# Prescribing Points

Volume 30 Issue 9 December 2020

NHS
Oxfordshire
Cinical Commissioning Group

*Volume 30 Issue 9 Date: December 2020*



**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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## EU Medication Exit Strategy

As 1st January 2021 and the exit from the EU draws nearer, OCCG has been involved in conversations with NHSE around national plans for the management of medication stocks at, what is likely to be, a challenging time.

NHSE has provided assurance that robust plans are in place to minimise the effect of disruption at the border which may cause a delay in medication reaching the UK market. These plans do, however, rely on prescribers, pharmacies and patients continuing to work in the same way they currently do and not changing prescribing habits and being mindful of the following;

- Prescribe and dispense as normal – extra medication should not be required and longer prescriptions should be avoided.
- Stockpiling is not necessary – the Government has put into place a plan for ensuring local stockpiling, which will put pressure on the availability of medicines, is not required.
- Business as usual shortages management applies – any stock shortages should be managed in the normal way.
- A national Medicines Shortage Group (MSRG) has been established to provide governance, communication and decision-making during the transition period.
- Familiarise yourself with the latest information on supply – CAS alerts and other centralized communications will continue to be shared with clinicians.

In due course the NHS will provide advice to patients regarding these plans in order to assure them and provide confidence that plans are in place to ensure everything is being done to avoid a shortage of medicines.

## BOB Antimicrobial Webinar - Recording

The recording for Berkshire, Oxfordshire and Buckinghamshire (BOB) Primary Care Antimicrobial Webinar held on 17th Nov 2020 is now available to watch here. The slides can also be downloaded here.

## SCAN Guideline Update

SCAN guideline version 3.0 was published in November 2020 and the updated pages are:

- Influenza
- Cellulitis
- Uncomplicated UTI in non-pregnant women
- Fluoroquinolones alert: cardiac risks

More information on how to download and access the app is available here.

## Antiphospholipid Syndrome (APS) Testing for Patients on Long-term Anticoagulation

We have been made aware that in some cases patients being transferred from warfarin to a DOAC for VTE are not being tested for APS as per the Medicines Management COVID-19 guidance. Please ensure patients are tested for APS where appropriate in line with this guideline. We would like to remind all prescribers:

- For patients anticoagulated due to VTE: clinician to screen for antiphospholipid syndrome in the following groups of patients. Request anti-cardiolipin and beta-2 gylcoprotein-1 antibodies **only** in the first instance and if antibody positive then discuss with haematology as DOAC might not be recommended.*
    - history of SLE or other autoimmune disease
    - presence of livedo reticularis
    - prolonged APTT prior to starting anticoagulation
    - recurrent thrombosis
    - VTE at an unusual site
    - history of arterial disease without a clear risk
    - thrombocytopenia
    - recurrent miscarriage/still birth/severe pre-eclampsia
    - aortic or mitral valve leaflet thickening or vegetations in the absence of another cause

* Please note, the OCCG VTE guideline advises to test for lupus anticoagulant, anti-cardiolipin and beta-2 gylcoprotein-1 antibodies. However, there is a risk during Covid-19 that the laboratory will not be able to quickly turn around lupus anticoagulant tests and so this is Covid-19 adapted guidance.

Some prescribers have told us that the tests required are difficult to find on ICE. If you search for 'cardio', cardiolipin antibodies appears as an option on a short list. Similarly if you search for 'beta', beta 2 glycoprotein appears as one of the options. Please also state the name of the anticoagulant the patient is taking in the clinical details for the request. We are also looking into whether these tests can be made more visible on ICE to prescribers for the future.

The Thrombosis team are happy to be contacted to discuss individual patients:

