Prescribing Points

Vol 29 Anticoagulation Special Edition
November 2019

Oxfordshire Cinical Commissioning Group

Volume 29, Date November 2019

This newsletter is written by the Medicines Optimisation Team, Oxfordshire CCG (OCCG), Jubilee House, Oxford Business Park South, Oxford, OX4 2LH. It is for all health professionals in Oxfordshire and is uploaded to the OCCG website. For queries, contact OCCG.medicines@nhs.net.

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Anticoagulation Optimisation and Support Service - Relaunch

Following on from a successful pilot project, a permanent Anticoagulation Optimisation and Support Service has been established. This service is being delivered by specialist anticoagulation pharmacists, with the assistance of a consultant haematologist. It is available to help support GPs and pharmacists in primary care to optimise anticoagulation. Services available include:

- Email advice line: doacsupport.ox@nhs.net
  (Please provide as much infomation as possible e.g. indication for anticoagulation, age, weight, recent eGFR/creatinine, LFTs, FBC, medicines, adherence, alcohol intake, need for dosette box etc.)

- Practice visit from specialist anticoagulation pharmacist to:
  - give education sessions on common pitfalls and practical prescribing points
  - provide a list of patients whose Time in Therapeutic Range (TTR) is < 65%
  - carry out a virtual review for patients on warfarin with low TTR
  - help assess patients with AF and a CHA_2DS_2-VASc ≥1 not anti-coagulated

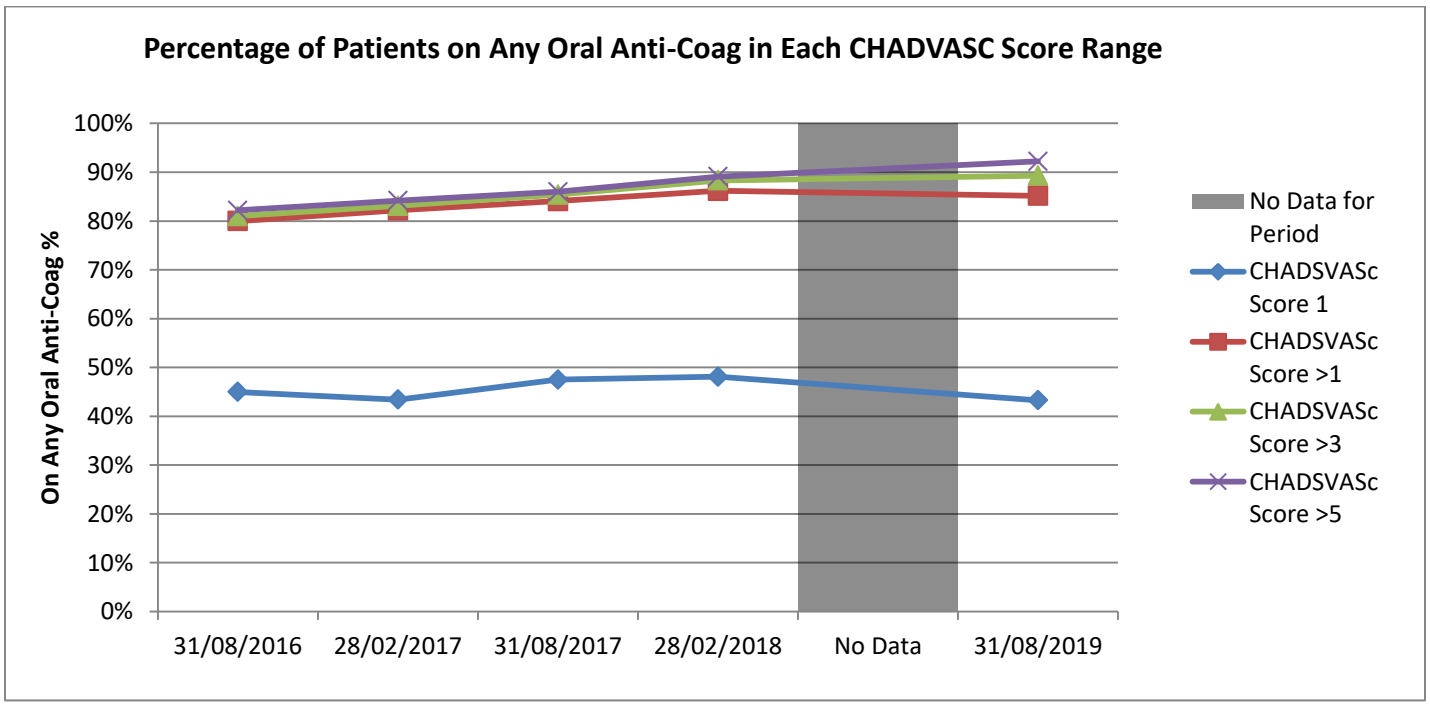
- Training for community pharmacists to counsel patients on DOACs and support provision of new medicines service (NMS) and Medicines Use Reviews (MURs).

