Prescribing Points

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Oxfordshire Cinical Commissioning Group

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Inside this issue:

OCCG COVID-19 Website

The CCG has set up a dedicated area for primary care in the restricted staff zone of the CCG's website. For those who cannot access the staff zone (N3 connection required), the document on medicines related Frequently Asked Qestions (FAQs) can also be found on ClinOx. The staff zone will be used to post key information, links to national updates and responses to FAQs. There are links to a number of additional guidance documents in the table at the bottom of this page and currently this includes diabetes patients; cancer referrals and wait times, cancer patient FAQs; and medicines related FAQs. Our team are continuoulsy updating the medicine related FAQs document with the most current information, if you have further questions please email occg.medicines@nhs.net.

Please note any general COVID-19 queries should be directed to the central email address at occg.emergencycontrol@nhs.net.

Prescribing Incentive Scheme 2019-20

We are suspending the requirements for any submission for the Prescribing Incentive Scheme (PIS) 2019-20. Three out of the four elements are already measured internally by the Medicines Optimisation team and require no submission. For the remaining element (Element 2: use of the PINCER IT tool), we will now assess achievement using prescribing data and will take a pragmatic and supportive approach in decision on payment. Therefore, practices are no longer required to submit anything for the PIS 2019-20.

Clozapine Shared Care Protocol

Clozapine is a third line antipsychotic used to for treatment resistant schizophrenia as per NICE recommendations. It is also licensed for the treatment of psychotic disorders occurring during the course of

Parkinson's disease where other treatments have failed. The updated Shared Care Protocol was approved at APCO in January 2020. Updates include:

- Amendments made to Adverse Drug Reactions based on the most recent Summary of Product Characteristics (SPC).
- Simplification of wording and improved clarity for issues such as blood monitoring and diabetes.
- It also specifies much more clearly that patients must remain open to the care of a secondary care consultant due to the terms of the UK product licence

For an update on clozapine prescribing and management during the COVID-19 pandemic please see the COVID-19: testing and medicines management in the community document. This covers how to manage testing for patients who are self isolating and how to manage prescrbing for patients with symptoms.

So What?

- Prescribers must ensure they use the updated Shared Care Protocol found on ClinOx here.
- Refer to the COVID-19: testing and medicines management in the community document for updates on current clozapine monitoring and prescribing.

Update to OCCG anticoagulation guidance and documents

For an update on warfarin and DOAC prescribing and management during the COVID-19 pandemic please see the COVID-19: testing and medicines management in the community document.

The OCCG Warfarin Shared Care Protocol, DOAC in AF and DOAC in VTE guidelines have been updated to reflect current terminology and practice (does not include COVID-19 updates, see separate document).
Key updates for the warfarin shared care protocol:

- Clarification of shared care responsibilities for the anticoagulation clinic, GP and patient.
- Updating monitoring requirement from 6 monthly to yearly in line with Primary Care Service For Warfarin Monitoring.

Key updates the DOAC in AF guidance are:

- Addition of drug interaction between primidone and DOACs
- Highlighting the lack of data for DOACs for use in patients with a body weight greater 120kg. For such patients warfarin is recommended.

Key updates the DOAC in VTE guidance are:

- Changes to dalteparin doses for patients weighing more than 98 kg. For these patients therapeutic dalteparin doses are to be given twice daily in line with OUH DVT protocols and ASH guidance.

- Addition of the management of patients with antiphospholipid syndrome (APS) and the use of DOACs in thromboembolism.

Blood Glucose Test Strips – A Case Study

A patient with Type 2 diabetes was referred to Ambulatory Assessment Unit by their GP for investigation of low blood glucose levels (2.3-5.5mmols) for period of 5 days. The GP had stopped all diabetes medications including insulin 3 days prior to referral to AAU as blood glucose levels had been low. The patient had no symptoms of hypoglycaemia. On arrival to AAU all observations were in normal limits except capillary blood glucose level of greater than 27.8mmols. The patient was referred to their Diabetes Specialist Nurses (DSN) for review, whilst visiting the patient the DSN observed that glucose strips had been dispensed and stored in a transparent plastic box. The DSN used one of these strips to test blood glucose levels which read as 5mmols, they then rechecked with new strips from pot that they came in and the reading was 24.4mmols. It is important to note that **strips stored incorrectly and exposed to light can give erroneous readings**. Patient advised to discard strips that had been dispensed and DSN provided new strips.

