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FDA Approves New 10 mg Dosing for XARELTO® (rivaroxaban) to Reduce the Continued Risk of Venous Thromboembolism (VTE)

XARELTO® is the only Factor Xa inhibitor to demonstrate superior efficacy in reducing the continued risk of recurrent VTE after initial treatment and with major bleeding rates similar to aspirin

Phase 3 EINSTEIN CHOICE study shows XARELTO® 10 mg reduced the risk of recurrent VTE by 74 percent

TITUSVILLE, NJ, OCTOBER 30, 2017 – Janssen Pharmaceuticals, Inc. announced today the U.S. Food and Drug Administration (FDA) approved the 10 mg once-daily dose of XARELTO® (rivaroxaban) for reducing the continued risk for recurrent venous thromboembolism (VTE) after completing at least six months of initial anticoagulation therapy. This approval follows a FDA Priority Review and is based on data from EINSTEIN CHOICE, the only clinical study to find that a Factor Xa inhibitor, specifically XARELTO®, demonstrates superior efficacy in reducing the continued risk of recurrent VTE and with major bleeding rates similar to aspirin.

VTE includes deep vein thrombosis (DVT), a blood clot in a deep vein (often the legs), and pulmonary embolism (PE), a clot that travels to the lung. It is the third most common cause of cardiovascular death worldwide, after heart attack and stroke.

"We believe the availability of the 10 mg XARELTO® dose will change clinical practice and the management of VTE recurrence," said Paul Burton, MD, PhD, FACC, Vice President, Medical Affairs, Janssen. "The landmark EINSTEIN program results yet again demonstrate XARELTO® is a safe and highly effective option, not only for the initial treatment of a VTE, but also for the continued prevention of a recurrent event."

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With this approval, the XARELTO® prescribing information provides instructions for physicians to begin treatment with XARELTO® 15 mg, dosed twice daily, for the first 21 days after a VTE occurrence. On day 22 through at least day 180, the daily dose decreases to XARELTO® 20 mg once daily. After at least 180 days (6 months), physicians can prescribe XARELTO® 10 mg once daily in patients at continued risk for DVT and/or PE.

"If anticoagulation therapy is stopped, up to 20 percent of patients will have a recurrent VTE within three years. To prevent this, physicians have long debated how best to extend anticoagulant use beyond the initial treatment window," said Jeffrey Weitz, MD, FRCP(C), FACP, Professor, Departments of Medicine and Biochemistry and Biomedical Sciences, McMaster University, and Executive Director, Thrombosis & Atherosclerosis Research Institute. "The FDA's approval of the 10 mg dose of XARELTO® for preventing recurrent VTE, along with clinical evidence confirming the superiority of XARELTO® over aspirin for extended VTE prevention, means we can finally put this debate to rest."

The FDA's approval of the XARELTO® 10 mg once-daily dose was based on the EINSTEIN CHOICE study results. The EINSTEIN CHOICE study evaluated patients with VTE who were already treated with six to 12 months of initial anticoagulation therapy and then received XARELTO® 10 mg once daily, XARELTO® 20 mg once daily or aspirin 100 mg once daily for up to an additional 12 months of treatment. Patients taking either XARELTO® dose had significantly fewer recurrent VTE compared to those taking aspirin. Specifically, XARELTO® 10 mg reduced the risk of recurrent VTE by 74 percent and XARELTO® 20 mg by 66 percent. All three treatment groups had low rates of major bleeding (0.4 percent with XARELTO® 10 mg, 0.5 percent with XARELTO® 20 mg, 0.3 percent with aspirin).

In September 2017, Janssen's development partner Bayer announced the Committee for Medicinal Products for Human Use of the European Medicines Agency granted a positive opinion to update the XARELTO® label to include the 10 mg once-daily dose in the European Union; the European Commission granted approval on October 19, 2017.