Oxfordshire Stroke Prevention Audit Results

For several years GP practices in Oxfordshire have participated in a bi-annual stroke prevention audit to identify the percentage of patients on any oral anticoagulant within a specific $CHA_2DS_2VAS_C$ score range. 100% of practices have participated in this audit. In August 2019, anticoagulation rates in practices ranges from 67% to 93% of patients with $CHA_2DS_2VAS_C$ scores of 2 or above, the average being 85%. This is a slight reduction from the last audit in February 2018, where anticoagulation rates ranged from 65.9% to 97.1% of patients with $CHA_2DS_2VAS_C$ scores of 2 or above. Each practice will be able to see their results on the CCG website here. Results are displayed by localities; however going forward results will be presented by PCNs. Please note that a secure N3 connection will be required to view these results.

Stroke Prevention Results - Percentage of Patients on Any Anti-Coag in each CHADVASC Score Range:

Data received from:	75 Practices			72 Practices			70 Practices			70 Practices			70 Practices		
Period As At:	31/08/2016			28/02/2017			31/08/2017			28/02/2018			31/08/2019		
Risk Score	On Any Oral Anti-Coag	Not on Any Oral Anti-Coag	On Any Oral Anti-Coag %	On Any Oral Anti-Coag	Not on Any Oral Anti-Coag	On Any Oral Anti-Coag %	On Any Oral Anti-Coag	Not on Any Oral Anti-Coag	On Any Oral Anti-Coag %	On Any Oral Anti-Coag	Not on Any Oral Anti-Coag	On Any Oral Anti-Coag %	On Any Oral Anti-Coag	Not on Any Oral Anti-Coag	On Any Oral Anti-Coag %
CHADSVASc Score 1	477	582	45.0%	501	653	43.4%	554	612	47.5%	619	668	48.1%	511	670	43.3%
CHADSVASc Score >1	8,021	2,003	**80.0%**	8,482	1,836	**82.2%**	9,004	1,699	**84.1%**	9,752	1,557	**86.2%**	10,038	1,747	**85.2%**
CHADSVASc Score >3	4,711	1,107	81.0%	4,992	1,013	83.1%	5,291	905	85.4%	5,684	753	88.3%	4,803	576	89.3%
CHADSVASc Score >5	1,280	278	82.2%	1,357	254	84.2%	1,436	234	86.0%	1,539	188	89.1%	1,199	101	92.2%



Update to VTE treatment with dalteparin guidelines

The guidelines for VTE treatment with dalteparin in cancer and non-cancer setting have been updated and can be found here. The main changes are in weight banding and the dosing schedule of dalteparin in patients requiring twice a day dosing due to high body weight. Twice a day dosing will now use the same strength pre-filled syringe for both doses.

Month 1 **- VTE treatment with dalteparin** (excluding pregnancy and the puerperium)

Body weight (kg)	Dose of dalteparin by subcutaneous injection using a pre-filled syringe (units)
Less than 46 Consider discussing with haem SpR if less than 40kg	7,500 once daily
46-56	10,000 once daily
57-68	12,500 once daily
69-82	15,000 once daily
83-98	18,000 once daily
99-112	10,000 **twice daily**
113-137	12,500 **twice daily**
138-165	15,000 **twice daily**
More than 166 Consider discussing with haem SpR if greater than 180kg	18,000 **twice daily**

The DVT protocol and the Guidelines for DOACs for Treatment and Secondary Prevention of VTE have also been updated. Please be reminded that;

- Anticoagulation should be supplied by the GP if diagnostic investigations are expected to take longer than 4 hours from the time of first clinical suspicion of DVT.
- Please note that for suspected pulmonary embolism refer patient to medical referral line on 01865 227591.

The dosing schedule for dalteparin from month 2 onwards is now as follows. Please reweigh the patient to determine the correct dose.

