About Xarelto® (Rivaroxaban)

What is Xarelto® (Rivaroxaban)?

'Xarelto' is a highly effective, novel oral anticoagulant (OAC) developed to prevent and treat dangerous blood clots, with the potential to improve clinical outcomes and quality of life for a broad range of patients with, or at risk of venous arterial thromboembolism (VAT).

Benefits of 'Xarelto' include[1]:

- Oral administration
- Rapid onset of action
- Predictable anticoagulation without need for routine monitoring or dose adjustment
- Low risk of drug-drug interactions
- No significant food interactions

'Xarelto' is approved for five indications in seven distinct areas of use, consistently protecting patients from blood clots across more VAT conditions than any other novel OAC[1]

VTE Prevention in Adult Patients Following Elective Hip or Knee Replacement Surgery:

For adult patients who have had major orthopaedic surgery, one 10 mg tablet, once-daily 'Xarelto' provides superior protection against venous thromboembolism (VTE) with similar safety compared to the low molecular weight heparin (LMWH) enoxaparin[2]. Patients on 'Xarelto' also experience fewer symptomatic VTEs and fewer bleeding complications post-surgery, resulting in shorter hospital stays[3,4].

PE Treatment and Prevention:

For adult patients with pulmonary embolism (PE), 'Xarelto' is the first single-drug solution and the only novel OAC approved for acute treatment and the prevention of recurrent VTE. As a single-drug solution, 'Xarelto' is highly effective in protecting against life-threatening PEs without the need for injections or routine coagulation monitoring[5], providing simplified patient management from hospital to home. Additionally,'Xarelto' significantly lowers the risk of major bleeding compared with the dual-drug approach of LMWH and VKA[6].

DVT Treatment and Prevention:

For adult patients with deep vein thrombosis (DVT), 'Xarelto' is the first single-drug solution and the only novel OAC approved for acute treatment and the prevention of recurrent VTE. As the single-drug solution, 'Xarelto' is highly effective in providing simplified patient management from hospital to home wihtout the need for injections or routine coagulation monitoring[1,5,6]. Additionally, 'Xarelto' has a similar low rate of major bleeding compared with the dual-drug approach of LMWH and vitamin K antagnoists (VKA)[5].

Stroke Prevention in Patients with Non-Valvular AF:

For adult patients with atrial fibrillation (AF), once-daily 'Xarelto' offers highly effective stroke prevention without the need for routine coagulation monitoring[1,7]. Importantly, 'Xarelto' can prevent stroke without increasing the risk of heart attack and lowers the rate of the most feared intracranial and fatal bleeds, compared with warfarin while providing similar overall bleeding rates[1,8]. It is also the only novel OAC with a specific dose evaluated for patients with renal impairment.

Prevention of Atherothrombotic Events after an ACS in Patients with Elevated Cardiac Biomarkers:

For patients with acute coronary syndrome (ACS), 'Xarelto' 2.5 mg twice daily in combination with standard antiplatelet therapy can help reduce atherothrombotic events (CV death, heart attack and stroke) by continuing to provide more complete long-term protection than antiplatelet therapy alone[9,10].

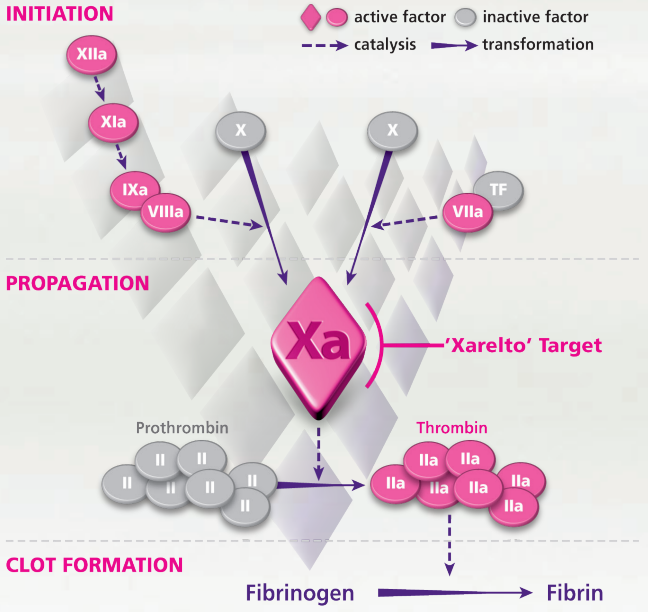
How Does 'Xarelto' Work?