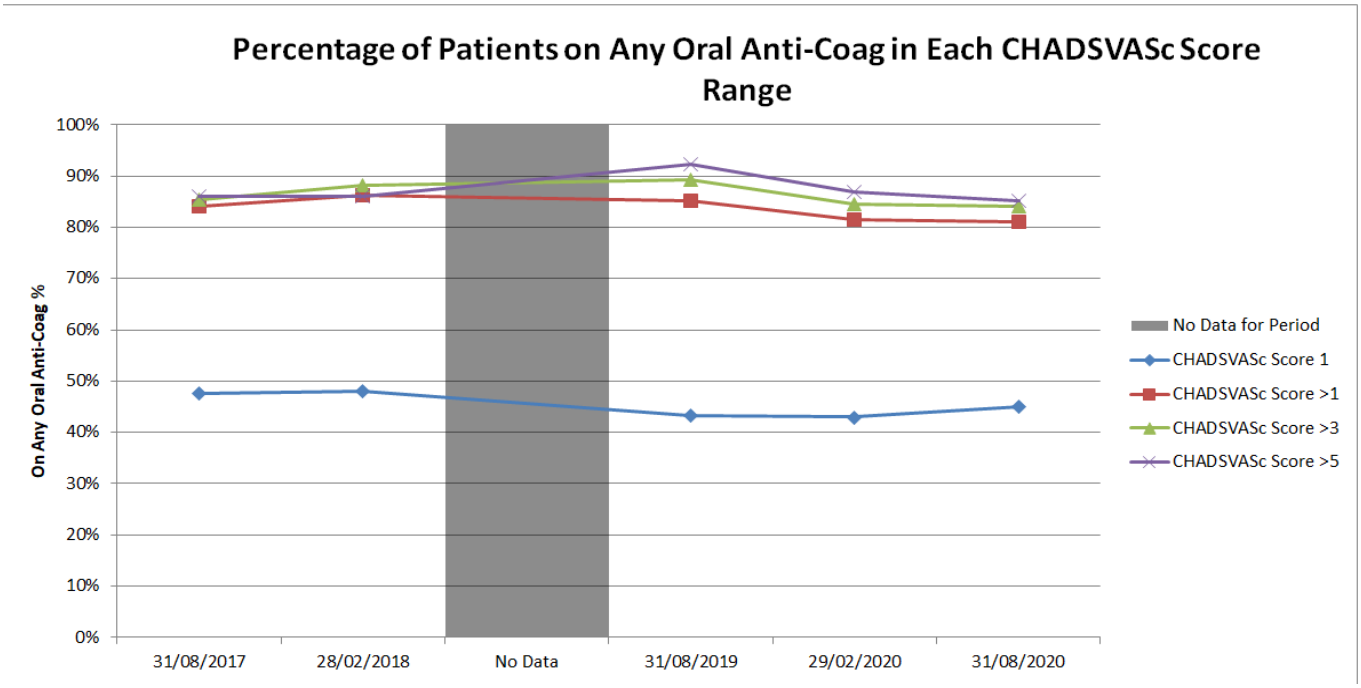
- Haematology registrar – bleep 5529 via the JR switchboard (0300 304 7777), or phone the haemophilia centre (01865-225316), or email haematologyregistrar.enquiries@nhs.net
- Anticoagulation pharmacists – bleep 4511 or 5036, or email doacsupport.ox@nhs.net.

## 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 CHA2DS2VASC score range. 98.5% of practices have participated in this audit. In August 2020, anticoagulation rates in practices ranges from 61.7% to 89.7% of patients with CHA2DS2VASC scores of 2 or above, with the average being 81.1%. This is a reduction from last year in August 2019, where anticoagulation rates ranged from 67% to 93% of patients with CHA2DS2VASC scores of 2 or above, when the average was 85.2%. Each practice is able to view the results for their practice here (results are displayed by localities). Please note that a secure N3 connection is required to view these results.

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

| Data received from: | 70 Practices | | | 70 Practices | | | 66 Practices | | | 67 Practices | | | 66 Practices | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Period As At: | 31/08/2017 | | | 28/02/2018 | | | 31/08/2019 | | | 29/02/2020 | | | 31/08/2020 | | |
| 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 | 554 | 612 | 47.5% | 619 | 668 | 48.1% | 511 | 670 | 43.3% | 511 | 679 | 42.9% | 549 | 672 | 45.0% |
| CHADSVASc Score >1 | 9,004 | 1,699 | 84.1% | 9,752 | 1,557 | 86.2% | 10,038 | 1,747 | 85.2% | 9,993 | 2,277 | 81.4% | 10,113 | 2,355 | 81.1% |
| CHADSVASc Score >3 | 5,291 | 905 | 85.4% | 5,684 | 753 | 88.3% | 4,803 | 576 | 89.3% | 4,702 | 859 | 84.6% | 4,915 | 932 | 84.1% |
| CHADSVASc Score >5 | 1,436 | 234 | 86.0% | 1,539 | 188 | 89.1% | 1,199 | 101 | 92.2% | 1,130 | 170 | 86.9% | 1,135 | 197 | 85.2% |




**So What?**

- Please review how your practice is performing and how improvements could be made.
- The Anticoagulation Optimisation Support Service Team will be contacting some practices directly to offer further support in the near future but if your practice would like some help and support in this area, please contact OCCG.medicines@nhs.net or doacsupport.ox@nhs.net.

