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**Janssen Submits Supplemental New Drug Application to FDA Seeking New Indications for XARELTO® (rivaroxaban) for Patients with Chronic Coronary and/or Peripheral Artery Disease (CAD/PAD)**

*Application seeks approval of the XARELTO® vascular dose (2.5mg BID) to reduce the risk of major cardiovascular events in patients with chronic CAD and/or PAD, and to reduce the risk of acute limb ischemia in patients with PAD*

*If approved, XARELTO® will be the only Factor Xa inhibitor indicated for these patient groups*

**RARITAN, NJ, December 11, 2017** – Janssen Research & Development, LLC (Janssen) today announced it has submitted a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for two new XARELTO® (rivaroxaban) vascular indications: reducing the risk of major cardiovascular (CV) events such as CV death, heart attack or stroke in patients with chronic coronary and/or peripheral artery disease (CAD/PAD), and for reducing the risk of acute limb ischemia in patients with PAD. This application is based on data

from the landmark COMPASS study, the only randomized trial to investigate a Factor Xa inhibitor for preventing major CV events in this population.

Both CAD and PAD occur when arteries become hardened or narrowed due to a buildup of cholesterol and plaque, limiting blood flow to parts of the body. While long-term aspirin use helps prevent CV events, it is only modestly effective and, despite use of preventative medicines as directed by current guidelines, an underlying thrombotic risk remains and people with CAD or PAD could still have a serious or fatal CV event.<sup>i</sup>

“Coronary artery disease (CAD) and peripheral artery disease (PAD) impact millions of Americans and can lead to heart attack, stroke, and death. At Janssen, we want to help prevent the potentially devastating and irreversible harm associated with CV events that often occur in these patients,” said James F. List, MD, PhD, Global Therapeutic Area Head, Cardiovascular & Metabolism, Janssen. “Based on the results of COMPASS, we believe the combination of the vascular dose of XARELTO<sup>®</sup> (2.5 mg twice daily) plus aspirin can provide important benefits and potentially change the way physicians treat patients with CAD and PAD, if approved.”

### **About COMPASS**

The COMPASS study showed that the XARELTO<sup>®</sup> vascular dose of 2.5 mg twice daily plus aspirin 100 mg once daily significantly reduced the risk of major CV events defined as CV death, heart attack or stroke by 24 percent in patients with chronic CAD and/or PAD compared to aspirin alone. This finding was driven by a robust 42 percent reduction in stroke and 22 percent reduction in CV death. The risk of major bleeding was significantly higher in patients taking the XARELTO<sup>®</sup>/aspirin regimen compared to aspirin alone, with no significant increase in fatal or intracranial bleeds. COMPASS was [stopped early](#), approximately one year ahead of schedule, due to efficacy, and its [results](#) were presented during a Hot Line session at the ESC Congress 2017 and simultaneously published in [The New England Journal of Medicine](#). In addition, two sub-analyses from COMPASS in patients with [PAD](#) and [CAD](#) were recently published in *The Lancet*.

COMPASS is a Phase 3 clinical study of 27,395 patients with chronic CAD and/or PAD from 33 countries that examined the use of XARELTO<sup>®</sup>, alone or in combination with aspirin, in the long-term prevention of major adverse cardiovascular (CV) events, including heart attack, stroke or CV-related death.

### **About EXPLORER**

The EXPLORER program is unmatched by any oral anticoagulant in the Factor Xa inhibitor class in its size, scope and ambition. A collaborative effort between Janssen and Bayer, EXPLORER seeks to generate important clinical evidence on the safety and efficacy of XARELTO<sup>®</sup> and its potential role in addressing critical unmet medical needs. Several of the studies, including COMPASS, are designed to seek additional indications or expand the label for XARELTO<sup>®</sup> to benefit more patients in need of additional therapies for their cardiovascular disease. By the time of its completion, more than 275,000 patients will have participated in the EXPLORER clinical development program, other completed and ongoing clinical trials, investigative registries and non-interventional studies.

### **WHAT IS XARELTO<sup>®</sup>?**

XARELTO<sup>®</sup> (rivaroxaban) is a prescription medicine used to reduce the risk of stroke and blood clots in people with atrial fibrillation, not caused by a heart valve problem. For patients currently well managed on warfarin, there is limited information on how XARELTO<sup>®</sup> and warfarin compare in reducing the risk of stroke.

XARELTO<sup>®</sup> is also a prescription medicine used to treat deep vein thrombosis (DVT) and pulmonary embolism (PE), and to reduce the risk of blood clots happening again in people who continue to be at risk for DVT or PE after receiving treatment for blood clots for at least 6 months.

XARELTO<sup>®</sup> is also a prescription medicine used to reduce the risk of forming a blood clot in the legs and lungs of people who have just had knee or hip replacement surgery.

