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U.S. FDA Approves XARELTO® (rivaroxaban) to Help Prevent Blood Clots in Acutely Ill Medical Patients

XARELTO® provides a new oral option to help prevent venous thromboembolism (VTE) and VTE-related death during hospitalization and post-hospital discharge in acutely ill medical patients at risk for VTE and not at high risk of bleeding

Despite being largely preventable, VTE, or blood clots, remains a significant risk for millions of Americans hospitalized with an acute medical illness

RARITAN, N.J., October 14, 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) has approved XARELTO® (rivaroxaban) for the prevention of venous thromboembolism (VTE), or blood clots, in hospitalized acutely ill medical patients at risk for thromboembolic complications who are not at high risk of bleeding. With the approval of this new indication, XARELTO® can be initiated for these patients during hospitalization and continued after discharge for a total recommended duration of 31 to 39 days. To date, the FDA has granted XARELTO® eight indications – the most of any direct oral anticoagulant (DOAC) – six of which are

specifically for the treatment, prevention and reduction in the risk of recurrence of VTE across a wide range of patient populations.

[Click to Tweet:](#) *New oral treatment option now approved to help prevent #bloodclots #VTE in adults hospitalized for an acute medical illness, providing an alternative to injectable anticoagulants, which have long been the standard of care*
<https://ctt.ec/UOp3r+>

“With this new approval, XARELTO® as an oral-only option now has the potential to change how acutely ill medical patients are managed for the prevention of blood clots, both in the hospital and for an extended period after discharge,” said Alex C. Spyropoulos, M.D., Professor of Medicine, The Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Northwell Health at Lenox Hill Hospital, New York, NY.¹ “The Phase 3 clinical studies in this high-risk patient group show us that XARELTO® at the 10mg dose is an effective and safe option to help prevent blood clots.”

More than seven million Americans are hospitalized each year with an acute medical illness, which is a broad term used to describe serious, yet common, medical conditions.ⁱ These patients are at increased risk of blood clots for up to three months after hospital discharge, with 80 percent of events happening within the first six weeks.^{ii,iii} In response to the burden of VTE in hospitalized patients, the Surgeon General issued a *Call to Action* in 2008 for key stakeholders to build a coordinated plan that could lead to a reduction in VTE across the U.S.^{iv} However, a recent study found that in-hospital VTE rates continue to rise and more work is needed to reduce the burden of VTE especially among those at lower risk.^v

Guidelines currently recommend that acutely ill medical patients at risk of VTE receive anticoagulants, typically injectable agents, in the hospital to protect them from blood clots, but advise against routine anticoagulant use after leaving the

¹ Dr. Alex C Spyropoulos served as a Member of the Steering Committee of the MAGELLAN trial and was compensated for his work.

hospital.^{vi,vii} Research shows that many patients refuse treatment with injectable anticoagulants out of fear, discomfort, anxiety or inconvenience.^{viii}

“Preventing blood clots is a critical priority for physicians treating patients with acute medical illnesses, which is why Janssen is pleased that the FDA approved the use of XARELTO[®] to address this often fatal, yet preventable condition,” said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular & Metabolism, Janssen Research & Development, LLC. “Rather than facing daily injections with older anticoagulants, patients now have a new oral treatment option that will help prevent blood clots, both in the hospital and after hospital discharge.”

About the Phase 3 Clinical Program

More than 20,000 patients with acute medical illnesses were evaluated in the Phase 3 clinical program^{ix,x}, which includes the MAGELLAN and MARINER studies.

[Published in 2013](#), MAGELLAN evaluated the use of XARELTO[®] in preventing VTE in hospitalized patients with an acute medical illness and restricted mobility, starting with their hospital stay and continuing through post-hospital discharge. The study met its two co-primary efficacy endpoints, with XARELTO[®] demonstrating non-inferiority to enoxaparin, a low-molecular-weight heparin (LMWH), in short-term use (10 ± 4 days) and superiority in long-term use (35 ± 4 days) compared to short-term use of enoxaparin followed by placebo. The combined rates of major and non-major clinically relevant bleeding were higher in the XARELTO[®] group.

An [important post-hoc analysis from MAGELLAN](#) found that, by applying five additional exclusionary criteria to remove patients at high risk for bleeding due to active gastroduodenal ulcer, recent bleeding, active cancer, history of severe bronchiectasis or pulmonary cavitation, or dual antiplatelet therapy at baseline, researchers established a favorable benefit-risk profile for VTE prevention with XARELTO[®].

Additionally, building on the foundation from MAGELLAN, the Phase 3 MARINER trial was conducted in a similar population of acutely ill medical patients. [Published in](#)

[2018](#), MARINER evaluated XARELTO® for the prevention of VTE and VTE-related death following hospital discharge compared to placebo. While XARELTO® did not reduce the composite endpoint of VTE and VTE-related death, it did significantly reduce symptomatic VTE with consistent and favorable safety, reinforcing the positive benefit-risk profile of XARELTO®.

MAGELLAN and MARINER are part of the EXPLORER clinical research program for XARELTO®. As a collaborative effort between Janssen and its development partner Bayer, EXPLORER has generated important clinical evidence on the safety and efficacy of XARELTO®. Many studies in the program are designed to seek additional indications or expand the label for XARELTO® to benefit more patients in need of therapies for their cardiovascular disease. By the time of its completion, more than 275,000 patients will have participated in the EXPLORER program, other completed and ongoing clinical trials, investigative registries and non-interventional studies.

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) or peripheral artery disease (a condition where the blood flow to the legs is reduced)

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, who have a history of blood clots.

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 or peripheral artery disease:**
 - Take XARELTO® 2 times a day with or without food.
 - If you miss a dose of XARELTO®, take your next dose at your regularly scheduled time.

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 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 see [accompanying or click here or attached — pick appropriate location] full Prescribing Information, including Boxed Warnings, and Medication Guide for XARELTO®.

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

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 (T2D) 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, and 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/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 XARELTO® (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 December 30, 2018, 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. 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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^{vii} Schünemann et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. *Blood Advances*. 2018;2:3198-3225.

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