About EINSTEIN CHOICE

EINSTEIN CHOICE is a Phase 3, global, randomized, double-blind, superiority study that compared the efficacy and safety of two doses of XARELTO® (10 mg and 20 mg once daily) with aspirin 100 mg once daily for the management of VTE. The study met its primary efficacy endpoint, finding both XARELTO® doses to be superior to aspirin in reducing the risk of recurrent VTE. There were 3,365 patients from 31 countries included in the study analysis. People who required extended anticoagulation at therapeutic doses were not included, as the study's objective was to investigate patients for whom the treating physician was uncertain about the need for continuing anticoagulant therapy.

Data from EINSTEIN CHOICE were presented during a joint American College of Cardiology/*Journal of the American Medical Association* Late-Breaking Clinical Trials session at the American College of Cardiology's 66th Annual Scientific Session in March 2017 and simultaneously published in *The New England*

Journal of Medicine.

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® and its potential role in addressing critical unmet medical needs. Several studies in the program, including EINSTEIN CHOICE, are designed to seek additional indications or expand the label for XARELTO® 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®?

XARELTO® 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® and warfarin compare in reducing the risk of stroke.

XARELTO® is also a prescription medicine used to treat deep vein thrombosis and pulmonary embolism, 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® 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.

MEDICATION GUIDE
XARELTO® (zah-REL-toe)
(rivaroxaban) tablets

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 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 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:
  - nose bleeds that happen often
  - unusual bleeding from the 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), loss of control of the bowels or bladder (incontinence).

- **XARELTO is not for patients with artificial heart valves.**

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. 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 lungs (pulmonary embolism)
    - 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.
    - reduce the risk of forming a blood clot in the legs and lungs of people who have just had hip or knee replacement surgery

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

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 in XARELTO. See the end of this leaflet for a complete list of ingredients in XARELTO.

Before you take XARELTO, tell your doctor about all of 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 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. It is not known if XARELTO passes into your breast milk. You and your doctor should decide if you will take XARELTO or 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 over-the-counter medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO 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 doses at the same times 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 tablet whole, talk to your doctor about other ways to take XARELTO.
- Your doctor will decide how long you should take XARELTO. Do not stop taking XARELTO without talking with your doctor first.
- 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 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.

What are the possible side effects of XARELTO?

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

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store XARELTO?

- Store XARELTO at room temperature between 68°F to 77°F (20° to 25°C).

Keep XARELTO and all medicines out of the reach of children.

General information about XARELTO.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use XARELTO for a condition for which it was not prescribed. Do not give XARELTO to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or doctor for information about XARELTO that is written for health professionals.

What are the ingredients in XARELTO?

Active ingredient: rivaroxaban

Inactive ingredients: croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and sodium lauryl sulfate.

The proprietary film coating mixture for XARELTO 10 mg tablets is Opadry® Pink and contains: ferric oxide red, hypromellose, polyethylene glycol 3350, and titanium dioxide.

The proprietary film coating mixture for XARELTO 15 mg tablets is Opadry® Red and contains: ferric oxide red, hypromellose, polyethylene glycol 3350, and titanium dioxide.

The proprietary film coating mixture for XARELTO 20 mg tablets is Opadry® II Dark Red and contains: ferric oxide red, polyethylene glycol 3350, polyvinyl alcohol (partially hydrolyzed), talc, and titanium dioxide.

Finished Product Manufactured by: Janssen Ortho, LLC Gurabo, PR 00778 or Bayer AG 51368 Leverkusen, Germany

Manufactured for: Janssen Pharmaceuticals, Inc. Titusville, NJ 08560 Licensed from: Bayer HealthCare AG 51368
Leverkusen, Germany

For more information call 1-800-526-7736 or go to www.XARELTO-US.com.

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Please click here for full Prescribing Information, including Boxed Warnings.

For more information about XARELTO®, visit www.xarelto.com.

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. Follow us on Twitter at @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 the availability and benefits of the 10 mg dose of 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 Pharmaceuticals, Inc., 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, 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.