News Release

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FDA Approves Expanded Peripheral Artery Disease (PAD) Indication for XARELTO® (rivaroxaban) Plus Aspirin to Include Patients After Lower-Extremity Revascularization (LER) Due to Symptomatic PAD

XARELTO® is the first and only therapy indicated for both coronary artery disease (CAD) and PAD, now including PAD patients post-LER

XARELTO® is the only anticoagulant in 20 years to show significant benefit in patients with PAD who remain at high risk for major thrombotic events, including acute limb ischemia and amputation

PAD impacts 20 million Americans[1] and is the leading cause of amputations in the U.S., with rates continuing to rise[2]

RARITAN, N.J., August 24, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the U.S. Food and Drug Administration (FDA) has approved an expanded peripheral artery disease (PAD) indication for the XARELTO® (rivaroxaban) vascular dose (2.5 mg twice daily plus aspirin 100 mg once daily) to include patients following recent lower-extremity revascularization (LER) due to symptomatic PAD. The approval is based on data from the Phase 3 VOYAGER PAD study. With this approval, XARELTO® is the first and only therapy indicated to help reduce the risks of major cardiovascular (CV) events in patients with coronary artery disease (CAD) and major thrombotic vascular events, such as myocardial infarction, ischemic stroke, acute limb ischemia, and major amputation of a vascular etiology, in

patients with PAD, including patients who have recently undergone LER due to symptomatic PAD.

CLICK TO TWEET: #BREAKINGNEWS: @US_FDA approves expanded #PeripheralArteryDisease #PAD indication for @JanssenUS treatment, evolving current standard of care for #PAD patients & how long-term prevention of persistent #bloodclot related events are managed. Learn more: bit.ly/33sm1yt

"For more than 20 years, many physicians have used dual antiplatelet therapy after lower extremity revascularization due to symptomatic PAD with limited data to support efficacy and safety in this setting. Now, the VOYAGER PAD and COMPASS clinical studies have demonstrated the utility of dual pathway inhibition in targeting both platelets and thrombin in patients with PAD. These data provide a new mechanism of treatment using an evidence-based strategy for this vulnerable population," said Marc P. Bonaca*, M.D., M.P.H., Department of Medicine, Division of Cardiovascular Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado. "This FDA approval of rivaroxaban plus aspirin is a major advancement for PAD management and sets the stage to evolve the current standard of care for patients with PAD."

PAD is a common chronic circulatory condition that causes blood vessels to narrow, thereby reducing blood flow to the limbs, most often the legs.[3] It is a disease which often goes undiagnosed and undertreated.[4] In fact, an estimated 20 million Americans are living with PAD, but only 8.5 million are currently diagnosed.[5] While it usually starts asymptomatically, PAD can progress to severe symptoms and require revascularization to avoid amputation.[6] PAD is the leading cause of amputations in the U.S. and results in high rates of fatal and non-fatal CV events.[6]

"PAD is a serious condition that is too frequently missed or often not even discussed by patients and their doctors due to lack of awareness and other health conditions that often take priority. It's important to understand the risk factors for PAD, including conditions such as diabetes, smoking and high blood pressure," said Ryan Gough, Executive Director of the Partnership to Advance Cardiovascular Health**, a

heart patient advocacy organization. "There's been a long-standing need across the healthcare community for increased education around PAD and better access to screening and innovative treatments. This is especially critical for patients in underserved communities, who are often at even greater risk for serious complications like amputation."

Amputations are a devastating complication of PAD and are associated with high mortality, despite being largely preventable.[6] In recent years, the rate of amputations in the U.S. has been increasing,[7] with studies showing Black Americans – who have a higher prevalence of asymptomatic PAD, less access to quality vascular care[6], and are at risk for delays in care[8] – are up to four times more likely to have an amputation as a result of PAD compared to White Americans.[1]

CLICK TO TWEET: #DYK Peripheral Artery Disease #PAD impacts 20M Americans and is the leading cause of amputations in the U.S., with rates continuing to rise? Learn more about PAD: bit.ly/3mjzSBT

XARELTO® now has nine indications in the U.S. – the most of any direct oral anticoagulant (DOAC). Today's approval is based on the Phase 3 VOYAGER PAD trial, which demonstrated the XARELTO® vascular dose (2.5 mg twice daily plus aspirin 100 mg once daily) reduced the risk of major adverse limb and cardiovascular events by 15 percent in patients with symptomatic PAD post-LER compared to aspirin alone.[9] The VOYAGER PAD trial saw no significant difference in TIMI[i] major bleeding between XARELTO® with aspirin compared to aspirin alone. The results from the VOYAGER PAD study complement findings from the landmark Phase 3 COMPASS trial, which also examined the dual pathway approach of XARELTO® with aspirin in CAD and/or PAD patients and further supports this FDA label extension in PAD patients.[10] Data from the Phase 3 COMPASS trial resulted in FDA approval in 2018 to reduce the risk of major cardiovascular events, such as heart attack, stroke and cardiovascular death in people with chronic PAD and CAD.[10] While there were more major bleeds with the