'Xarelto' is an oral direct Factor Xa Inhibitor, protecting against blood clots by selectively targeting Factor Xa, an enzyme which acts at a pivotal point in the blood-clotting (coagulation) process.

Coagulation requires a complex series of chemical reactions and body signals. This process of chemical reactions is often referred to as the 'Clotting Cascade'. One of the many clotting factors (blood clot proteins) is Factor Xa. Factor Xa is needed to produce thrombin that promotes the formation of blood clots. One molecule of Factor Xa catalyses the formation of approximately 1,000 thrombin molecules via what is known as a 'thrombin burst'[11,12].

Directly targeting and inhibiting Factor Xa prevents the thrombin burst. Selectivity to Factor Xa has been proven to be clinically meaningful. Studies have demonstrated an increase in the anticoagulant efficacy of heparin-based drugs as their selectivity for Factor Xa increases[11].

Targeting Factor Xa to Inhibit Thrombin Generation



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RIVAROXABAN

About Xarelto® (Rivaroxaban) continued...

'Xarelto' has demonstrated clinical benefit in comparison to standard therapy in a broad range of acute and chronic blood-clotting disorders

The Clinical Trial Programme for 'Xarelto'

- The ongoing Clinical Trial Programme investigates 'Xarelto' for the prevention and treatment of a broad range of VAT conditions
- Completed studies in the extensive clinical trial programme involve nearly 100,000 patients making it the most studied and widely published novel OAC in the world today. All ten completed Phase III pivotal trials across five acute and chronic conditions have successfully met or exceeded their primary endpoints, in preventing and or treating VAT disorders

'Xarelto' Regulatory Milestones

Rivaroxaban was discovered by Bayer HealthCare, and is being jointly developed with Janssen Research & Development, LLC. 'Xarelto' is marketed outside the U.S. by Bayer HealthCare and in the U.S. by Janssen Pharmaceuticals, Inc. (a Johnson & Johnson Company).

'Xarelto' Dosing

Prevention of Stroke and Systemic Embolism
in adults with non-valvular Atrial Fibrillation with one or more risk factors

- **20 mg OD** — Patients with CrCl > 49 mL/min with food
- **OR**
- **15 mg OD** — Patients with CrCl 15 to 49 mL/min* with food

Treatment of DVT and PE...
...and Extended Treatment for prevention of recurrent DVT and PE in adults

- **15 mg BID** — Patients with CrCl > 15 mL/min* with food

AFTER 3 WEEKS TRANSITION TO

- **20 mg OD** — Patients with CrCl > 15 mL/min* with food

Prevention of VTE in adults undergoing elective hip or knee replacement surgery

- **10 mg OD** — Patients with CrCl > 15 mL/min*

The initial dose should be taken 6 to 10 hours after surgery once haemostasis has been established

Secondary Prevention of ACS in Combination with Standard Antiplatelet Therapy[a]
in adults with elevated cardiac biomarkers[b]

- **2.5 mg BID** — Patients with CrCl > 15 mL/min*

The initial dose should be taken after stabilization of the ACS event

[a] ASA alone or in combination with a thienopyridine (clopidogrel or ticlopidine) [b] Troponin-I/T; creatine kinase-muscle and brain isoenzyme (CK-MB) * Not indicated in patients with CrCl < 15 ml/min; use with caution in patients with CrCl 15-29 ml/min

To learn more about thrombosis, please visit www.thrombosisadviser.com
To learn more about VAT, please visit www.VATspace.com
To learn more about 'Xarelto', please visit www.xarelto.com

References

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