Rivaroxaban in Venous Thromboembolism (VTE)

Venous Thromboembolism (VTE)

Venous thromboembolism (VTE) is the most common, avoidable cause of hospital death[1].

- The worldwide incidence of VTE is 1 per 1000[2]
- In the EU, more than twice as many people die from VTE than from breast cancer, prostate cancer, AIDS and traffic accidents combined[3]

VTE kills one person every 37 seconds in the Western World[3,4]

37 seconds

Europe alone

>500,000[3,5]

VTE deaths annually

VTE encompasses two serious conditions:

Deep vein thrombosis (DVT) is a blood clot that forms in the veins that lie deep within the muscles, usually in the leg or pelvis. If all or part of the DVT breaks off and the blood clot moves to block a vessel in the lungs, it is known as a **pulmonary embolism (PE)[6]**, which can be rapidly fatal.

Deep vein thrombosis (DVT)

- Even in the absence of a PE, DVT alone can have burdensome and costly consequences such as post-thrombotic syndrome[7]
- The rate of VTE recurrence remains high, with hospital readmission for DVT at 19%[8]

Pulmonary embolism (PE)

- About 1 in 10 deaths that occur in the hospital is caused by pulmonary emboli[10]
- 10–25% of PEs are rapidly fatal[7, 11], usually within 2 hours of the onset of symptoms[12]. PE can reoccur, and if it does, it is usually fatal[13]

Annual estimated incidence of DVT

= 100,000 incidences of DVT

Annual estimated incidence of acute PE

= 100,000 incidences of acute PE

VTE can be difficult to diagnose, so it is important people are aware of the signs and symptoms

Symptoms of DVT can include:
Pain, swelling, redness of the area usually the leg, and dilation of the surface veins; the skin may also be warm to the touch

Symptoms of PE can include:
Acute shortness of breath, chest pain, rapid heart rate and light headedness; some people may also cough blood

Who is at Risk of VTE?

- Patients undergoing major orthopaedic surgery for hip or knee replacement or major surgery for cancer
  - Without preventative treatment, the absolute DVT risk after hip or knee surgery is between 40% and 60%[1]
- Patient-related, predisposing risk factors include inherited thrombophilia, advanced age, obesity, prior VTE and varicose veins[1]
- Patients admitted to hospital for an acute medical condition

Economic burden

The complications associated with VTE and its treatment are frequent and costly. The main drivers of these VTE costs are initial and recurrent events requiring hospitalisation.

- In Europe, the annual cost of managing all-cause VTE has been estimated at approximately €4,000 per patient[14]

€3.1bn[9]
= estimated total annual cost for VTE associated care in Europe

VTE Prevention and Treatment

Anticoagulants are the cornerstone of therapy for prevention and treatment of potentially deadly blood clots, but widely used older therapies are associated with significant drawbacks for the patient that challenge optimal treatment.

- The older therapy for **prevention of VTE** associated with orthopaedic surgery is a class of injectable anticoagulant drugs known as low molecular weight heparins (LMWH)
- The older therapy for **treatment of VTE and long-term prevention** is the complex dual-drug treatment of daily injections of LMWH followed by a transition to long-term oral therapy with a vitamin K antagonist (VKA), such as warfarin. As well as its complex dosing, the dual-drug treatment carries an increased risk of major bleeding[15]

Limitations of older VTE therapies may contribute to their under-utilisation[16], creating challenges for patients and leaving them at risk.

Novel oral anticoagulants (OACs) can overcome the limitations of older anticoagulants to prevent and/or treat venous and arterial thromboembolic (VAT) conditions.

VTE Treatment and Prevention of Recurrence: For adult patients with DVT and PE, rivaroxaban was the first novel OAC approved for acute treatment and the prevention of recurrent VTE.

As the oral, single-drug treatment, rivaroxaban 15 mg twice daily offers fast and effective blood clot regression and protection from early recurrence in the first 21 days without the need for injections or routine coagulation monitoring[17,18,19,20]. Then once-daily rivaroxaban 20 mg can provide enduring protection from the danger of DVT and/or PE recurrence[21] for as long as treatment is needed. Furthermore, oral once-daily rivaroxaban offers patients greater convenience and satisfaction (compared to dual-drug treatment), supporting aherence and persistence that are critical for good patient outcomes[22].