[i] Thrombolysis in Myocardial Infarction

XARELTO® vascular dose in COMPASS, there was no significant difference in rates of fatal bleeding, intracranial bleeding or symptomatic bleeding into a critical organ.[9,10]

"We're thrilled to bring XARELTO® to even more patients with PAD who have been living for two decades without any new innovation in the antithrombotic space," said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular and Metabolism, Janssen Research & Development, LLC. "Today's approval underscores Janssen's commitment to transform care for people living with PAD and make XARELTO® available to even more patients in need."

About VOYAGER PAD

The Phase 3 VOYAGER PAD study included 6,564 patients from 542 sites across 34 countries worldwide. Patients were randomized in a 1:1 ratio and received either the XARELTO® vascular dose (2.5 mg twice daily plus aspirin 100 mg once daily) (n=3,286) or aspirin alone (100 mg once daily) (n=3,278). Patients were stratified by revascularization procedure type (endovascular vs. surgical) and use of clopidogrel, which was administered at the treating physician's discretion. Patients were followed for a median of 28 months.

The VOYAGER PAD study met its primary efficacy and principal safety endpoints, demonstrating the XARELTO® vascular dose was superior to aspirin alone in reducing the risk of major adverse limb and cardiovascular events by 15 percent in patients with symptomatic PAD after lower-extremity revascularization. The benefit of adding XARELTO® to aspirin was apparent early, was consistent among major subgroups and continued to accrue over time. There was no significant increase in TIMI major bleeding observed in patients treated with the XARELTO® vascular dose compared to aspirin alone (2.65 percent vs. 1.87 percent respectively).

More on COMPASS

COMPASS, the largest clinical study of XARELTO® to date, enrolled a total of 27,395 patients with chronic CAD and/or PAD. Patients were randomized in a 1:1:1 ratio, with one group receiving the XARELTO® vascular dose (2.5 mg twice daily plus aspirin 100 mg once daily), another group receiving rivaroxaban 5 mg twice daily, and the final

group receiving aspirin 100 mg once daily. COMPASS was stopped approximately one year ahead of schedule due to efficacy.

COMPASS met its primary efficacy endpoint, with the XARELTO® vascular dose shown to be superior to aspirin alone, reducing major CV events by 24 percent. This finding was driven by a robust 42 percent reduction in any stroke and 22 percent reduction in CV death. While the risk of major bleeding was significantly higher in patients taking the XARELTO® vascular dose compared to aspirin alone, there was no significant difference between the treatment groups in fatal bleeds, intracranial bleeds, symptomatic bleeding into a critical organ, or bleeding into the surgical site requiring reoperation.

WHAT IS XARELTO®?

XARELTO® is a prescription medicine used to:

- reduce the risk of stroke and blood clots in people who have a medical condition called atrial fibrillation that is not caused by a heart valve problem. With atrial fibrillation, part of the heart does not beat the way it should. This can lead to the formation of blood clots, which can travel to the brain, causing a stroke, or to other parts of the body
- treat blood clots in the veins of your legs (deep vein thrombosis or DVT) or lungs (pulmonary embolism or PE)
- 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
- help prevent a blood clot in the legs and lungs of people who have just had hip or knee replacement surgery
- help prevent blood clots in certain people hospitalized for an acute illness and after discharge, who are at risk of getting blood clots because of the loss of or decreased ability to move around (mobility) and other risks for getting blood clots, and who do not have a high risk of bleeding

XARELTO® is used with low dose aspirin to:

- reduce the risk of serious heart problems, heart attack and stroke in people with coronary artery disease (a condition where the blood supply to the heart is reduced or blocked)
- reduce the risk of a sudden decrease in blood flow to the legs, major amputation, serious heart problems or stroke in people with peripheral artery disease (a condition where the blood flow to the legs is reduced), and includes people who have recently had a procedure to improve blood flow to the legs

It is not known if XARELTO® is safe and effective in children.

IMPORTANT SAFETY INFORMATION

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

XARELTO® may cause serious side effects, including:

- **Increased risk of blood clots if you stop taking XARELTO®.** People with atrial fibrillation (an irregular heart beat) that is not caused by a heart valve problem (nonvalvular) 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.