## Switching from Existing DOAC to Edoxaban

It has come to light that some practices may be considering switching patients from their existing choice of DOAC to edoxaban. Edoxaban does offer a small cost saving but there are many clinical reasons as to why this agent is not routinely used in Oxfordshire. A switch to edoxaban should not be viewed as a simple task. Prescribers should consider very carefully on a case by case basis whether this is an appropriate switch to be carried out. The anticoagulation team at OUH have concerns regarding a switch to edoxaban in primary care for patients who are otherwise well controlled on another DOAC. If the patient is not well controlled on their existing DOAC please get in touch with them for advice (Doacsupport.ox@nhs.net).

Patients are not started on edoxaban in OUH. Apixaban is the DOAC that is favoured at OUH for many reasons:

- In AF - apixaban 5mg has been shown to be more efficacious when compared to warfarin. Edoxaban showed similar efficacy to warfarin. There have been no head-to head trials comparing different DOACs.
- In AF - gastro-intestinal bleeding is more common with edoxaban 60mg than warfarin, this was not observed with apixaban.
- In acute VTE - there is the need for 5 days of LMWH before starting edoxaban so practically this is not favourable for the DVT clinic, ambulatory or inpatients.
- In long term secondary prevention of VTE – there is no reduced dose for edoxaban (as opposed to apixaban 2.5mg or rivaroxaban 10mg). A reduced dose of DOAC is associated with a reduced bleeding risk.
- There is some concern over using edoxaban in patients with high renal clearance (see section 4.4. of the SmPC for full details).
- A reduction in the dose of edoxaban is needed if combined with a course of erythromycin.

In order to switch safely from one DOAC to another, the prescriber would need to ensure they had upskilled their knowledge sufficiently in this area. There are a number of agents on the market, all with different indications, doses, cautions and monitoring requirements etc. DOACs can be viewed as straightforward by some, whilst in reality the prescribing can be complicated and confusing.

Patients would also need additional counselling and therefore careful planning is needed as to who would do this, how it will be managed and to ensure there is sufficient time available. General practice is under immense pressure at present due to COVID-19 and other factors and prescribers must ensure that patient safety is not compromised if a switch is carried out.

**So What?**

- OCCG does not recommend carrying out a switch to edoxaban if the patient is well controlled on another DOAC.
- If this switch is carried out, it should be done on a case by case basis after very careful consideration of all the clinical factors involved.
- Contact the anticoagulation team doacsupport.ox@nhs.net for further support and advice.

## Updated Interim Thromboprophylaxis Guidance for Patients with Suspected or Proven COVID-19

OUH have updated their interim guidance regarding thromboprophylaxis that was previously agreed in May. Patients with suspected or proven COVID-19 are offered extended standard dose LMWH thromboprophylaxis

on discharge for 7 days. It has now been agreed that if patients are unable to administer LMWH, rivaroxaban 10mg once daily (prophylactic dose) may be given as an alternative (this is an unlicensed indication). If a patient is considered to be particularly high risk of VTE because of additional VTE risk factors, such as previous VTE, then extended post-discharge thromboprophylaxis for up to 30 days may be considered on a case by case basis.

Patients under ambulatory care will also be considered for 7 days of VTE prevention on an individual basis taking into account additional VTE risk factors. If patients are unable to administer LMWH, rivaroxaban 10mg daily (prophylactic dose) is an alternative (unlicensed indication).

It is acknowledged that there is a lack of good-quality evidence specific to patients with COVID-19 and this guidance uses clinical knowledge and experience to build on the limited evidence base to develop the recommendations. It has been agreed that the VTE prophylaxis will be prescribed and supplied by the OUH in these circumstances. Any queries regarding this please contact occg.medicines@nhs.net.

