About programme updates
CPPE has a quality assurance process called programme guardians. A programme guardian is a recognised expert in an area relevant to the content of a learning programme who reviews the programme every six to eight months. Following the regular programme guardian review we have developed this update to inform you of any necessary corrections, additions, deletions or further supporting materials. We recommend that you check you have the most recent update if you are using a programme more than six months after its initial publication date.

This update has been prepared by Dr Frances Akor and should be read in conjunction with the Advances in anticoagulation: new oral treatments learning@lunch flex programme. We have indicated the relevant section and page number of the original document wherever we provide updated information.

Learning with CPPE
The Centre for Pharmacy Postgraduate Education (CPPE) offers a wide range of learning opportunities in a variety of formats for pharmacy professionals from all sectors of practice. We are funded by Health Education England to offer continuing professional development for all pharmacists and pharmacy technicians providing NHS services in England. For further information about our learning portfolio, visit: www.cppe.ac.uk

A note about web links
Where we think it will be helpful we have provided web links to take you directly to an article or specific part of a website. However, we are aware that web links can change. If you have difficulty accessing any web links we provide, please go to the organisation’s home page or your preferred internet search engine and use appropriate key words to search for the relevant item.

All web links were accessed on 18 January 2016.

Access to the BNF online
You can access the BNF online through MedicinesComplete. If you are not already registered, you will need to do so. UK-based individuals working for or on behalf of the NHS can register for free and access the BNF and BNF for children. To register, go to: www.medicinescomplete.com/about/subscribe.htm

Assessment
As part of your learning for this programme, you may wish to undertake the associated e-assessment. To access the assessment, go to: www.cppe.ac.uk/assessment

References in the programme to competency frameworks
In this programme we may map our learning objectives against the Royal Pharmaceutical Society of Great Britain’s competency framework, the General Level Framework or the Knowledge and Skills Framework. You can easily map the learning objectives against a competency framework that is relevant to your practice.
Pre-session handout

Task 1 – reflective questions

Question 1
Replace the entire question with:

1. Apixaban, dabigatran, edoxaban and rivaroxaban are recommended by the National Institute for Health and Care Excellence (NICE) as options for the prevention of stroke in people with non-valvular atrial fibrillation. What risk factors must a patient have in order to be eligible for treatment with these medicines?

Question 2
Replace the entire question with:

2. It is important to give advice to patients who are taking a new oral anticoagulant. What would you discuss with a patient starting on apixaban?

Task 2 – reading

Question 1
Remove the bullet point and reference to the article: ‘Will you supply as much warfarin in 2015?’ and add in the following articles and documents to the suggested pre-reading:


Question 2
Add this text to the bullet points at the end of this question:

The following NICE technology appraisals and clinical guidelines should also be read alongside the existing list:

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Learning portfolio

Case studies

Replace the text in the second paragraph to:
The cases are designed to illustrate some of the difficult decisions involved in developing appropriate treatment strategies for patients who require anticoagulation therapy and allow you to discuss the challenges and solutions to these with your colleagues. The cases focus on two of the non-vitamin K antagonist (VKA) oral anticoagulants: dabigatran and rivaroxaban.

Case study 2 – Delia

Remove the following question from the case study:
If dabigatran is not fully approved for use in your trust, what pathway would you have to go through to gain approval for its use?

This is because dabigatran, alongside apixaban and rivaroxaban and vitamin K antagonists should all be offered as choices for anticoagulation as per NICE Clinical guideline 180 – Atrial fibrillation: the management of atrial fibrillation.

Replace the question with:
In your trust, are all the non-VKA oral anticoagulants available for use, or are there some restrictions? If there are restrictions, do you know what they are?

Case Study 3 – Daryl

Add the following before the second question on this page:
Please read that Daryl’s renal function has deteriorated and his creatinine clearance has reduced to 30 mLs/min.