So What?

- Blood Glucose Test Strips stored incorrectly and exposed to light can give erroneous readings.
- If a patient presents with low blood glucose levels, check how they stored to rule out strip error before adjusting medication.

SGLT2 Inhibitors and Foot Disease

The local specialist team have identified several patients on SGLT2 inhibitors with active foot disease. There is an increased risk of lower limb amputation (mainly toes) in patients on Canagliflozin, and this may be a class effect (see MHRA warning). NICE (2015) and MHRA (2017) have provided advice on reducing the risk of lower limb amputation when using SGLT2 inhibitors in type 2 diabetes:

- Check feet regularly and follow preventative care.
- Report any foot infection or ulceration.
- Avoid initiation of SGLT2 inhibitors if active foot ulceration or if previous lower limb amputation.
- If develops foot ulcer stop SGLT2 inhibitor as a precaution, and consider other treatments
- Be cautious about initiating SGLT2 inhibitors in people with peripheral vascular disease.
- Consider stopping SGLT2 inhibitors in cases of foot ulceration, osteomyelitis or gangrene.

So What?

- Follow advice above on reducing the risk of lower limb amputation when using SGLT2 inhibitors in type 2 diabetes.

Emergency Ketone Testing Kits

Ketone testing for people with Type 1 Diabetes is key to support self-management in illness. If you are unable to access ketone meters or test strips via normal supply routes, please contact OCDEM or Community Diabetes Team who will be able to support supply of an emergency kit. This arrangement is in place as a

preventative measure, currently there are no issues with normal supply routes. The OCCG Ketone Testing Guidelines and following leaflets from TREND UK can be used to support Sick Day Rule discussions with patients:

- What to do when you are unwell Type 1 Diabetes
- What to do when you are unwell Type 2 Diabetes
- Hypoglycaemia Explained

So What?

- Continue to provide ketone test strips/monitors as normal for appropriate patients. If any issues occur, contact OCDEM or Commuity Diabetes Team.

Supply Issues and Product Discontinuation

Please note this is not an exhaustive list. Some information on long-term supply issues can be found on Clinox website. Please check the COVID-19 Medicines Related FAQ document for information on shortages related to the pandemic.

Supply Issue: Fluoxetine 10mg Tablets

Fluoxetine 10mg tablets are out of stock until late 2020. Fluoxetine 10mg capsules and fluoxetine 20mg/5ml oral solution remain available. A serious shortage protocol (SSP) has been issued on 12/3/2020.
Please note that the oral solution has the same bioavailability as the tablets/capsules - so can be used to make up the equivalent dose if required e.g.

- 10mg = 2.5ml; 30mg = 7.5ml; 40mg = 10ml

So What?

- For patients with insufficient supplies, clinicians should consider prescribing an alternative formulation of fluoxetine.
- Community pharmacists may supply fluoxetine 10mg capsules against the SSP for eligible patients.

Supply Issue: Promazine 25mg & 50mg Tablets

Promazine 25mg and 50mg tablets are out of stock with anticipated resupply date of mid-April 2020. Alternative formulations, including unlicensed import, are available – see 'So What' below.

For patients with insufficient supplies during this period, clinicians should first of all consider reviewing patients to establish if continued treatment is required, in accordance with UKMi advice:

• Promazine is an antipsychotic drug from the phenothiazine class (group 1), which is generally characterised by pronounced sedative effects. It is licensed for the management of agitation and restlessness in the elderly, and as short-term adjunctive management of psychomotor agitation.

• In elderly patients with dementia, antipsychotic drugs are associated with a small increased risk of mortality and an increased risk of stroke or transient ischaemic attack, therefore they are not recommended to treat mild to moderate psychotic symptoms.