## Freestyle Libre 2

Abbott have released the updated Freestyle Libre System (Freestyle Libre 2), which will be officially launched in January 2021. The original Freestyle Libre system will still be available and is not being discontinued, so there is no immediate rush to switch patients and no need for wastage of sensors. Some points to note:

- Currently, Freestyle Libre 2 sensors are 'non-formulary' in Oxfordshire **so we are not encouraging active switching until it has been approved by APCO and added to the formulary.** The sensors are likely to be added as a formulary option in January.
- Abbott will upgrade readers for free – the patient should contact Abbott for the new reader. For those who use the app, an update is available to allow access to the Freestyle Libre 2 features.
- Once the patient has their new reader, the prescriber can switch the sensors over to Freestyle Libre 2 sensors. However, there is no immediate rush and no need for wastage, as the original sensors will still work with the Freestyle Libre 2 reader. However, if the original sensors are used, the extra functions (e.g. optional alarms) will not work. Encourage patients to use their original sensors up first and delay switching where possible until the updated sensors have been added to the formulary.
- Improved features of Freestyle Libre 2 include improved accuracy and optional alarms for high or low glucose levels.
- Freestyle Libre 2 sensors are the same price as the original, so there is no cost impact in switching.

So What?

- Freestyle Libre 2 sensors will be considered at APCO in January.
- If patients wish to upgrade their reader now (via Abbott), the original sensors can still be used with the new reader. However, upgraded features will not be accessible until the new sensors are issued.
- Patients should use their supplies of original sensors first before switching to avoid wastage.

## Amino Acid Infant Formula Prescribing in Oxfordshire

Amino Acid Infant Formulas (AAF) are used in infants with Cow's Milk Protein Allergy (CMPA) where at least one of the following criteria are met:

- Persistent symptoms after 4 weeks on an Extensively Hydrolysed formula (EHf)
- Severe CMPA such as faltering growth and severe GI symptoms
- A history of anaphylactic reaction to cow's milk formula
- Persistent symptoms in breast fed infants unresponsive to maternal dairy free diet for 4 weeks, or mother does not wish to continue breast feeding

AAF should only be prescribed on advice and recommendation of a paediatric consultant. GPs can contact the consultant-led paediatric allergy advice service via oxon.paedsallergyadvice@nhs.net for specialist advice on appropriateness of AAF before starting it in new patients.

OCCG firstline AAF is **Alfamino**, followed by **Nutramigen PurAmino** and **Neocate LCP**. Elecare is also on the formulary and is suitable for infants requiring a low osmolarity feed with medium chain triglycerides (MCTs).

****NB Neocate Syneo should not be prescribed in Primary Care as it was black-listed by APCO in November 2019 due to a lack of evidence to support its use. ****

**So What?**

- If Cow's Milk Protein Allergy is suspected and at least one of the criteria above is met, email the Paeds Allergy Advice (oxon.paedsallergyadvice@nhs.net ) for input with which infant formula to prescribe.
- Only prescribe items on the OCCG formulary.
- Any questions please contact OCCG Prescribing Support Dietitian on occg.dietitian@nhs.uk.

## Hydroxychloroquine Shared Care Protocol

The Hydroxychloroquine Shared Care Protocol was updated in September 2019 in line with the retinopathy guidelines produced by the Royal College of Ophthalmologists. The RCO guidelines highlight that recent data suggests hydroxychloroquine retinopathy may be more common than previously reported and that, overall, 7.5% of individuals (usually classified at the start of treatment as 'high risk') taking hydroxychloroquine for more than **five** years *may* have some signs of retinal damage detected on specialised tests. It notes that the risk is increased for patients taking more than **5mg/kg/day**, those also taking **tamoxifen**, and those with **renal impairment**. Clinicians at the OUH **are** fully aware of the above guidance and OCCG has been in discussion with them to develop a long term solution for ensuring safe monitoring, including the removal of patients from this treatment wherever possible and the alternative use of other medications. They are working on these lists now to reduce the numbers of patients on this drug as quickly as is practical in the current climate. We now have a workable solution to the monitoring issue which will be rolled out very early in the new year, mindful of the current situation.

We understand the concerns that individual prescribers have currently, as they are not able to comply fully to the requirements of the shared care protocol and RCO guidance. As with all shared care, if the GP does not

feel comfortable taking clinical responsibility for the prescribing due to aspects of the protocol not being met, then it can be passed back to secondary care. However, we would like to reassure you that a solution will be available shortly and ask that any decisions about who should take responsibility for continuing care or treatment should be based on the patient's best interests. Please contact occg.medicines@nhs.net if you have any questions and look out for further communications on a screening service in GP Bulletin next week.