Learning Checklist

Add in NICE Technology appraisals 275 and 355, and Clinical guideline 180 to the second box in the activity column relating to reading NICE technology appraisals and guidance.

Suggested Answers

Add the following at the bottom of the suggested answer to question 1 to contain information about apixaban and edoxaban:
Apixaban is recommended as an option in people with one or more of the following risk factors:
- they have had a stroke or transient ischaemic attack in the past
- they are over 75 years of age
- they have hypertension
- they have diabetes mellitus
- they have symptomatic heart failure.6

Edoxaban is recommended as an option in people with one or more of the following risk factors:
- they have heart failure, high blood pressure or diabetes
- they have had a stroke or transient ischaemic attack before
- they are over 75 years of age.7

You should explain briefly what apixaban is, how it works and why it has been prescribed. If relevant you may wish to explain the key differences between apixaban and warfarin. It is helpful to tell the patient how long they would be expected to take the apixaban for, this is dependent on the indication. Discuss with the patient how and when they should take apixaban; one tablet swallowed with water, with or without food, twice daily, at the same time each day. If the dose is missed, the patient should take it immediately and then continue with twice daily intake as before. If the patient is having problems remembering to take their medication, they should discuss this with their GP or pharmacist. It is important to highlight the risks of patients missing doses of apixaban (exposing them to increased risk of thrombosis) and, therefore, remembering to take it is really important.

Provide information on common side-effects, including nausea, haemorrhage and bruising. Provide advice on what the patient should do if they experience a bleed, explaining the less obvious signs of bleeding (black tarry stool) with the more obvious types. If the bleeding is self-limiting, they should speak to their GP at the next opportunity. If the bleeding is ongoing or severe, they should attend their local accident and emergency department.

Ask patients to tell all of their healthcare providers, including community pharmacists and dentists, they are taking apixaban, and to speak to their GP or pharmacist before starting any new medicines. Check that the patient has been provided with an apixaban alert card – this should be carried around with them at all times and shown to healthcare professionals. (Note – some areas are choosing to use a generic anticoagulant card for use with all new oral anticoagulants (NOAC) rather than specific alert cards for the individual NOACs).

If you are talking to a woman of childbearing age, it is important to stress to them that they should not get pregnant while taking apixaban as the safety of treatment during pregnancy has not been established. Also inform them that apixaban should not be used during breastfeeding.
Please note that dabigatran requires the patient to have at least annual renal function and liver function tests.

Prothrombin time (PT) can also be used as a qualitative assessment of rivaroxaban.

If clinically indicated, rivaroxaban, apixaban and edoxaban levels can be measured by calibrated quantitative anti-factor Xa tests.

**Case Study 1 – Faye**

Replace the text in the first suggested answer to:
Stop warfarin and administer a dose of phytomenadione 1 – 5 mg by mouth. Discuss with Faye the reasons behind her raised INR. Has she been taking her warfarin as directed? Has she been following her usual patterns of eating and drinking? Has she taken any new medicines? Invite her back for another INR check in a few days’ time to ensure the INR is falling.

**Low molecular weight heparin (LMWH) subcutaneous injection:**
- Disadvantages: note that protamine only partially reverses LMWH, and the effects of LMWH can persist for up to 24 hours after administration.

**Apixaban:**
- Advantages: fixed dose schedule, unlike warfarin, and no food - drug interactions and the treatment is not affected by alcohol.
- Disadvantages: It may be difficult to identify non-adherence to this treatment and currently there is no reversal agent should bleeding occur.

**Dabigatran:**
- Advantages: fixed dose schedule, unlike warfarin and no food - drug interactions and the treatment is not affected by alcohol.
- Disadvantages: requires five days parenteral anticoagulant prior to starting the dabigatran, currently no reversal agent should bleeding occur.
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Edoxaban:
- Advantages: once daily dosing, unlike warfarin and no food - drug interactions and the treatment is not affected by alcohol.
- Disadvantages: requires five days parenteral anticoagulant prior to starting the edoxaban, currently no reversal agent should bleeding occur.