• Patients on long term treatment should be reviewed and treatment stopped if they are not getting a clear ongoing benefit from taking them and after discussion with the person taking them and their family members/ carers. In people living with dementia, psychosocial and environmental interventions are the preferred management options to reduce distress.

• Antipsychotics should only be considered for people living with dementia who are either at risk of harming themselves or others or they are experiencing agitation, hallucinations or delusions that are causing them severe distress. If treatment is considered necessary, a licensed oral solution is available, as are unlicensed imports.

So What?
For patients with insufficient supplies during this period, clinicians should consider:
• reviewing patients to establish if continued treatment is required (as per UKMi advice) or;
• prescribing promazine 25mg/5ml or 50mg/5ml oral syrup (Rosemont Pharmaceuticals); or
• prescribing unlicensed promazine 25mg or 50mg tablets (in accordance with national guidance and local policy)

Diamorphine Hydrochloride powder for reconstitution and injection 5mg & 10mg ampoules

The two suppliers of diamorphine hydrochloride 5mg and 10mg in the UK, Wockhardt and Accord, have both reported shortage issues:

• Accord is out of stock of both 5mg and 10mg strengths, with a re-supply date of Summer 2020.
• Wockhardt are expecting to be out of stock of 5mg vials from week commencing (w/c) 2nd March and 10mg vials from w/c 16th March until w/c 6th April 2020.

Diamorphine hydrochloride 30mg, 100mg, 500mg are available but manufacturers are unable to support an increase in demand on these strengths. Morphine sulfate solution for injection 10mg/ml has been identified by clinical experts as the most likely first-line alternative, however, morphine and diamorphine are not equipotent, and care should be taken when switching patients or amending guidelines. There are sufficient supplies of morphine sulfate 10mg/ml injection (preservative free) from Ethypharm and Hameln to support this supply disruption.

So What?

Primary care providers should ensure that the steps taken are now made **permanent**:

- identify a local lead within their organisation to manage the delivery of actions as advised in this document where possible;
- review and update guidelines and protocols, moving to morphine sulfate injection as opioid of choice, where clinically appropriate, in place of diamorphine 5mg and 10mg;
- identify and deliver required education and training to General Practice and community nursing teams to support the switch over to morphine;
- ensure no new patients are started on diamorphine hydrochloride 5mg or 10mg injection;
- review patients currently receiving diamorphine 5mg or 10mg injection and manage the switch to an alternative opioid;
- not switch patients to higher strengths of diamorphine injection as there is insufficient stock to support increased use;
- consider morphine 10mg/ml injection as the first line opioid as supplies of alternative opioid agents are limited and these should be prescribed for patients where morphine is not clinically appropriate; and
- place orders for morphine sulfate 10mg/1ml solution for injection ampoules (Ethypharm (Martindale) and Hameln) from major wholesalers.

Supply Issue: Genotropin®

There is temporary supply issue with Genotropin®, for an overview of availability please see the table below:

Dose/Device	Status	Comment
12mg Refill Cartridge	Out of Stock	• Full resupply planned for April 2020
5.3mg Refill Cartridge	Low Stock	• Limited supplies **until** w/c 24th February 2020
12mg GoQuick	Out of Stock	• Full resupply planned for April 2020
5.3mg GoQuick	In Stock	• No expected interruption to supply
0.6mg MiniQuick	Out of Stock	• Full resupply planned for April 2020
0.8mg MiniQuick	V. Low Stock	• Full resupply planned for April 2020 with limited supplies available during Feb/March 2020
All other MiniQuick Products	In Stock	• No expected interruption to supply

Product doses with limited availability are still available to order via Alliance Account. For patients who are required to switch their device as a result of this issue, Pfizer will provide free device training through the homecare provider. If this is required, the homecare company should be informed of a change to prescription and a request for patient training. Alternatively, please contact endocrinecare@pfizer.com for additional support.