Single-Drug Approach

15 mg BID

After 3 weeks Transition to 20 mgOD

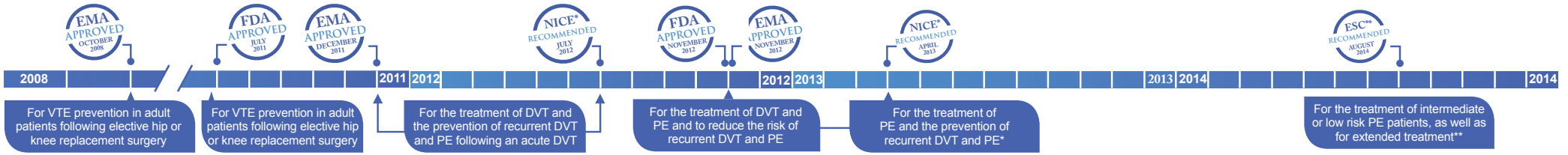
Additionally, rivaroxaban was shown to halve the risk of major bleeding in these patients compared with the dual-drug treatment of LMWH and VKA. Clinically relevant bleeding was comparable with dual-drug treatment[15,23].

ESC Guidelines on the diagnosis and management of acute PE (updated August 2014) recommend rivaroxaban as a treatment option for intermediate or low risk PE patients, as well as for extended treatment[24]

VTE Prevention in Adult Patients Following Elective Hip or Knee Replacement Surgery: For adult patients who have had hip or knee replacement surgery, one 10 mg tablet of rivaroxaban, once-daily provides superior protection against VTE with similar safety compared to the LMWH enoxaparin[17,25,26,27]. In real-world settings, patients on rivaroxaban were also shown to experience fewer symptomatic VTEs and similar rates of major bleeding complications post-surgery compared to older treatments[28].

Rivaroxaban in Venous Thromboembolism (VTE) - Continued

Rivaroxaban VTE Regulatory Milestones



*UK's NICE issued Final Guidance in July 2012 recommending rivaroxaban for National Health Service (NHS) use for the treatment of DVT and the prevention of recurrent DVT and PE following an acute DVT in adults. In April 2013 NICE also issued Final Guidance recommending rivaroxaban for NHS use for the treatment of PE and the prevention of recurrent DVT and PE. The positive NICE appraisals were based on detailed analysis of the clinical and cost-effectiveness benefits of rivaroxaban[29,30] **European Society of Cardiology (ESC) published updated Guidelines on the diagnosis and management of acute PE in August 2014 recommending rivaroxaban as a treatment option for patients with intermediate or low risk of PE, as well as for extended treatment[24]

About Rivaroxaban

Rivaroxaban is the most broadly indicated and most prescribed novel OAC[31] and is marketed under the brand name Xarelto®. Rivaroxaban is approved for five indications across seven distinct areas of use, protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other novel OAC:

- The prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factors
- The treatment of deep vein thrombosis (DVT) in adults
- The treatment of pulmonary embolism (PE) in adults*
- The prevention of recurrent DVT and PE in adults
- The prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip replacement surgery
- The prevention of VTE in adult patients undergoing elective knee replacement surgery
- The prevention of atherothrombotic events (cardiovascular death, heart attack or stroke) after an acute coronary syndrome in adult patients with elevated cardiac biomarkers when co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine

Whilst licences may differ from country to country, across all indications rivaroxaban is approved in more than 125 countries. Rivaroxaban was discovered by Bayer HealthCare, and is being jointly developed with Janssen Research & Development, LLC. Rivaroxaban is marketed outside the U.S. by Bayer HealthCare and in the U.S. by Janssen Pharmaceuticals, Inc. (a Johnson & Johnson Company).

Anticoagulant medicines are potent therapies used to prevent or treat serious illnesses and potentially life threatening conditions. Before initiating therapy with anticoagulant medicines, physicians should carefully assess the benefit and risk for the individual patient. Responsible use of rivaroxaban is a very high priority for Bayer, and the company has developed a Prescribers Guide for physicians and a 'Xarelto' Patient Card for patients to support best practice.

To learn more, please visit https://prescribe.xarelto.com
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

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