Case Study 2 – Delia
(page 23 – amendment and deletion)
The second paragraph in the suggested answers should be replaced with:
The decision about whether to start treatment with dabigatran should be made after an informed discussion between the clinician and Delia about the risks and benefits of dabigatran compared with warfarin, as per recommendation in NICE Clinical guideline 180. Warfarin may still be a suitable option if her confusion settles after treatment of her UTI. If, after considering the pros and cons, warfarin is not felt to be appropriate due to the variable dose that Delia will need to manage herself with and the frequent anticoagulation appointments that she will need to attend (although, this might not be such an issue if domiciliary appointments are available in your area), then dabigatran may be the agent of choice as long as Delia has a creatinine clearance of over 30 mL/min.

Remove the second question and suggested answer from the case study entirely.

(page 24 – amendment)
Replace the final sentence of the suggested answer with:
You may want to check clotting factors to ensure that there are no raised parameters and perform a hemoclot thrombin inhibitor assay test; this may be used to measure bleeding risk if an overdose or major haemorrhage occurs.

(page 25 – amendment)
Amend the final sentence of the suggested answer to:
If the patient requires stenting then this may affect what is recommended and you may wish to consult a cardiology specialist for further advice because in general NOACs are not being used concomitantly with the new oral antiplatelets.

Discussion points
(page 25 – amendment)
Replace both paragraphs with:
Reanalysis of the Randomized Evaluation of Long-term Anticoagulant Therapy (RE-LY) study data and meta-analysis regarding myocardial infarction (MI) indicated that there was no significant increased risk of MI with dabigatran when compared with warfarin. However, the data does indicate that rivaroxaban, apixaban or warfarin may be a more suitable option for patients who have had acute coronary syndrome.
In addition, there is data in the ATLAS-ACS 2 TIMI 51 (Anti-Xa therapy to lower cardiovascular events in addition to standard therapy in subjects with acute coronary syndrome-thrombolysis in myocardial infarction) trial regarding treatment with low-dose rivaroxaban and aspirin and clopidogrel for acute coronary syndrome. Rivaroxaban is licensed and recommended by NICE for use as an option alongside aspirin and clopidogrel, or aspirin alone, for preventing atherothrombotic events in patients who have an acute coronary syndrome with elevated cardiac biomarkers.

The following information should be added to the first suggested answer box:
The manufacturers of dabigatran have produced a specific monitored dosage system (MDS) which holds dabigatran only. If a blister pack is required both rivaroxaban and apixaban can be put into an MDS.

Case Study 3 – Daryl
Please read that Daryl’s renal function has deteriorated and his CrCl has reduced to 30 mLs/min.

Discussion point
Please remove the discussion point referring to interactions between rivaroxaban and NSAID.

In the suggested answer, in paragraph three, bullet point four should be replaced with:
• Blood product transfusion: consider a platelet transfusion if levels are less than 60 to 80 x 10^9/L or the patient is on an antiplatelet agent; consider performing a red cell transfusion if the bleeding is ongoing

Add this additional bullet point at the end of the suggested answer in paragraph three:
• Consider mechanical compression, eg, for severe epistaxis

In cases of severe or life-threatening bleeding, consider the following:
• The patient’s suitability for haemofiltration or dialysis (if they are on dabigatran and if feasible)
• Administering activated prothrombin complex concentrate or activated VIIa, however note data is limited. Discuss these possible treatments with the on-call haematology consultant.

References
Please add the following references to the end of this section:
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References for this update

Further suggested reading

Feedback
We hope you find this learning programme useful for your practice. Please help us to assess its value and effectiveness by visiting your learning record in the *My CPPE* section on our website: www.cppe.ac.uk/mycppe/record

Alternatively, please email us at: feedback@cppe.ac.uk

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