

# About Xarelto® (rivaroxaban)

## Fast facts

- ◆ Xarelto® (rivaroxaban) is a once-daily, oral direct Factor Xa inhibitor approved in more than 100 countries worldwide for the prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery
- ◆ Rivaroxaban does not require coagulation monitoring<sup>1</sup>
- ◆ Rivaroxaban is in advanced development in a range of other indications for the prevention and/or treatment of potentially deadly blood clots<sup>2</sup>
- ◆ The extensive clinical trial program for rivaroxaban makes it the most studied oral Factor Xa inhibitor in the world today<sup>3</sup>
- ◆ Rivaroxaban has the most extensive Phase III Clinical Trial Program of any new oral anticoagulant\*
- ◆ Rivaroxaban has been successfully launched in more than 75 countries by Bayer Schering Pharma and has reached the market leader position amongst the new oral anticoagulants

## What is Xarelto® (rivaroxaban)?

Xarelto® (rivaroxaban) is a novel once-daily, oral direct Factor Xa inhibitor<sup>4</sup> approved in more than 100 countries worldwide for the prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery. By targeting Factor Xa at a pivotal stage in the blood-clotting process, rivaroxaban inhibits thrombin generation rather than inhibiting the action of thrombin itself.<sup>1</sup> Thrombin is an enzyme in the blood clotting cascade that promotes the formation of blood clots.<sup>5</sup>

Rivaroxaban requires no dose adjustment for age, sex or body weight and no routine coagulation monitoring due to its predictable pharmacokinetic (PK) and pharmacodynamic (PD) profile.<sup>3,5,6</sup> Due to this, rivaroxaban promises to overcome the disadvantages of current standard treatments in the out-patient setting, such as the need for regular injections, and coagulation monitoring, as well as frequent food and drug interactions.<sup>1,7</sup>

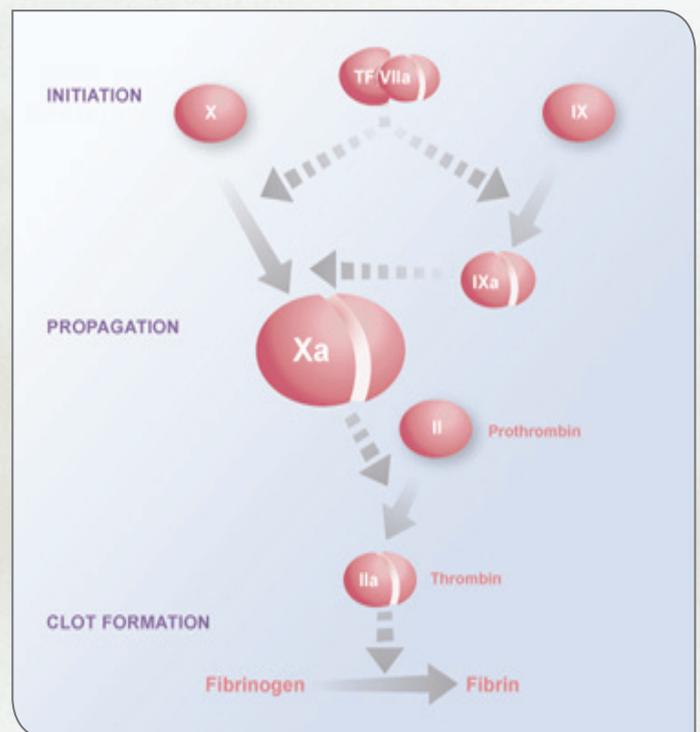


Fig.1 Simplified coagulation cascade  
Source: [www.thrombosisadviser.com](http://www.thrombosisadviser.com)

## Efficacy and Safety at a Glance

Rivaroxaban is the only new oral anticoagulant that has consistently demonstrated superior efficacy over enoxaparin in VTE prevention in adult patients following elective hip or knee replacement surgery.<sup>8,9,10,11</sup>

In the pooled analysis of RECORD 1-3, rivaroxaban was shown to be significantly more effective at two weeks than injectable

enoxaparin at reducing the composite of symptomatic VTE and all-cause mortality following major orthopedic surgery. The analysis also demonstrated that patients treated with rivaroxaban experienced no significant difference in the rate of major bleeding compared to enoxaparin-treated patients.<sup>6</sup>

## Value of the new oral anticoagulants

Property	Benefit	Therapies without this benefit
<b>Oral administration</b>	Convenient use both in and out of hospital	Parenteral drugs, such as the heparins
<b>Predictable PK/PD profile</b>	Safe and effective regulation of coagulation from the first dose and throughout therapy	Warfarin/vitamin K antagonists
<b>Fixed dose</b>	No dose adjustment for majority of patients	Warfarin/vitamin K antagonists
<b>No routine coagulation monitoring</b>	Saves healthcare costs (fewer hospital/physician visits) and patients' time	Warfarin/vitamin K antagonists
<b>Rapid onset and offset of action</b>	Anticoagulation from the first dose, which stops quickly after cessation of therapy	Warfarin/vitamin K antagonists
<b>Low risk of food and drug interactions</b>	Hassle-free use regardless of concomitant use of other medication/diet	Warfarin/vitamin K antagonists

## RECORD: Venous Blood Clot Prevention in Major Orthopedic Surgery

*Regulation of Coagulation in major Orthopedic surgery reducing the Risk of DVT and PE.*<sup>8,9,10,11</sup> RECORD is a global program of four trials in more than 12,500 patients, comparing rivaroxaban taken as one tablet, once daily with subcutaneous enoxaparin in the prevention of VTE after elective (planned) hip or knee replacement surgery.