### **IMPORTANT SAFETY INFORMATION**

**What is the most important information I should know about XARELTO<sup>®</sup> (rivaroxaban)?**

- **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 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.**

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

- **XARELTO® can cause bleeding**, which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner medicine (anticoagulant) 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 take 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®)
- Selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs)
- Other medicines to prevent or treat blood clots

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:**

- Unexpected bleeding or bleeding that lasts a long time, such as:
  - Nosebleeds that happen often
  - Unusual bleeding from gums
  - Menstrual bleeding that is heavier than normal, or vaginal bleeding
- Bleeding that is severe or you cannot control
- Red, pink, or brown urine
- Bright red or black stools (looks 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

- **Spinal or epidural blood clots (hematoma):** People who take a blood thinner medicine like XARELTO<sup>®</sup>, and have medicine injected into their spinal and epidural area, or have a spinal puncture, have a risk of forming a blood clot that can cause long-term or permanent loss of the ability to move (paralysis). Your risk of developing a spinal or epidural blood clot is higher if:
  - A thin tube called an epidural catheter is placed in your back to give you certain medicine
  - You take NSAIDs or a medicine to prevent blood from clotting
  - You have a history of difficult or repeated epidural or spinal punctures
  - You have a history of problems with your spine or have had surgery on your spine

If you take XARELTO<sup>®</sup> and receive spinal anesthesia or have a spinal puncture, your doctor should watch you closely for symptoms of spinal or epidural blood clots. Tell your doctor right away if you have back pain, tingling, numbness, muscle weakness (especially in your legs and feet), or loss of control of the bowels or bladder (incontinence).

- **XARELTO<sup>®</sup> is not for people with artificial heart valves.**

**Do not take XARELTO<sup>®</sup> if you:**

- Currently have certain types of abnormal bleeding. Talk to your doctor before taking XARELTO<sup>®</sup> if you currently have unusual bleeding.
- Are allergic to rivaroxaban or any of the ingredients of XARELTO<sup>®</sup>.

Before taking XARELTO<sup>®</sup>, tell your doctor about all your medical conditions, including if you:

- Have ever had bleeding problems
- Have liver or kidney problems
- Are pregnant or plan to become pregnant. It is not known if XARELTO<sup>®</sup> will harm your unborn baby.
  - Tell your doctor right away if you become pregnant during treatment with XARELTO<sup>®</sup>. Taking XARELTO<sup>®</sup> while you are pregnant may increase the risk of bleeding in you or in your unborn baby.
  - If you take XARELTO<sup>®</sup> during pregnancy, tell your doctor right away if you have any signs or symptoms of bleeding or blood loss. **See “What is the most important information I should know about XARELTO<sup>®</sup>?” for signs and symptoms of bleeding.**
- Are breastfeeding or plan to breastfeed. XARELTO<sup>®</sup> may pass into your breast milk. You and your doctor should decide if you will take XARELTO<sup>®</sup> or breastfeed.

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

**Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO<sup>®</sup> works. Certain medicines may increase

your risk of bleeding. See **“What is the most important information I should know about XARELTO®?”**

### **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.
- Your doctor may change your dose if needed.
- If you take XARELTO® for:
  - **Atrial Fibrillation:**
    - Take XARELTO® **1 time a day with your evening meal.**
    - If you miss a dose of XARELTO®, take it as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
  - **Blood clots in the veins of your legs or lungs:**
    - Take XARELTO® **1 or 2 times a day** as prescribed by your doctor.
    - For the **15-mg and 20-mg doses**, XARELTO® **should be taken with food.**
    - For the **10-mg dose**, XARELTO® **may be taken with or without food.**
    - Take your XARELTO® dose(s) at the same time each day.
    - If you miss a dose:
      - **If you take the 15-mg dose of XARELTO® 2 times a day (a total of 30 mg of XARELTO® in 1 day):** Take XARELTO® as soon as you remember on the same day. You may take 2 doses at the same time to make up for the missed dose. Take your next dose at your regularly scheduled time.
      - **If you take XARELTO® 1 time a day:** Take XARELTO® as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
  - **Hip or knee replacement surgery:**
    - Take XARELTO® 1 time a day with or without food.
    - If you miss a dose of XARELTO®, take it as soon as you remember on the same day. Take your next dose at your regularly scheduled time.
- If you have difficulty swallowing the XARELTO® tablet whole, talk to your doctor about other ways to take XARELTO®.
- Your doctor will decide how long you should take XARELTO®.
- 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 have XARELTO® available to avoid missing any doses.

- If you take too much XARELTO<sup>®</sup>, go to the nearest hospital emergency room or call your doctor right away.

#### **WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO<sup>®</sup>?**

- See “What is the most important information I should know about XARELTO<sup>®</sup>?”

**Call your doctor for medical advice about side effects. 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 (1-800-526-7736).

Please click [here](#) for full Prescribing Information, including Boxed Warnings, and Medication Guide.

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#### **About the Janssen Pharmaceutical Companies**

*At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science.*

*We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at [www.janssen.com](http://www.janssen.com). Follow us on Twitter at [@JanssenUS](https://twitter.com/JanssenUS).*

#### *Cautions Concerning Forward-Looking Statements*

*This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding development of, and potential approval of new indications for, XARELTO<sup>®</sup> (rivaroxaban). 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 known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting*

*in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2017, including under "Item 1A. Risk Factors," its most recently filed Quarterly Report on Form 10-Q, including under the caption "Cautionary Note Regarding Forward-Looking Statements," and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at [www.sec.gov](http://www.sec.gov), [www.jnj.com](http://www.jnj.com) or on request from Johnson & Johnson. Neither the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.*

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<sup>1</sup> Bhatt DL, Eagle KA, Ohman EM, et al. Comparative determinants of 4-year cardiovascular event rates in stable outpatients at risk of or with atherothrombosis. *JAMA* 2010;304:1350-7.