- **Increased risk of bleeding.** XARELTO® can cause bleeding which can be serious, and may lead to death. This is because XARELTO® is a blood thinner medicine (anticoagulant) that lowers blood clotting. During treatment with XARELTO® you are likely to bruise more easily, and it may take longer for bleeding to stop. You may be at higher risk of bleeding if you take XARELTO® and have certain other medical problems.

  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
  - Long-term (chronic) use of 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 (anticoagulant) like XARELTO®, 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® 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® is not for use in people with artificial heart valves.

XARELTO® is not for use in people with antiphospholipid syndrome (APS), especially with positive triple antibody testing.

Do not take XARELTO® if you:

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

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

- Have ever had bleeding problems
- Have liver or kidney problems
- Have antiphospholipid syndrome (APS)
- Are pregnant or plan to become pregnant. It is not known if XARELTO® will harm your unborn baby.
    - **Tell your doctor** right away if you become pregnant during treatment with XARELTO®. Taking XARELTO® while you are pregnant may increase the risk of bleeding in you or in your unborn baby.
    - If you take XARELTO® 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®?" for signs and symptoms of bleeding.**
- Are breastfeeding or plan to breastfeed. XARELTO® may pass into your breast milk. Talk to your doctor about the best way to feed your baby during treatment with XARELTO®.

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 over-the-counter medicines, vitamins, and herbal supplements.

Some of your other medicines may affect the way XARELTO® works, causing side effects. 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.
- Your doctor will decide how long you should take XARELTO®.
- XARELTO® may need to be stopped for one or more days before any surgery or medical or dental procedure. Your doctor will tell you when to stop taking

XARELTO® and when to start taking XARELTO® again after your surgery or procedure.

- If you need to stop taking XARELTO® for any reason, talk to the doctor who prescribed XARELTO® to you to find out when you should stop taking it. Do not stop taking XARELTO® without first talking to the doctor who prescribes it to you.
- If you have difficulty swallowing XARELTO® tablets whole, talk to your doctor about other ways to take XARELTO®.
- Do not run out of XARELTO®. Refill your prescription of 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 take too much XARELTO®, go to the nearest hospital emergency room or call your doctor right away.

If you take XARELTO® for:

- **Atrial Fibrillation that is not caused by a heart valve problem:**
  - 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 **10-mg dose**, XARELTO® **may be taken with or without food.**
  - For the **15-mg and 20-mg doses**, take XARELTO® **with food 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.
- **Blood clots in people hospitalized for an acute illness:**
  - Take XARELTO® 1 time a day, with or without food, while you are in the hospital and after you are discharged as prescribed by your doctor.
  - 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.

- **Reducing the risk of serious heart problems, heart attack and stroke in coronary artery disease:**
  - Take XARELTO® 2.5 mg 2 times a day with or without food.
  - If you miss a dose of XARELTO®, take your next dose at your regularly scheduled time.
  - Take aspirin 75 to 100 mg once daily as instructed by your doctor.
- **Reducing the risk of a sudden decrease in blood flow to the legs, major amputation, serious heart problems or stroke in people with peripheral artery disease, including those who have recently had a procedure to improve blood flow to the legs:**
  - Take XARELTO® 2.5 mg 2 times a day with or without food.
  - If you miss a dose of XARELTO®, take your next dose at your regularly scheduled time.
  - Take aspirin 75 to 100 mg once daily as instructed by your doctor.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

XARELTO® may cause serious side effects:

- See **"What is the most important information I should know about XARELTO®?"**

The most common side effect of XARELTO® was bleeding.

Call your doctor for medical advice about side effects. **You may report side effects to the FDA at 1-800-FDA-1088.** You may also report side effects to Janssen Pharmaceuticals, Inc., at 1-800-JANSSEN (1-800-526-7736).

Please read full Prescribing Information, including Boxed Warnings, and Medication Guide for XARELTO®.

About Janssen Cardiovascular & Metabolism

In Cardiovascular & Metabolism (CVM), we take on the most pervasive diseases that burden hundreds of millions of people and healthcare systems around the world. As part of this long-standing commitment and propelled by our successes in treating type 2 diabetes and thrombosis, we advance highly differentiated therapies that prevent and treat life-threatening cardiovascular, metabolic and retinal diseases. Uncovering new therapies that can improve the quality of life for this large segment of the population is an important endeavor – one which Janssen CVM will continue to lead in the years to come. Our mission is global, local and personal. Together, we can

reshape the future of cardiovascular, metabolic and retinal disease prevention and treatment. Please visit www.janssen.com/cardiovascular-and-metabolism.

About the Janssen Pharmaceutical Companies of Johnson & Johnson
At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal. Janssen Research & Development, LLC, is part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements
This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding 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 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of 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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