So What?

Please contact occg.medicines@nhs.net if you have any questions and look out for further communications on a screening service in GP Bulletin next week.

## Supply Issues

### Supply Issues Affecting Primary Care

Please note this is not an exhaustive list. Some information on long-term supply issues can be found on Clinox website.

| Supply Issue/ Manufacturer | Resupply date | Comment |
|---|---|---|
| Bisacodyl (Dulcolax) 5mg and 10mg suppositories/ Sanofi | Bisacodyl 5mg suppositories- Early January 2021<br><br>Bisacodyl 10mg suppositories limited supplies expected January 2021, full resupplies expected in March 2021. | • There are alternative laxatives that can be used via the oral or rectal route for constipation. |
| Haloperidol 5mg/5ml oral solution sugar free /Thame Laboratories | Out of stock (OOS) until March 2021 | • Haloperidol (Haldol®) 2 mg/ml oral solution is the only licensed oral solution that can support an uplift in demand.<br>• Haloperidol 500microgram, 1.5mg, 5mg and 10mg tablets remain available.<br>• Specials manufacturers have confirmed they can manufacture haloperidol 5mg/5ml oral solution sugar free. |
| H2-antagonists/ Various brands | Various updates | • Please refer to the local Ranitidine Switch Protocol for use in primary care.<br>• See here for updates on resupply dates. |
| Oral contraceptive tablets/ Various brands | Various updates | See here for more information. |
| Normacol Plus/ Target Healthcare | W/c 21st December 2020 (updated) | See here for more information. |
| Pregaday Tablets | Mid-December 2020 (updated) | See here for more information. |
| Trifluoperazine 1mg/5ml syrup/ Advanz Pharma | OOS until April 2021 | • Trifluoperazine 1mg and 5mg tablets remain available |

| | | |
|---|---|---|
| | | • Trifluoperazine 5mg/5ml oral solution remains available. Patients must be counselled on the change in strength and equivalent volume required.<br><br>• Trifluoperazine 1mg/5ml oral suspension may be ordered as Specials.<br>• See here for more information. |
| Zonisamide 25 mg and 50mg capsules/Teva | OOS until mid-February 2021 | • Alternative manufacturer's Zonisamide capsules remain available.<br>• Prescribers should closely monitor patients for any changes in seizure frequency and/or breakthrough seizures when they are switched over to alternative manufacturer's zonisamide capsules (MHRA category 2 anti-epileptic drug).<br>• See here for more information. |

## Recall of Contaminated Betahistine Tablets

MHRA was informed by Kent Pharmaceutical Ltd that some batches of betahistines 8mg and 16mg tablets are contaminated with theophylline due to a cross-contamination issue identified with an excipient that was used in the manufacture of the finished product. Therefore, a decision was taken to recall the affected batches – details of the affected batches can be found here.

The risk of adverse reactions is low with respect to the level of contamination. However, prescribers and pharmacists should be aware of this alert if patients report of any experience of side effects related to hypersensitivity or those not normally experienced with betahistine. Any suspected side effects should also be reported via the Yellow Card scheme.

## Drug Safety Updates

## Modafinil (Provigil): increased risk of congenital malformations if used during pregnancy

MHRA has issued a safety update that states modafinil potentially increases the risk of congenital malformations when used in pregnancy and should not be used during pregnancy. Women of childbearing potential must use effective contraception during treatment and for 2 months after stopping modafinil. Modafinil may reduce the effectiveness of steroidal contraceptives, including oral contraceptives, therefore alternative or concomitant methods of contraception are required. See here for more details.

## Bupropion (Zyban): risk of serotonin syndrome with use with other serotonergic drugs

Cases of serotonin syndrome have been reported in association with bupropion, especially in overdose or when bupropion is co-administered with other drugs with a serotonergic effect, for example selective

serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine re-uptake inhibitors (SNRI). If concomitant prescribing with other serotonergic drugs is clinically warranted, MHRA advises of the following:

- do not exceed the recommended dose
- remind patients of the milder symptoms of serotonin syndrome at initiation of treatment and at any change of dose and the importance of seeking medical advice if they occur
- if serotonin syndrome is suspected, either decrease the dose of bupropion or withdraw therapy depending on the severity of the symptoms.

See the safety update here for more details.