- ◆ RECORD1 and 2: total **hip** replacement surgery
- ◆ RECORD3 and 4: total **knee** replacement surgery

The results confirm that rivaroxaban was superior to enoxaparin-based treatment regimens for the prevention of VTE after total hip or knee replacement surgery with low rates of major bleeding that were not statistically different from the comparator.

## Other Rivaroxaban Phase III Clinical Trials

The extensive program of clinical trials evaluating rivaroxaban makes it the most studied oral, direct Factor Xa inhibitor in the world today.<sup>3</sup> In total, more than 65,000 patients will be enrolled into the rivaroxaban clinical development Phase II and III program which, in addition to RECORD includes:

- ◆ **EINSTEIN:** Treatment and secondary prevention of VTE
- ◆ **ROCKET AF:** Stroke prevention in patients with atrial fibrillation (SPAF)
- ◆ **MAGELLAN:** Prevention of VTE in medically ill patients
- ◆ **ATLAS ACS TIMI 51:** Secondary prevention of acute coronary syndrome (ACS)



## Development and Availability

Rivaroxaban was developed in Bayer Schering Pharma's Wuppertal laboratories in Germany, and is being jointly developed by Bayer HealthCare and Johnson & Johnson Pharmaceutical Research & Development, L.L.C. The therapy

is approved in more than 100 countries worldwide and has been successfully launched in 75 countries by Bayer Schering Pharma, where it has reached the market leader position among the new oral anticoagulants.

\* <http://clinicaltrials.gov>

**RECORD1:** Eriksson BI, et al. *N Engl J Med.* 2008;358(26):2765-2775

**RECORD2:** Kakkar AK, et al. *Lancet.* 2008;372(9632):29-37

**RECORD3:** Lassen MR, et al. *N Engl J Med.* 2008; 358(26):2776-2786

**RECORD4:** Turpie AGG, et al. *Lancet.* 2009;373(96761):1673-1680

**MAGELLAN:** <http://clinicaltrials.gov/ct2/show/NCT00571649>

**EINSTEIN DVT:** <http://clinicaltrials.gov/ct2/show/NCT00440193>

**EINSTEIN PE:** <http://clinicaltrials.gov/ct2/show/NCT00439777>

**EINSTEIN EXT:** Buller HR. Abstract presented at 51<sup>st</sup> ASH annual meeting and exposition, New Orleans, USA, December 5-8, 2009

**ROCKET AF:** <http://clinicaltrials.gov/ct2/show/NCT00494871>

**J-ROCKET AF:** <http://clinicaltrials.gov/ct2/show/NCT00973323>

**ATLAS ACS TIMI 51:** <http://clinicaltrials.gov/ct2/show/NCT00809965>

## References

- 1 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
- 2 Khoo CW, Tay KH, Shantsila E, Lip GYH. Novel oral anticoagulants. *Int J Clin Pract.* 2009;63:630-641
- 3 International Congress on Thrombosis: Rivaroxaban is first novel oral anticoagulant to significantly reduce the composite outcome of symptomatic VTE and death [press release]. Leverkusen, Germany: Bayer HealthCare AG; June 30, 2008
- 4 Perzborn E. In vitro and in vivo studies of the novel antithrombotic agent BAY 59-7939 – an oral, direct Factor Xa inhibitor. *J Thromb Haemost.* 2005;3:514-21
- 5 Medline Plus Medical Dictionary, Thrombin, 2009 <http://www2.merriamwebster.com/cgi-bin/mwmednlm?book=Medical&va=thrombin>
- 6 Eriksson BI, Kakkar AK, Turpie AG et al. Oral rivaroxaban for the prevention of symptomatic venous thromboembolism after elective hip and knee replacement. *The J Bone Joint Surg. Br.* 2009;91-B:644-52
- 7 Haas S. New oral Xa and IIa inhibitors: updates on clinical trial results. *J Thromb Thrombolysis.* 2008;25:52-60
- 8 Kakkar AK, Brenner B, Dahl OE et al. Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty; A double-blind, randomised controlled trial. *Lancet.* 2008;372:31-9
- 9 Lassen MR, Angeno W, Borris LC et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *N Engl J Med.* 2008;358:2776-86
- 10 Turpie AG, Lassen MR, Davidson BL et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): a randomized trial. *Lancet.* 2009;373:1673-80
- 11 Eriksson BI, Borris LC, Friedman RJ et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Eng J Med* 2008;358:2765-75

To learn more about thrombosis please visit [www.thrombosisadviser.com](http://www.thrombosisadviser.com)

To learn more about 'Xarelto' please visit [www.xarelto.com](http://www.xarelto.com)



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