About Stroke Prevention in Atrial Fibrillation (AF)

What is Atrial Fibrillation (AF)?
Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder and affects approximately 10 million people in Europe, up to 5.1 million people in the U.S. and more than 800,000 people in Japan.

In AF, the upper chambers (atria) of the heart contract irregularly. 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.

What is Stroke?
A stroke is the rapidly developing loss of brain function. Strokes are caused by a lack of blood supply to the brain due to a blood clot or haemorrhage, causing rapid brain-cell death that may result in severely restricted movement paralysis, loss of speech or vision which may be permanent or even death. Strokes can be classified into two major categories:

♦ Ischaemic strokes occur due to an interruption of the blood supply due to a blockage (e.g. a blood clot)
♦ Haemorrhagic strokes occur due to rupture of a blood vessel which leads to bleeding inside the brain

Stroke, from any cause, is the second most common cause of death worldwide, responsible for 5 million deaths each year. Stroke is also the leading cause of permanent disability among adults in the U.S.

AF-Related Stroke
AF-related stroke devastates lives and is a major healthcare burden. AF is a strong, independent risk factor for stroke and accounts for approximately 1 in 5 ischaemic strokes (strokes caused by a blood clot blocking a blood vessel in the brain). Patients with AF are five times more likely to have a stroke compared with the general population. Moreover, previously 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.
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)\(^\text{12}\).

**The Burden of AF-Related Stroke**

Patients with AF who have multiple co-morbidities have a greater risk of stroke\(^\text{12}\) 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\(^\text{13,14,15}\). AF-related strokes are also associated with a 50% likelihood of death within one year\(^\text{15}\).

Importantly, the burden of AF-related stroke is likely to become more marked in years to come because the number of people with AF is forecast to increase approximately 2.5-fold by 2050\(^\text{16,2}\) due to ageing of the population\(^\text{17}\) and to improved survival following conditions that predispose to AF (such as heart attack)\(^\text{18}\).

**Current Treatments and Clinical Challenges**

Vitamin K antagonists (VKAs) such as warfarin are no longer the preferred option for stroke prevention for most AF patients, according to the current ESC Guidelines\(^\text{19}\). The limitations of VKAs can leave patients unprotected. When taking VKAs, patients can be ‘over-anticoagulated’, which can lead to bleeding, particularly intracranial haemorrhage (ICH), or ‘under-anticoagulated’, which increases the risk of a stroke. Other problems with VKAs include unpredictable levels of anticoagulation, the need for routine coagulation monitoring or frequent dose adjustment, drug-drug interactions and dietary restrictions\(^\text{20}\).

Current ESC Clinical Guidelines (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. Since clinical experience remains limited, the novel oral anticoagulants are recommended with strict adherence to approved indications and careful post-marketing surveillance.

**Novel oral anticoagulants** hold the promise of overcoming the limitations of traditional anticoagulants to prevent and or treat venous and arterial thromboembolic (VAT) disease that is responsible for a number of serious and life threatening conditions including deep vein thrombosis (DVT), pulmonary embolism (PE) and stroke. Benefits of novel oral anticoagulants
include predictable anticoagulation without the need for routine coagulation monitoring or frequent dose adjustment, low risk of drug-drug interactions and no dietary restrictions.

**Xarelto® (rivaroxaban) protects patients** from blood clots across more venous and arterial thromboembolic conditions than other novel oral anticoagulants. For AF patients, ‘Xarelto’ combines highly effective stroke protection and similar overall bleeding rates compared to warfarin, but importantly with fewer of the most feared intracranial and fatal bleeding. ‘Xarelto’ also provides these patients a reassuring cardiovascular profile with no increase in myocardial infarctions.21

♦ In November 2011, ‘Xarelto’ received approval in the U.S. to reduce the risk of stroke and systemic embolism in patients with non-valvular AF

♦ In December 2011, ‘Xarelto’ received further marketing approval in the EU for the prevention of stroke and systemic embolism in patients with non-valvular AF, offering a one tablet, once-daily, fixed dose treatment option for patients at risk of stroke, including those with multiple comorbidities who are considered more difficult to protect21

♦ In May 2012, the UK’s National Institute for Health and Clinical Excellence (NICE) issued a Final Appraisal Determination (FAD) recommending ‘Xarelto’ as a therapeutic option for adult National Health Service (NHS) patients in England and Wales with diagnosed non-valvular AF with one or more risk factors for stroke. Importantly, this includes AF 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 guidance follows a rigorous assessment by NICE of the clinical and cost-effectiveness benefits of ‘Xarelto’22
References
About Xarelto® (Rivaroxaban)
Rivaroxaban is the most broadly indicated novel oral anticoagulant and is marketed under the brand name Xarelto®. To date, Xarelto has been approved for use in the following venous arterial thromboembolic (VAT) indications:

- The prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factors in more than 70 countries worldwide
- The treatment of deep vein thrombosis (DVT) and prevention of recurrent DVT and pulmonary embolism (PE) in adults in more than 70 countries worldwide
- The prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery in more than 120 countries worldwide

Since the first approval of Xarelto in 2008 in the orthopaedic setting, more than two and a half million patients worldwide have received Xarelto in daily clinical practice in this indication alone.

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 high priority for Bayer, and the company has developed a Prescribers Guide for physicians and a Xarelto Patient Card for patients to support best practices. 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