DEGAM S1- procedure recommendation

New oral anticoagulants

(in non-valvular atrial fibrillation)

Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin

Version 1.0 (July 2013)

Question of care:

The standard for oral anticoagulation is the treatment with vitamin K antagonists (VKAs)[1]. Recently newer agents, the so-called new oral anticoagulants (NOACs) have been approved for the indication of nonvalvular atrial fibrillation[2]. There are varying recommendations and ratings concerning the use of the NOACs.

This recommendation and the following algorithm contain advice from the German Society of General Practice and Family Medicine (Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin, DEGAM) on the use of NOACs and is solely intended for use in outpatient care in general practitioners' practices. This recommendation is meant to support general practitioners in making necessary decisions in daily practice. It does not claim to be comprehensive and is only valid until newer recommendations replace it.

Please check the DEGAM homepage for updates: http://www.degam.de.

This procedure recommendation refers solely to patients with non-valvular atrial fibrillation and an indication for long-term anticoagulation according to the $CHADS_2$ - or CHA_2DS_2VASc-Score.

Chances and risks of NOAC:

NOACs are a possible alternative for patients who are not eligible for VKA (see page 2). Coagulation monitoring is not necessary (and not possible).

Before and during the use of NOACs the renal function (creatinine clearance according to Cockcroft-Goult, http://www.medcalc.com) should be monitored. The dose has to be adapted depending on the substance used and patient-specific comorbidities, as well as renal insufficiency, higher age, certain co-medications, low body weight, intestinal problems and/or a high risk for bleeding.

Indication, contra-indication, posology and warnings on the summary of product characteristics have to be taken into account.

Every patient with NOAC should receive a patient ID card, be informed about the risks of the therapy and the necessity of regular controls, as well be aware of the problem of a lacking antidote.

Statement:

Overall in Germany, the DEGAM found no advantage in treating patients with atrial fibrillation (who can be easily treated with VKAs) with NOACs instead of VKAs as a prophylaxis of cardioembolic diseases.

Criticism of the three registration trials which are non-inferiority trials has to be taken seriously. Furthermore, the clinical relevance of an ascertained marginal risk-reduction[3] – especially in patients who are well-managed or control their INR themselves – remains unclear.

There are unknown risks for patients with higher age, low body weight, polymedication, uncertain adherence, intake of anti-platelet agents and/or NSAID, multimorbidity, gastric- and bleeding disorders and an elevated risk of bleeding.

The lack of long-term experience in general use has to be taken into account. NOACs require a higher attentiveness.

Adverse events should be reported at the Drug Commission of the German Medical Association (Arzneimittelkommission der Deutschen Ärzteschaft, AkdÄ) http://www.akdae.de.

Further information:

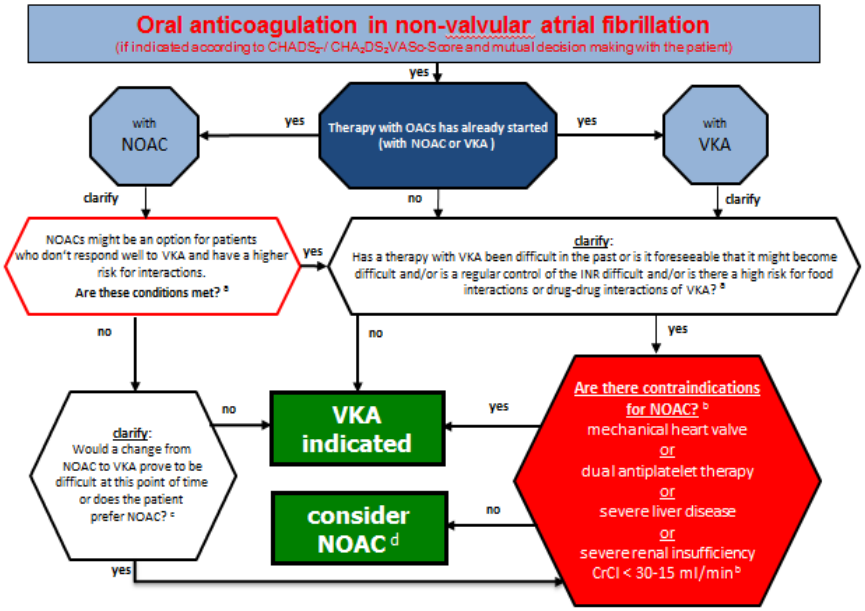
note: link leeds to the updated version 2.0; Sept. 2016

AkdÄ : Orale Antikoagulation bei nicht-valvulärem Vorhofflimmern (~~Version 1.0, September 2012~~).

Canadian Agency for Drugs and Technologies in Health: Antithrombotic agents for the prevention of stroke and systemic embolism in patients with atrial fibrillation, http://www.cadth.ca
Ottawa: The Agency; 2013. (CADTH Therapeutic Review; vol.1, no. 1b).

Scottish Intercollegiate Guidelines Network (SIGN): Antithrombotics: indications and management, http://www.sign.ac.uk
Edinburgh: SIGN; 2012. (SIGN publication no. 129). [August 2012].

[1] VKA/Coumarins: phenprocoumon (Marcumar®, Falithrom®, generics) or warfarin (Coumadin®).
[2] NOACs: Factor Xa- inhibitor rivaroxaban (Xarelto®) and apixaban (Eliquis®) and the thrombin inhibitor dabigatran (Pradaxa®)
[3] In the ARISTOTLE Trial the Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG) has included patients aged ≥ 65 in the VKA population in its benefit assessment according to § 35a SGB V as of 27.03.2013
Evidence for an additional benefit of apixaban in comparison to warfarin has been found.



OAC: oral anticoagulant; **NOAC:** new oral anticoagulant; **VKA:** vitamin-K-antagonist; **CrCl:** creatinine clearance; **NSAID:** non steroidal anti inflammatory drug; **INR**: international normalized ratio

[a] **No indication for NOACs**: good response to VKA - INR stably within target range – high risk of bleeding, high HAS BLED-Score, http://www.medcalc.com >2 (caution: missing antidote) – bleeding under VKA in INR target range

[b] **Further contraindications for NOAC**: pregnancy, breastfeeding, children and adolescents, systemic antimycotics, macrolide antimycotics, HIV protease inhibitors, dialysis, CrCl < 30 ml/min with dabigatran, else < 15 ml/min, high risk of bleeding

[c] **A change from NOAC to VKA** should always be well reflected upon and planned. In principle, there is an elevated risk for bleeding and thromboembolism during the changeover period. *From dabigatran to VKA:* CrCl ≥ 50 ml/min: VKA parallelly for three days (two days if CrCl 30 to 50 ml/min). INR-test two days after cessation of NOAC at the earliest. *From rivaroxaban or apixaban to VKA:* VKA parallelly until INR ≥ 2,0. INR-test 24 hours after cessation of NOAC at the earliest.

[d] **NOAC only after thorough assessment** (shared decision making). **Reasons against NOACs**: Age > 80 years, body weight < 60 kg, renal insufficiency (reduction of dose od contraindication), polymedication, uncertain adherence, antiplatelet therapy and/or NSAID intake, multimorbidity, history of gastric- or bleeding disorders

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