Other Short-term Supply Issues

Supply Issue	Updated resupply date
Phenelzine (Nardil) 15mg tablets	Unable to advise resupply date
Clonidine 25mcg tablets	End of April 2020
Lorazepam (Ativan®) 4mg/ml injection (Pfizer)	w/c 23 March 2020
Penicillamine 125mg and 250mg tablets	Late March 2020

Safety Alerts

Restrictions in use of cyproterone due to meningioma risk

The EMA's safety committee has recommended that the antiandrogen medicines cyproterone at a daily dose of 10 mg or more should only be used for androgen-dependent conditions (such as hirsutism, alopecia and seborrhoea) when other treatment options have failed, including treatment with lower doses of cyproterone. Cyproterone should also only be used for the control of libido when other treatment options are not suitable.

These restrictions are in light of a safety review that has identified an increased risk of meningioma (a non-cancerous brain tumour) at higher doses (primarily 25 mg daily and over). There is no change for use in prostate cancer, and available data suggest no increased risk with low-dose (1 to 2 mg) cyproterone-containing medicines, although these will now also be contraindicated in patients with a history of meningioma.

So What?

- Healthcare professionals should monitor patients for clinical signs and symptoms of meningioma in line with clinical practice. Symptoms may be unspecific and include changes in vision, hearing loss or ringing in the ears, loss of smell, headaches that worsen with time, memory loss, seizures or weakness in extremities.
- If a patient treated with cyproterone acetate is diagnosed with meningioma, treatment with all cyproterone-containing products must be permanently stopped.
- For more information please see the EMA website.

Esmya (ulipristal acetate): suspension of the licence due to risk of serious liver injury

Ulipristal acetate 5mg (Esmya) is authorised for moderate to severe symptoms of uterine fibroids in women who had not reached the menopause. Since authorisation and to date, the MHRA have received 19 suspected adverse drug reaction reports of liver disorders with the use of Esmya in the UK. None report liver transplant or death. Approximately 2,865 treatment courses of Esmya were dispensed in the UK in 2019.

Following a further case (5th case worldwide) of liver injury requiring transplant, the licence for Esmya has been suspended to protect public health while a safety review is conducted by the European Medicines Agency (EMA). The MHRA has issued a recall of Esmya from pharmacies, wholesalers, and patients, and the manufacturer will send a letter to UK prescribers and dispensers shortly. Please note the emergency

contraceptive EllaOne also contains ulipristal acetate (single dose, 30mg), however there are no concerns with this medicine at this time.

So What?

- contact patients currently being treated with Esmya as soon as possible and stop their treatment; discuss alternative treatment options for uterine fibroids as appropriate.
- do not start any new patients on Esmya
- advise recent users to seek immediate medical attention if they develop signs and symptoms of liver injury (nausea, vomiting, malaise, right hypochondrial pain, anorexia, asthenia or jaundice)
- perform liver function tests 2–4 weeks after stopping Esmya as recommended in the product information
- report suspected adverse drug reactions without delay to the Yellow Card Scheme.

Benzodiazepines and opioids: reminder of risk of potentially fatal respiratory depression

Benzodiazepines (and benzodiazepine-like drugs) and opioid medicines can both cause respiratory depression; when used together, additive effects on the central nervous system increase the risks of sedation, respiratory depression, and coma, which can be fatal if not recognised in time.

Following a Coroner report in relation to death by respiratory arrest of a man given the benzodiazepine clonazepam, and among other drugs, the opioid methadone, the MHRA has issued a safety alert regarding co-prescribing of benzodiazepines and opioids: healthcare professionals are reminded of the risk of (additive) respiratory depression when co-prescribed, advice to minimise risk and advice to supply to patients.

So What?

- only prescribe benzodiazepines (or benzodiazepine-like drugs) and opioids together if there is no alternative
- if a decision is made to co-prescribe, use the lowest doses possible for the shortest duration of time and carefully monitor patients for signs of respiratory depression
- if there is any change in prescribing such as new interactions or dose adjustments, re-introduce close monitoring of the patient
- if co-prescribing methadone with a benzodiazepine or benzodiazepine-like drug, closely monitor for respiratory depression for at least 2 weeks following initiation or changes to prescribing because the respiratory depression effect of methadone may be delayed.
- advise patients of the symptoms of respiratory depression and sedation and the need to seek immediate medical attention if these occur.