Johnson & Johnson

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Pooled Analysis Confirms XARELTO® has Similar Efficacy and Reduces the Incidence of Major Bleeding by Nearly Half Compared to Standard of Care in Treatment of DVT and PE

Analysis Published in the Thrombosis Journal

RARITAN, N.J., September 20, 2013 - Janssen Pharmaceuticals, Inc. (Janssen) announced today a newly published, pooled analysis of the Phase III EINSTEIN trial program, showing XARELTO® (rivaroxaban) is as effective as the standard of care in reducing the risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) in people with symptomatic DVT or PE, while reducing the incidence of major bleeding by 46 percent. The analysis also found safety and efficacy outcomes for XARELTO® were consistent across four subgroups of participants: fragile subjects, those with cancer, subjects with a history of a recurrent venous thromboembolism (VTE) and those presenting with a large clot. These findings were published in Volume 11, Issue 21 of the Thrombosis Journal.

DVT is a condition in which blood clots form in one of the large, deep veins, usually in the legs. PE is a serious condition that most commonly occurs when part or all of a DVT dislodges and travels to the lung, via the heart, where it can partially or completely block a branch of the pulmonary artery. When PE occurs with large clots, multiple clots, or when the patient already has pre-existing heart or lung disease, the event may be fatal. Each year up to 900,000 Americans experience a DVT or PE, resulting in up to 300,000 deaths.

"The current standard of care for treatment of DVT and PE requires a two-drug regimen: a rapidly acting, injectable anticoagulant followed by long-term treatment with an oral Vitamin K antagonist, such as warfarin," said Jack E. Ansell, M.D., MACP, Professor of Medicine at New York University School of Medicine*. "This analysis confirms an oral, single-drug option like XARELTO® can simplify treatment and has a lower incidence of major bleeding compared to standard of care. It effectively reduces the risk of DVT and PE while eliminating the need for routine blood monitoring and frequent dose adjustments."

This pre-specified pooled analysis included results from the EINSTEIN-DVT and EINSTEIN-PE studies. The analysis included more than 8,000 participants, split between the DVT (3,449) and PE (4,833) studies, indicating the XARELTO® treatment benefit can be expected for subjects with either condition. Results from this pooled analysis were presented at the 54th American Society of Hematology (ASH) Annual Meeting in Atlanta in December 2012.

XARELTO® is the most-prescribed novel oral anticoagulant in the U.S. market today and is approved for six clinical uses in the U.S. It has earned the broadest reimbursement profile among novel anticoagulants, with 85 percent of patients on Medicare Part D and 85 percent of commercial patients covered at the lowest branded co-pay. To date, more than 5 million patients have received XARELTO® worldwide and more than 3 million prescriptions have been written for XARELTO® in the U.S.

The EINSTEIN-PE study was an open-label, randomized, non-inferiority trial. The trial compared oral rivaroxaban - 15 mg twice daily for three weeks, followed by 20 mg once daily - with the current standard of care (enoxaparin followed by a Vitamin K Antagonist [VKA]) in subjects with acute symptomatic PE with or without symptomatic DVT. Patients received treatment for six or 12 months. EINSTEIN-PE enrolled 4,833 participants and is the largest study ever conducted in the acute treatment of PE. Results from EINSTEIN-PE were presented at the American College of Cardiology Annual Scientific Sessions, and published in the New England Journal of Medicine in March 2012 (n engl j med 10.1056).

The EINSTEIN-DVT study compared the safety and efficacy of oral rivaroxaban -administered at 15 mg twice daily for three weeks followed by 20 mg once daily - with standard therapy. More than 3,400 participants with acute symptomatic DVT in the deep veins of the knee or thigh, but without any symptoms of PE, were enrolled and received treatment for three, six or 12 months. Results from EINSTEIN-DVT were presented at the annual European Society of Cardiology Congress in August 2010.

This pooled analysis of the EINSTEIN-DVT and -PE studies was pre-specified to be able to assess the overall efficacy and safety of XARELTO® for the treatment of VTE.