Month 2 onwards**- VTE treatment with dalteparin** (excluding pregnancy and the puerperium)

NB. Ensure patient is reweighed

Body weight (kg)	Dose of dalteparin by subcutaneous injection using a pre-filled syringe (units)
Less than 57	7,500 once daily
57-68	10,000 once daily
69-82	12,500 once daily
83-98	15,000 once daily
99-112	18,000 once daily
113-137	10,000 **twice daily**
138-165	12,500 **twice daily**
166 or more	15,000 **twice daily**

DVT / Anticoagulation update

Superficial vein thrombosis:

Mild to moderate cases of superficial vein thrombosis can be managed in primary care. For guidance on how to manage superficial vein thrombosis please see:

- https://www.ouh.nhs.uk/services/referrals/specialist-medicine/documents/dvt-protocols.pdf
- https://www.oxfordshireccg.nhs.uk/gp-bulletins/gp-weekly-bulletin-19-december-2018/77810

If you suspect the superficial vein thrombosis is close to a deep venous junction or that there may be a concurrent deep venous thrombosis please refer the patient to the DVT clinic for investigation by telephoning 01865 225629 or emailing dvt.service@nhs.net out of hours.

D dimers:

The Oxfordshire DVT clinic has been operating at full capacity during the last year which has at times meant that clinicians have been unable to secure same day scan slots for new patients with suspected DVT.

In order to free up scan slots by reducing the need for repeat scan appointments it is imperative that unless a patient is already on an anticoagulant a D dimer blood sample is taken *prior to administration of interim anticoagulation*. The sample should be filled to the top of the label on in a blue citrate tube and can be sent with the patient to their DVT clinic appointment. The samples are stable at room temperature for up to 24 hours.

DOACs:

If you wish to start a warfarin patient on a Direct Oral Anticoagulant (DOAC) please complete a 'stopping warfarin form' on EMIS which must be sent to the anticoagulation service (ac.service@nhs.net) who will facilitate the transition. Please note that before the transition can be made the patients must have received verbal and written counselling and be in possession of the DOAC.

Please take note of the below contraindications/cautions when prescribing DOACs:

Metallic heart valve	Contraindicated
Pregnancy or breastfeeding	Contraindicated
Weight over 120kg	Not recommended based on International Society on Thrombosis and Haemostasis guidelines; limited data available and concern about under-dosing based on decreased drug exposures, reduced peak concentrations and shorter half-lives with increasing weight.
Renal impairment using calculated CrCl	Less than 30ml/min: Warfarin preferred. Dabigatran contraindicated. Use Xa inhibitors with caution (limited data available) Less than 15ml/min: All DOACs contraindicated
Patients with INR target ranges other than 2-3	Not suitable. All trial data comparing a DOAC with warfarin was for a patient group with a standard INR range of 2-3.
Interacting medications	Check individual SPC for each medicine. Common examples to avoid in combination are HIV protease inhibitors, azole-antimycotics (e.g. ketoconazole, itraconazole, voriconazole and posaconazole, rifampicin, phenytoin, carbamazepine, phenobarbital, primidone and St. John's Wort. Dabigatran – caution with amiodarone and verapamil Edoxaban – dose reduce with ciclosporin, dronedarone, erythromycin or ketoconazole

Calculating renal function

Please note recent MHRA alert regarding use of appropriate estimate of renal function to avoid the risk of adverse drug reactions.

Creatinine clearance (CrCl) should be calculated using the Cockcroft-Gault formula to determine dosage adjustments for:

- **direct-acting oral anticoagulants (DOACs)**
- patients taking nephrotoxic drugs (examples include vancomycin and amphotericin B)
- **elderly patients (aged 75 years and older)**
- patients at extremes of muscle mass (BMI <18 kg/m2 or >40 kg/m2)
- patients taking medicines that are largely renally excreted and have a narrow therapeutic index, such as digoxin and sotalol

Management of patients with antiphospholipid syndrome (APS) and the use of DOACs in thromboembolism

The EMA and MHRA have recently issued a warning about the use of DOACs in patients who are known to have APS following the results of a randomised clinical trial of patients with triple positive APS. 'Triple positive APS' refers to a patient who fulfils the clinical criteria for APS and who is also positive for all three of the laboratory tests used to diagnose APS. These tests are: lupus anticoagulant; anticardiolipin antibody and anti-beta2-glycoprotein 1 antibody tests which should be tested and confirmed to be positive on two separate occasions, 3 months apart.
Considering these data, we would like to recommend the following management for patients known to have APS, or those potentially at risk of APS.

