The Development of Anticoagulants

1930s

Heparin (unfractionated)[1]

✓ Effective (as used according to prescriber information)

Injection

1940s

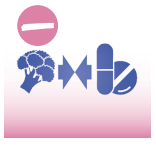
Vitamin K Antagonists (VKAs) e.g. warfarin[1]

✓ Effective (if INR is in therapeutic range)

✓ Oral administration

Regular coagulation monitoring

Dose adjustment



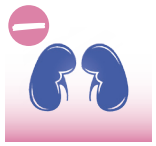
Many food and drug interactions

1980s

Low Molecular Weight Heparins (LMWHs) e.g. enoxaparin[2]

✓ Effective (as used according to prescriber information)

Injection



Can accumulate in patients with kidney impairment

2000s

Novel Oral Anticoagulants (OACs)

- Direct Factor Xa Inhibitors (Xabans) e.g. rivaroxaban, apixaban and edoxaban[3]
- Direct Thrombin Inhibitors (DTIs) e.g. dabigatran[4]

Rivaroxaban

Now approved in five indications in seven areas of use, it is the most prescribed novel OAC in the world and its investigation - both completed and ongoing - will include more than 275,000 patients in clinical trials and real world settings[6,7]

Xabans can overcome the limitations of older anticoagulants to prevent and/or treat venous and arterial thromboembolic (VAT) conditions[5]

Oral administration

Rapid onset of action

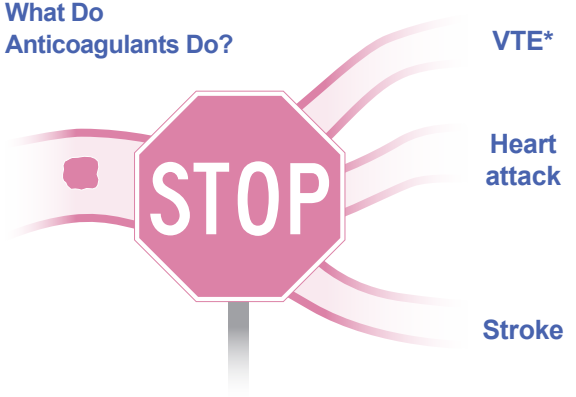
Predictable anticoagulation without need for routine monitoring or dose adjustment

Low risk of drug-drug interactions

No significant food interactions

It is important doctors and patients discuss the benefits and risks of the different anticoagulants to help identify the best treatment for optimal protection that is suited to maintain their quality of life

What Do Anticoagulants Do?



Anticoagulants are one of the first lines of defence against blood clots

*Venous thromboembolism (VTE)

References: **1)** Ansell J, et al. The pharmacology and management of the vitamin K antagonists: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004. 126 (3 Suppl): 204S-233S **2)** Hirsh J, Anand SS, Halperin JL, et al. Guide to anticoagulant therapy: Heparin : a statement for healthcare professionals from the American Heart Association. Circulation. 2001;103,(24)2994-3018 **3)** Graff J, Harder S. Anticoagulant therapy with the oral direct factor Xa inhibitors Rivaroxaban, apixaban and edoxaban and the thrombin inhibitor dabigatran etexilate in patients with hepatic impairment. Clin Pharmacokinet. 2013; 52(4) 243-54 **4)** Lee CJ, Ansell JE. Direct thrombin inhibitors, BJCP. 2011. 72(4) 581-592 **5)** Cohen AT, Imfeld S, et al. Phase III Trials of New Oral Anticoagulants in the Acute Treatment and Secondary Prevention of VTE: Comparison and Critique of Study Methodology and Results. Adv Ther (2014) 31:473–493 **6)** Xarelto Summary of Product Characteristics as approved by the European Commission **7)** IMS Health MIDAS, Database: Monthly Sales January 2015.