September
2014

Do the "NOACs" change the deal in Insurance?

Author
Dr John Evans and
Dr Dominique Lannes
Underwriting and Claims
R&D Center

Cardiovascular diseases are the main cause of mortality in the world and insurers have to take into consideration any significant changes in this field... The arrival of the long-awaited Novel Oral AntiCoagulant drugS or "NOACS", specifically targeting blood clotting factors thrombin or Xa, has been hailed as an important therapeutic advance over traditional oral vitamin K antagonists.

We set out to explain the potential advantages and limitations of NOACs and their potential impact on life insurance practices.

The therapeutic armamentarium for the prevention of arterial and venous thrombo-embolic disease has recently been enhanced by the approval of the use of **novel oral anticoagulant (NOACs)** drugs. Traditionally, in these indications, physicians have **used oral vitamin K antagonists (VKA)** which act by depleting the blood of active coagulation factors. They have been shown to significantly reduce the risk of stroke and total mortality when used prophylactically.

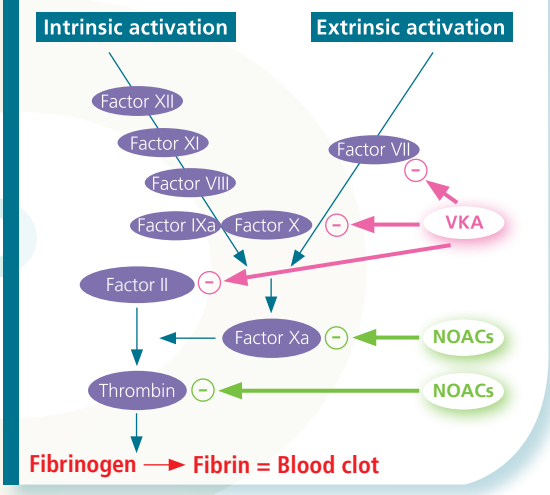
VKA inhibit the synthesis by the liver of the clotting factors II, VII, IX, X. They have a **non-specific** mode of action - Figure 1 - resulting in variable pharmacokinetics/dynamics and interactions with concurrently used drugs. In fact, only half of patients treated with VKA are in the therapeutic range and only for 50% of the time despite regular, at least monthly, blood testing for titration of dosage. The main consequence is an increased risk of side effects, especially bleeding.

VKA act by the inhibition of epoxide reductase in the liver, so preventing the recycling of oxidised Vitamin K to Vitamin K resulting in a depletion of reduced Vitamin K. Reduced Vitamin K catalyses the carboxylation of inactive prothrombin, and factors VII, IX and X to their active functional forms and, therefore, its depletion results in a lack of active coagulation factors.

NOACs either directly inhibit thrombin production (Rivaroxaban) or the formation of factor Xa (Dabigatran etexilate) - Figure 1. Because NOACs have **specific** sites of action, their pharmacokinetic and pharmacodynamics properties are more predictable than the VKA. Moreover, they do not interact as much as the VKA with foods and other drugs. **The practical advantage is that they have fixed dosing schedules which do not require blood testing for anticoagulation titration.**

(Figure 1)

Site of action of VKA and NOACs in the coagulation process



Editor
Paolo De Martin

SCOR Global Life SE
Societas Europaea with
a capital of 274 540 000
5, avenue Kléber
75795 Paris Cedex 16
France
RCS Paris 433 935 558

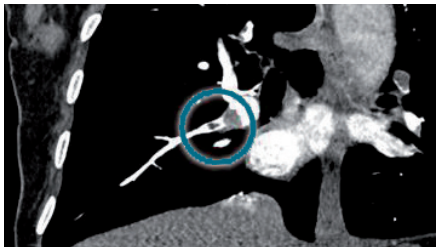
www.scor.com

SCOR Global Life

Do the "NOACs" change the deal in Insurance?

(Figure 2)

Pulmonary embolism



Pulmonary CT angiography a clot blocking the right pulmonary artery : this is a pulmonary embolism
Source: Imaging centre IMFM Paris

The question is : when there is a serious risk of blood clot and embolism will this new anticoagulant treatment (NOACs) replace traditional oral vitamin K antagonists (VKA) because the new drugs have the same efficacy but a better risk profile without the necessity of regular blood tests?

The answer is probably YES. The use of NOACs has been approved for the prevention of stroke and arterial embolism in patients with non-valvular atrial fibrillation and for primary prevention of venous thromboembolism during hip and knee replacement surgery. One of them has also been approved for the prevention of recurrent deep vein thrombosis and pulmonary embolism - Figure 2.

Special attention has to be given when using these NOACs in certain patient populations, in particular in patients with renal insufficiency, those receiving additional antithrombotic therapy, those with questionable compliance, patients of child bearing potential and those with a high risk of gastrointestinal bleeding. Other disadvantages include the absence of a readily available antidote in case of overdosage and the lack of long term experience compared with VKA.

However, actually VKA remain the only oral anti-coagulant drugs which can be used for example in patients with prosthetic heart valves and atrial fibrillation with valvular heart disease.

VKA & NOAC's drugs in the world

	International Non-proprietary Name (INN)	Trade Mark
VKA	Warfarin	Coumadin, Jantoven, Lawarin, Marevan, Waran, Warfant ...
	Acenocoumarol	Sintrom, Mini-Sintrom, Sinkumar, Ascumar ...
	Fluindione	Previscan
NOACs	Rivaroxaban	Xarelto
	Dabigatran etexilate	Pradaxa, Pradax, Rendix

Practical implications for the insurer:

There would seem to be no reason to change our life ratings according to the type of oral anticoagulant drug used in the indications which have been approved.

There is no doubt that the cost of NOACs is much higher than that of traditional VKA but substantial gains in cost-effectiveness have been predicted in terms of stroke prevention, reduced morbidity from bleeding and absence of monthly anticoagulation tests.

Moreover, in view of the better safety profile of the NOACs, it is to be expected that **more patients will be treated effectively by anticoagulation** instead of platelet anti-aggregant therapy for stroke and DVT prevention which will, no doubt, **increase costs to health insurers.**