Anticoagulation management in known APS:

1. **APS and arterial thrombosis**: we strongly recommend that these patients are anticoagulated with warfarin
2. **APS and venous thrombosis**:
    a. **Triple positive APS patients** (i.e. anticardiolipin Ab, β2-GP1 Ab and lupus anticoagulant positive) should be offered warfarin as first line therapy.
    b. **Non-triple positive patients**. There is no evidence to support the choice of anticoagulant for this patient group. A discussion should be had with the patient about the clinical uncertainty around whether a DOAC is as effective at preventing thrombotic events as warfarin. A shared decision, taking the patient's wishes into consideration, should be made and documented. It is recognised that if a patient has been stable and has not developed a further thrombotic event whilst on a DOAC, that it is reasonable to continue that medication.

Anticoagulation management in patients with unknown APS status:

1. **Patients with a newly diagnosed unprovoked VTE:** It is recommended that from now on all patients with a newly diagnosed unprovoked VTE who are considered for long-term anticoagulation are tested for APS. This will be done at a three month thrombosis review clinic at the Churchill Hospital.

2. **Switching from warfarin to a DOAC in patients on long-term anticoagulation for VTE prevention**: For patients already taking long-term anticoagulation for unprovoked VTE (if a VTE cannot be established as provoked, it should be treated as unprovoked), and who are being considered by their GP for a medication switch from warfarin to a DOAC, the GP should test the patient for APS prior to switching. The tests are listed on ICE as lupus screen; Cardiolipin Antibodies and beta2 glycoprotein 1. Please state the name of the anticoagulant the patient is taking in the clinical details for the request. If the initial tests are negative then the patient can be switched from warfarin to a DOAC. If the initial tests are positive then the patient should not be switched and repeat tests should be conducted after 3 months (12 weeks). If the results are still positive then follow the advice in the paragraph above on "anticoagulation management in known APS". If the results are negative on repeat testing then switching from warfarin to a DOAC can be considered.

   The Thrombosis team are happy to be contacted to discuss individual patients:
   - Haematology registrar – bleep 5529 via the JR switchboard (0300 304 7777), or phone the haemophilia centre (01865-225316), or email haematologyregistrar.enquiries@nhs.net
   - Anticoagulation pharmacists – bleep 4511 or 5036, or email doacsupport.ox@nhs.net

Drug information booklets

- Warfarin – NPSA "yellow book"
  - Booklets and patient alert cards can be ordered via the Primary Care Support England (PCSE) supply system.
- Apixaban (Eliquis®)
  - Booklets and patient alert cards can be ordered (free of charge) from Bristol-Myers Squibb Medical Information (Telephone: 0800 731 1736; E-mail: medical.information@bms.com).
  - Apixaban Educational Risk Minimisation Materials to help reduce the risk associated with using this medicine can also be found on the Electronic Medicines Compendium website.
- Dabigatran (Pradaxa®)
  - Booklets and patient alert cards can be ordered (free of charge) from Boehringer Ingelheim Medical Information (Telephone: 0134 474 2579, E-mail: medinfo@bra.boehringer-ingelheim.com).
  - Dabigatran Educational Risk Minimisation Materials to help reduce the risk associated with using this medicine can also be found on the Electronic Medicines Compendium website.
- Edoxaban (Lixiana®)
  - Booklets and patient alert cards can be ordered (free of charge) from Daiichi Sankyo Medical Information (Telephone: 0800 028 5122, E-mail: medinfo@daiichi-sankyo.co.uk).
  - Edoxaban Educational Risk Minimisation Materials to help reduce the risk associated with using this medicine can also be found on the Electronic Medicines Compendium website.
- Rivaroxaban (Xarelto®)
  - Booklets and patient alert cards can be ordered (free of charge) from Bayer plc Medical Information (Telephone: 0118 206 3000, E-mail: Medical.information@bayer.co.uk).
  - Booklets and alert cards can be downloaded and printed from http://www.xarelto-info.co.uk/hcp/.
  - Rivaroxaban Educational Risk Minimisation Materials to help reduce the risk associated with using this medicine can also be found on the Electronic Medicines Compendium website.