO[®]

WHAT SHOULD I TELL MY DOCTOR BEFORE OR WHILE TAKING XARELTO[®]?

Before taking XARELTO[®] tell your doctor if you:

- Have ever had bleeding problems
- Have liver or kidney problems
- Have any other medical condition
- Are pregnant or planning to become pregnant
- Are breastfeeding or plan to breastfeed

Tell all of your doctors and dentists that you are taking XARELTO[®]. They should talk to the doctor who prescribed XARELTO[®] for you before you have any surgery, medical or dental procedure.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO[®] works. Certain medicines may increase your risk of bleeding.

Especially tell your doctor if you take:

- ketoconazole (Nizoral[®])
- itraconazole (Onmel[™], Sporanox[®])
- ritonavir (Norvir[®])
- lopinavir/ritonavir (Kaletra[®])
- indinavir (Crixivan[®])
- carbamazepine (Carbatrol[®], Equetro[®], Tegretol[®], Tegretol[®]-XR, Teril[™], Eptitol[®])
- phenytoin (Dilantin-125[®], Dilantin[®], Phenobarbital, Solfoton[™])
- rifampin (Rifater[®], Rifamate[®], Rimactane[®], Rifadin[®])
- St. John's wort (*Hypericum perforatum*)

Ask your doctor if you are not sure if your medicine is one listed above. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

HOW SHOULD I TAKE XARELTO[®]?

Take XARELTO[®] exactly as prescribed by your doctor. **Do not change your dose or stop taking XARELTO[®] unless your doctor tells you to.**

For people who have:

- **atrial fibrillation:** Take XARELTO[®] 1 time a day **with your evening meal. Stopping XARELTO[®] may increase your risk of having a stroke or forming blood clots in other parts of your body.**
- **hip or knee replacement surgery:** Take XARELTO[®] 1 time a day **with or without food.**
- Your doctor may stop XARELTO[®] for a short time before any surgery, medical or dental procedure. Your doctor will tell you when to start taking XARELTO[®] again after your surgery or procedure.
- Do not run out of XARELTO[®]. Refill your prescription for XARELTO[®] before you run out. When leaving the hospital following a hip or knee replacement, be sure that you will have XARELTO[®] available to avoid missing any doses.
- If you miss a dose of XARELTO[®], take it as soon as you remember on the same day.
- If you take too much XARELTO[®], go to the nearest hospital emergency room or call your doctor right away.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO[®]?

XARELTO[®] can cause bleeding which can be serious, and rarely may lead to death. *Please see "What is the most important*

information I should know about XARELTO®?"

Tell your doctor if you have any side effect that bothers you or that does not go away.

Discuss any side effects with your doctor. You are also encouraged to report side effects to the FDA: visit <http://www.fda.gov/medwatch> or call 1-800-FDA-1088. You may also report side effects to Janssen Pharmaceuticals, Inc. at 1-800-JANSSEN (526-7736).

Please click [here](#) for full prescribing information, including **Boxed Warnings** and the [Medication Guide](#).

Trademarks are those of their respective owners.

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to, general industry conditions and competition; economic factors, such as interest rate and currency exchange rate fluctuations; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approvals; challenges to patents; changes in behavior and spending patterns or financial distress of purchasers of healthcare products and services; changes to governmental laws and regulations and domestic and foreign health care reforms; trends toward health care cost containment; and increased scrutiny of the healthcare industry by government agencies. A further list and description of these risks, uncertainties and other factors can be found in Exhibit 99 of Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2012. Copies of this Form 10-K, as well as subsequent filings, are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. Neither Janssen Research & Development, LLC nor Johnson & Johnson undertake to update any forward-looking statements as a result of new information or future events or developments.)