*Dr. Ansell was not associated with the EINSTEIN clinical trials and was not compensated for any media work. He has been a paid consultant to Janssen Pharmaceuticals, Inc.

About XARELTO® (rivaroxaban)
XARELTO® works by blocking the blood clotting Factor Xa. XARELTO® does not require routine blood monitoring. Cardiologists start more patients on XARELTO® than any other anticoagulant and it is the only Factor Xa inhibitor approved for six distinct uses:

1. To reduce the risk of blood clots in the legs and lungs of people who have just had knee replacement surgery.
2. To reduce the risk of blood clots in the legs and lungs of people who have just had hip replacement surgery.
3. 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.
4. To treat people with deep vein thrombosis (DVT).
5. To treat people with pulmonary embolism (PE).
6. To reduce the risk of recurrence of DVT or PE following an initial six months of treatment for acute venous thromboembolism.

The extensive program of clinical trials evaluating rivaroxaban makes the compound the most studied oral, Factor Xa inhibitor in the world today. By the time of its completion in 2018, more than 100,000 patients will have participated in EXPLORER, a comprehensive, global research program for XARELTO®.

Janssen Research & Development, LLC, and Bayer HealthCare together are developing rivaroxaban.

For more information about XARELTO®, visit www.xarelto-us.com. The XARELTO® CarePath™ Support Program is a resourc designed for healthcare providers, patients and caregivers. Visit www.xareltocarepath.com or call 1-888-XARELTO to learn more about the XARELTO® CarePath™ resources focused on access, education and adherence.

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®)
  - 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 that 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 tingling, numbness, or muscle weakness, especially in your legs and feet.

XARELTO® is not for patients with artificial heart valves.

WHO SHOULD NOT TAKE XARELTO®?
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®.

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 plan to become pregnant. It is not known if XARELTO® will harm your unborn baby. Tell your doctor right away if you become pregnant while taking XARELTO®. If you take XARELTO® during pregnancy, tell your doctor right away if you have bleeding or symptoms of blood loss.
- 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 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.**See "What is the most important information I should know about XARELTO®?"**

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™, Epitol®)
- 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.

- Your doctor will tell you how much XARELTO® to take and when to take it.
- 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® once or twice a day as prescribed by your doctor.
  - Take XARELTO® with food at the same time each day.
  - If you miss a dose of XARELTO®:
    - **and take XARELTO® 2 times a 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.
    - **and 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 to 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 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®, go to the nearest hospital emergency room or call your doctor right away.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

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.

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 see full Prescribing Information, including Boxed Warnings, and Medication Guide.

About Janssen Pharmaceuticals, Inc.
As a member of the Janssen Pharmaceutical Companies of Johnson & Johnson, Janssen Pharmaceuticals, Inc. is dedicated to addressing and resolving the major unmet medical needs of our time. Driven by our commitment to patients, healthcare professionals, and caregivers, we strive to develop sustainable and integrated healthcare solutions by working in partnership with all stakeholders on the basis of trust and transparency. Our daily work is guided by meeting goals of excellence in quality, innovation, safety, and efficacy in order to advance patient care.

Our company provides medicines for an array of illnesses and disorders in several therapeutic areas. Innovative therapies that Janssen Pharmaceuticals, Inc. offers include ACIPHEX® (rabeprazole sodium), ELMIRON® (pentosan polysulfate sodium), INVEGA® SUSTENNA® (paliperidone palmitate) extended-release injectable suspension, INVOKANA® (canagliflozin tablets), NUCYNTA® ER (tapentadol extended-release tablets), RISPERDAL® CONSTA® (risperidone) Long-Acting Injection and XARELTO® (rivaroxaban). The full prescribing information for INVEGA® SUSTENNA®, NUCYNTA® ER, RISPERDAL® CONSTA® and XARELTO®, including boxed warnings, are available here, here, here, and here.

For more information on Janssen Pharmaceuticals, Inc., visit us at www.janssenpharmaceuticalsinc.com or follow us on Twitter at www.twitter.com/JanssenUS and on YouTube at www.Youtube.com/JanssenUS.

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