About Stroke Prevention in Atrial Fibrillation (AF)

Atrial Fibrillation (AF)

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder.

In AF, the upper chambers (atria) of the heart contract irregularly[1]. As a result, the atria do not empty completely and blood does not flow properly, potentially allowing blood clots to form. These blood clots can break loose and travel to the brain, resulting in a stroke[2].

The number of people with AF is forecast to increase approximately 2.5-fold by 2050[3,4] due to ageing of the population[5] and improved survival following conditions that predispose to AF (such as heart attack)[6].

AF Prevalence Data

AF and Stroke

AF is a strong, independent risk factor for stroke[9]. Undiagnosed AF is a probable cause of many strokes of unknown origin (so-called 'cryptogenic' strokes), and stroke may be the first manifestation of AF.

About Stroke

Stroke is the **second most** common cause of **death worldwide,** responsible for **5 million deaths** each **year**[11]

Strokes can be classified into two major categories:

Ischaemic Stroke
Cause: Interruption of the blood supply due to a blockage (e.g. a blood clot)[12]

Haemorrhagic Stroke
Cause: Rupture of a blood vessel which leads to bleeding inside the brain[12]

Stroke may result in severely restricted movement, paralysis, loss of speech or vision which may be permanent or even death. Stroke is also the leading cause of permanent disability among adults in the U.S.[13]

Approximately **1 in 5** ischaemic strokes are caused by AF[14]

Burden of AF Related Stroke

AF-related stroke devastates lives and is a major healthcare burden.

AF-related strokes are also associated with a **50% likelihood** of **death** within **one year**[18]

The risk of stroke in patients with AF increases with age and with the addition of other risk factors (e.g. high blood pressure, previous stroke, and diabetes)[15]. Patients with AF who have multiple co-morbidities have a greater risk of stroke[15] and represent the population most difficult to protect.

Furthermore, AF-related strokes are more severe, causing disability in more than half of patients and a worse outcome than strokes in patients without AF[16,17,18]. Importantly, the burden of AF-related stroke is likely to become more marked in years to come as the number of people with AF increases.

Current Treatments and Clinical Challenges

Traditional therapy with Vitamin K antagonists (VKAs) such as warfarin makes effective anticoagulation harder than it needs to be for patients and physicians. The limitations of VKAs can leave patients unprotected and for most AF patients, VKAs are no longer the recommended option for stroke prevention[19].

ESC Guidelines for the management of atrial fibrillation (updated August 2012) state that novel oral anticoagulants offer better efficacy, safety and convenience compared with VKAs. The guidelines recommend novel oral anticoagulants as broadly preferable to VKAs in the vast majority of patients with non-valvular AF[19]

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

Benefits of novel OACs include[20]:

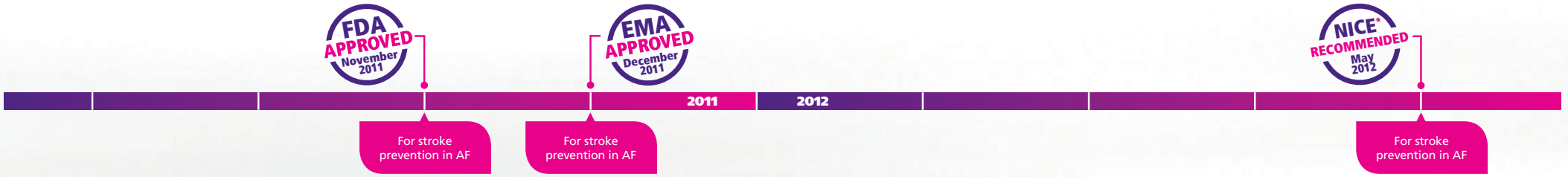
- Predictable anticoagulation without the need for routine coagulation monitoring or frequent dose adjustment
- Low risk of drug-drug interactions
- No significant food interactions

Xarelto® (rivaroxaban) protects patients from blood clots across more VAT conditions than any other novel OAC. For adult patients with AF, once-daily 'Xarelto' offers highly effective stroke prevention without the need for routine coagulation monitoring[20,21]. In general, a once-daily closing regimen has been shown to be preferred by patients and is associated with improved patient adherence compared with regimens with higher dosing frequency.

Importantly, 'Xarelto' prevents 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[20,22]. It is also the only novel OAC with a specific dose evaluated for patients with renal impairment.

About Stroke Prevention in Atrial Fibrillation (AF) continued...

'Xarelto' Stroke Prevention in AF Regulatory Milestones



*UK's NICE issued Final Guidance recommending 'Xarelto' for adult National Health Service (NHS) patients in England and Wales with diagnosed non-valvular AF with one or more risk factors for stroke including patients who are not receiving warfarin due to the challenges and limitations it presents, as well as those who are not achieving stable INR control. The positive NICE appraisal was based on detailed analysis of the clinical and cost-effectiveness benefits of 'Xarelto'[23]

About 'Xarelto'

Rivaroxaban is the most broadly indicated novel oral anticoagulant and is marketed under the brand name Xarelto®. To date, 'Xarelto' is approved for five indications across seven distinct areas of use, consistently 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 venous thromboembolism (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 a thienopyridine (clopidogrel or ticlopidine)

Whilst licences may differ from country to country, across all indications 'Xarelto' is approved in more than 120 countries.

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).

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 'Xarelto' 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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