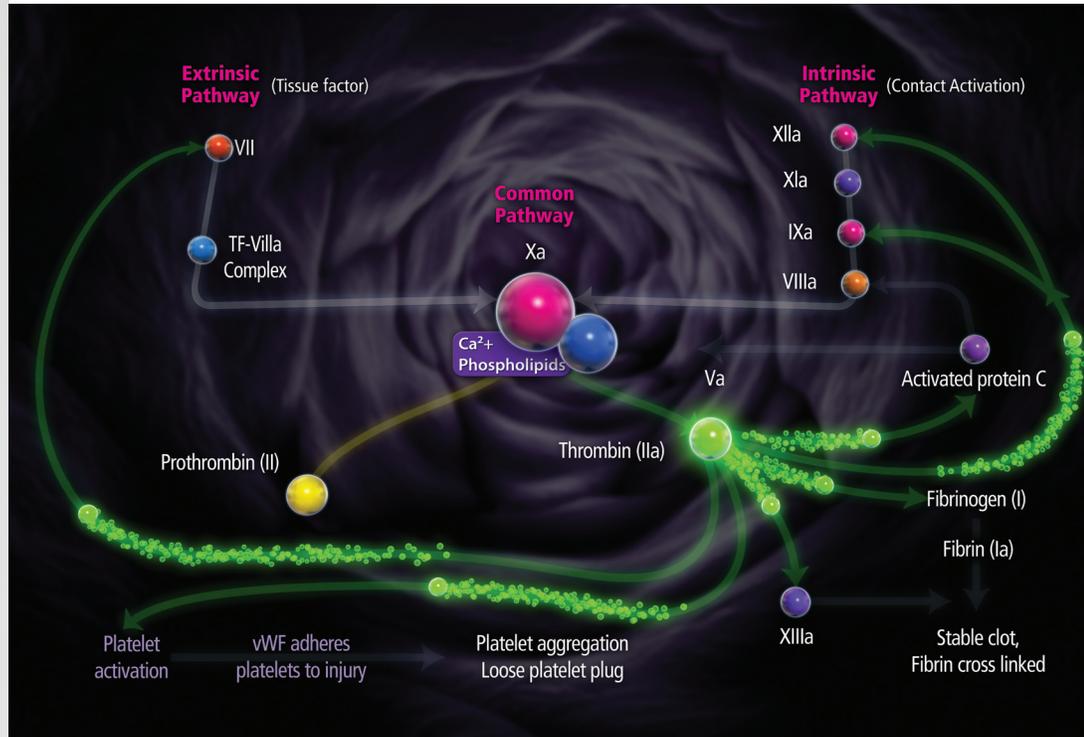


FAST FACTS

About XARELTO[®] (rivaroxaban)

How XARELTO[®] works

- ◆ XARELTO[®] is a once-daily, oral anti-coagulant approved in the United States by the U.S. Food and Drug Administration (FDA):
 - To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (AFib). There are limited data on the relative effectiveness of XARELTO[®] and warfarin in reducing the risk of stroke and systemic embolism when warfarin therapy is well-controlled
 - For the prevention (prophylaxis) of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE) in patients following knee or hip replacement surgery
- ◆ The extensive program of clinical trials evaluating XARELTO[®] in these and other potential indications makes it the most studied and published oral Factor Xa inhibitor in the world today¹
- ◆ To date, XARELTO[®] is approved in more than 110 countries worldwide and has been successfully launched by Bayer HealthCare in more than 80 countries including Australia, Canada, China, Mexico and within the European Union for the prevention of venous thromboembolism in adult patients undergoing elective knee or hip replacement surgery. Janssen Pharmaceuticals, Inc. holds marketing rights for XARELTO[®] in the U.S.
- ◆ Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD) and Bayer HealthCare are developing XARELTO[®] jointly for a broad range of disorders in which blood clotting plays a major role



By selectively binding to Factor Xa, rivaroxaban inhibits the conversion of prothrombin to thrombin

XARELTO[®] is a Factor Xa inhibitor.² Factor Xa has emerged as a target for new anticoagulants due to its pivotal role in the coagulation cascade where it stimulates the production of thrombin, the enzyme that promotes clot formation.^{2,3}

Factor Xa regulates thrombin generation, instead of inhibiting the action of thrombin, which may allow for other coagulation processes to continue.³ Selective inhibition of Factor Xa is expected to help modulate the formation of the prothrombinase complex to reduce the so-called "thrombin burst."^{3,4}



Clinical trial program

Johnson & Johnson Pharmaceutical Research & Development, L.L.C. and Bayer HealthCare are developing rivaroxaban jointly. The companies are evaluating rivaroxaban in clinical trial programs for a broad range of disorders in which blood clotting plays a major role. The extensive program of clinical trials evaluating rivaroxaban makes it the most studied oral, Factor Xa inhibitor in the world today.¹ By the time of its completion, more than 75,000 patients will have participated in the rivaroxaban clinical development program.

Important Safety Information

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 an 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 or forming blood clots in other parts of your body.**

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

For all people taking XARELTO®:

- ◆ XARELTO® can cause bleeding which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner 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®)
- prasugrel (Effient®)
- ticagrelor (Brilinta®)

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:

- ◆ tingling, numbness or muscle weakness, especially in your legs. This is particularly important if you had a procedure called spinal or epidural puncture as part of your anesthesia during surgery.
- ◆ any unexpected bleeding, or bleeding that lasts a long time (such as nose bleeds that happen often, unusual bleeding from gums, or 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 (look 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

WHO SHOULD NOT TAKE XARELTO®?

Do not take XARELTO® if you:

- ◆ currently have abnormal or 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 planning to become pregnant
- ◆ Are breastfeeding or plan to 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.

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.**

For people who have:

- ◆ **atrial fibrillation:** Take XARELTO® 1 time a day **with your evening meal.** Stopping XARELTO® may increase your risk of having a stroke or forming blood clots in other parts of your body.
- ◆ **hip or knee replacement surgery:** Take XARELTO® 1 time a day **with or without food.**

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 will have XARELTO® available to avoid missing any doses.

If you miss a dose of XARELTO®, take it as soon as you remember on the same day.

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®?

XARELTO® can cause bleeding which can be serious, and rarely may lead to death. *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.

Discuss any side effects with your doctor. 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 (526-7736).

Please see full **Product Information**, including **Medication Guide**.

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References:

1. Lopes RD, Piccini JP, Hylek EM, et al. Antithrombotic therapy in atrial fibrillation: guidelines translated for the clinician. *J Thromb Thrombolysis* 2008; 26:167-174.
2. Perzborn E, Strassburger J, Wilmen A, et al. In vitro and in vivo studies of the novel antithrombotic agent BAY 59-7939 – an oral, direct Factor Xa inhibitor. *J Thromb Haemost* 2005; 3: 514-521.
3. Turpie AG. Oral, direct factor Xa inhibitors in development for the prevention and treatment of thromboembolic diseases. *Arterioscler Thromb Vasc Biol* 2007; 27:1238-1247.
4. Hoffman M, Monroe DM. Coagulation 2006: a modern view of hemostasis. *Hematol Oncol Clin North Am.* 2007; 21(1):1-11.