

About Rivaroxaban

a. What is rivaroxaban?

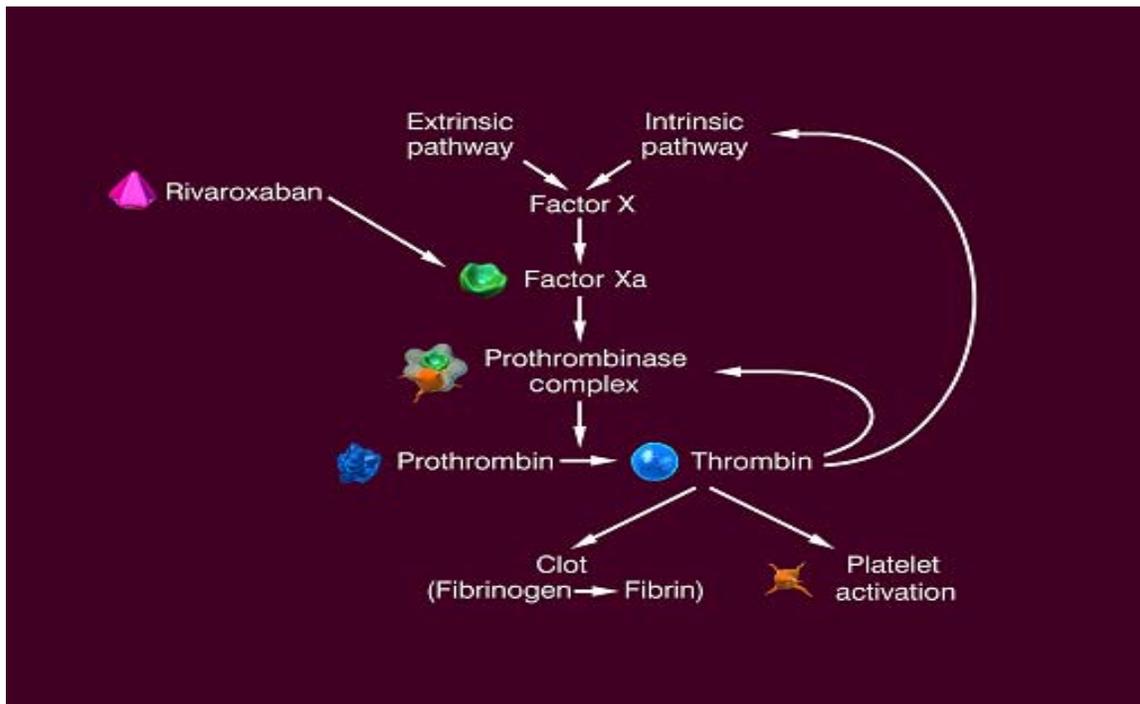
Rivaroxaban is an investigational, oral, once-daily, anticoagulant in advanced clinical development for a range of patients who could benefit from the prevention and/or treatment of blood clots. Blood clots and resulting complications, such as embolisms, are one of the leading global causes of mortality and a concern for many patient populations, including:

- Those undergoing major orthopedic surgery of the lower limbs (venous thromboembolism [VTE] prevention after elective, major orthopedic surgery)
- Those with heart rhythm disturbances at risk for stroke (stroke prevention in patients with atrial fibrillation)
- Those at risk for acute heart attack (secondary prevention in acute coronary syndrome)
- Patients suffering from deep vein thrombosis or pulmonary embolism (VTE treatment)

Rivaroxaban is a direct Factor Xa inhibitor. By specifically inhibiting the action of Factor Xa,¹ rivaroxaban targets the blood coagulation cascade at a pivotal point where thrombin, the enzyme that promotes clot formation, is generated.

Factor Xa has emerged as an attractive target for new anticoagulant² therapies due to its central point in the blood-clotting cascade, where it stimulates the production of thrombin, the enzyme that promotes clot formation.³ By regulating the production of thrombin, direct Factor Xa inhibitors control the blood-clotting process at a pivotal point in the coagulation cascade. One molecule of Factor Xa leads to the formation of about 1,000 thrombin molecules,⁴ suggesting that direct Factor Xa inhibitors may be able control the clotting process before it becomes too difficult to manage. The targeted action of direct Factor Xa inhibitors regulates thrombin generation rather than inhibiting the action of thrombin itself, which is required for maintaining blood coagulation in response to tissue damage.

Oral direct Factor Xa inhibitors also allow patients to be on the same treatment in the hospital and at home, where they may require treatment to deal with continued risk of developing life-threatening complications.



Simplified blood-clotting cascade and inhibition by Factor Xa inhibitors

b. Clinical trials program

To date, rivaroxaban is the most studied oral, direct Factor Xa inhibitor in development. More than 20,000 patients have been evaluated in the completed Phase II programs and enrolled thus far in the Phase III programs. Almost 50,000 patients are expected to be enrolled in the rivaroxaban clinical development program, which will evaluate rivaroxaban in the prevention and treatment of a broad range of acute and chronic blood-clotting disorders listed below:

- **RECORD:** VTE prevention in orthopedic surgery patients (Phase III)
- **EINSTEIN:** VTE treatment (Phase III)
- **ROCKET AF:** Stroke prevention in patients with atrial fibrillation (Phase III)
- **ATLAS ACS TIMI 46:** Secondary prevention of acute coronary syndrome (Phase II)

Specific information on these trials may be found on www.clinicaltrials.gov

The RECORD data presented at the 49th Annual Meeting of the American Society of Hematology (ASH) in December 2007, showed that rivaroxaban was statistically superior to enoxaparin, the current standard of care, for the prevention of venous blood clots in patients undergoing total hip or knee replacement surgery, with similar rates of major and non-major bleeding episodes.

Rivaroxaban is being jointly developed by Bayer HealthCare AG and Johnson & Johnson Pharmaceutical Research & Development, L.L.C. Bayer HealthCare submitted a regulatory filing to the European Agency for the Evaluation of Medicinal Products (EMA) at the end of October 2007 for approval to market rivaroxaban in the EU for the prevention of VTE in patients undergoing major orthopedic surgery of the lower limbs. Upon regulatory approval, rivaroxaban will be commercialized in Europe by Bayer Schering Pharma. A filing for rivaroxaban for a similar indication in the United States is planned in 2008, where upon approval, it will be commercialized by Scios Inc. and Ortho-McNeil, Inc., both of which are wholly-owned subsidiaries of Johnson & Johnson.

References

1. Perzborn E. J Thromb Haemost 2005; 3: 514-21.
2. Eriksson BI. J Thromb Haemost 2006; 4: 121-8.
3. Turpie AG. J Thromb Haemost 2005; 3: 2479-86.
4. Agnelli G. Circulation 2007; 116: 180-7.