Oxfordshire
Cinical Commissioning Group

Prescribing Points

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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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Inside this issue:

Guidelines on Prescribing Specialist Infant Formulas in Primary Care

The infant formula prescribing guideline has been updated and is now available on the OCCG website here. The guidelines outline recommendations for the safe, appropriate and cost-effective prescribing of specialist infant formula for children up to the age of 18 months in the Oxfordshire area. It covers:

- Over-the-counter (OTC) products available wherever appropriate
- Quantities to prescribe
- Which products to use for different clinical conditions
- Initiating, reviewing and discontinuing prescriptions
- When to refer to dietitians and/ or secondary or specialist care

In this update the main changes are:

- New sections added with advice for GORD, lactose intolerance, faltering growth and pre-term infants
- Clarified that anti-reflux pre-thickened formula and thickening formula, soya formula and lactose-free formula are all classified as black on the Oxfordshire formulary – all can be purchased OTC
- Amino acid formulas (AAf) are classified as amber continuation on the Oxfordshire formulary – should only be prescribed on the advice or recommendation of a Paediatric Consultant
- A summary of the prescribing guidelines has been added (available as a standalone document here). This should not be used for diagnosis but summarises the advice for the various conditions covered by the guideline including formula choices.

So what?
Prescribers can use the guideline to ensure appropriate prescribing of specialist infant formulas. Specific queries can also be directed to the Prescribing Support Dietitian via occg.dietitian@nhs.net

Maintenance Management of Asthma – Inhaled and Oral Therapies (adults)

A new document outlining the local formulary choice of inhalers and other therapies at the various stages of asthma treatment is now available on the CCG website here. This has been developed in conjunction with representatives from respiratory teams in Oxford Health, Oxford University Hospital as well as GPs, practice nurses and the CCG Medicines Optimisation Team.

This document brings together previous local formulary choices/prescribing policies for the treatment of asthma and clarifies any areas that may not have previously had a specific formulary choice. It also aims to highlight which steroid inhalers are considered low, medium or high dose and provides images of each inhaler to aid decision making.

Key points:

- Not intended as a full guideline but may be used as a decision support tool focusing on consistency of inhaler device, cost effectiveness and choice of dose
- Range of inhalers given as either a metered dose (MDI) or dry powder (DPI) pathway
- Clenil Modulite (MDI) and Pulmicort Turbohaler (DPI) both included as main low dose inhaled steroid (ICS) choices
- Alvesco (ciclesonide) MDI included as a 2nd line ICS option for patients who have unacceptable oral side effects caused by corticosteroid despite thorough post-dose mouth rinsing, use of a spacer and treatment of candidiasis.
- Fostair MDI and NEXThaler both included as main choices for MDI and DPI pathway when a combination inhaler is indicated (low, medium and high dose)
- **Airflusal MDI (fluticasone/salmeterol combination inhaler) included as an option if a medium or high dose combination MDI is indicated. A switch from Seretide Evohaler can be considered as this is an equivalent device and a considerable cost saving (see below). Airflusal must be prescribed by brand for the saving to be realised.**

Dose	AirFluSal MDI list price	Salmeterol/fluticasone MDI (Seretide) Drug Tariff Price
25/125 µg	£18.50	£35
25/250 µg	£29.95	£59.48

Please note, Seretide 50 evohaler should be used if a low dose combination is indicated

- Relvar Ellipta can be considered as an alternative option if a medium or high dose DPI is indicated and a once daily regimen would be beneficial
- Symbicort turbohaler also included as an alternative option as a low, medium and high dose DPI
- Formulary choices for add on therapies also included

So what?
Prescribers should ensure that the new formulary choices are considered when starting a patient on new treatment or when reviewing existing treatment

Generalised Anxiety Disorder Guideline (GAD) - Update

The GAD guidance has been updated by Oxford Health and is available on the CCG website here. The changes include:

- **Pregabalin** can now be started in primary care for this indication (3rd line option). Patients can still be referred to secondary care for an assessment if necessary. Information on dosing has been added to the guideline as well as clarification about when pregabalin should be added to selective serotonin reuptake inhibitors (SSRI) or serotonin and noradrenaline reuptake inhibitors (SNRI) therapy and when it should be used alone.
- **Escitalopram** has been included as an alternative 1st line option (as a licensed SSRI for GAD)

- **Serotonin and noradrenaline reuptake inhibitors** (SNRIs) – duloxetine or venlafaxine are 2nd line options for treatment. Evidence for both medications is similar and guidance clarifies that duloxetine is currently the more cost effective option.

So what?
Prescribers should ensure that the latest version of the guidance is followed and be aware of the above changes

Extended ticagrelor therapy for the prevention of atherothrombotic events after myocardial infarction

NICE TA420 recommends Ticagrelor (Brilique) 60mg twice daily, in combination with aspirin 75mg to 150mg within its marketing authorisation as an option for preventing atherothrombotic events in adults who have a history of myocardial infarction (MI) of at least one year and who are at high risk of a further event.
Ticagrelor 60 mg twice daily is the recommended dose when an extended treatment is required following one year of 90mg twice daily treatment. Treatment may be started without interruption as continuation therapy after the initial one-year treatment with Ticagrelor (Brilique) 90 mg in acute coronary syndrome (ACS) patients at high risk of an atherothrombotic event. Treatment can also be initiated up to 2 years from the MI, or within one year after stopping previous Ticagrelor 90mg. Treatment should be stopped when clinically indicated or at a maximum of 3 years.
From October 2017 OUH Cardiology will identify relevant patients and notify GPs via discharge letter and reference to the 'Extended ticagrelor therapy for the prevention of atherothrombotic events after myocardial infarction, Amber Continuation Guideline.'
The discharge letter will confirm that the patient has been identified as high risk and request 3 year continuation treatment with 60mg dose following one initial year at 90mg.
This treatment option, however, should be available for appropriate patients from March 2017.It is therefore proposed that patients who have been initiated on Ticagrelor 90mg post-MI between March 2016 and October 2017, should be identified by their GP practice and risk assessed according to the criteria from the PEGASUS-TIMI54 study (see table below).

OUH deal with approximately 1000 ACS patients per annum (some will be out of area). NICE estimates the number of relevant patients to be 2 per 100,000 and therefore there should only be a small number of patients at each practice to be reviewed and noted for continuation therapy.

Patient criteria for Ticagrelor continuation treatment

High risk criteria: 1 or more of the following high risk features:	
• Aged 65 years or older	• Diabetes requiring medication
• Multi-vessel coronary artery disease	• Chronic non-end stage kidney disease (Creatinine clearance less than 60ml/min)
• More than one previous MI	

The Medicines Optimisation Team can assist with patient identification for review. An EMIS search has been constructed to produce the patient list (patients starting Ticagrelor 90mg since March 2016). A template letter is available to inform patients of the planned additional treatment.

So What?
Actions for practices
- Identify patients initiated on ticagrelor 90mg since March 2016
- Review patients in line with high risk criteria
- Add clinical note or screen message to records of identified high risk patients, to commence 60mg continuation treatment following completion of one year on 90mg
- Send letter to inform patient
- Consider adding start and stop dates to prescription direction information to ensure patient and pharmacist are aware.

Vitamin D in Pregnancy

A guideline on Vitamin D Supplementation in Pregnancy has been produced by Oxford University Hospitals, approved by APCO and is now available on the CCG website here, along with a quick reference algorithm here.
The aim of the guidance is to ensure all pregnant women are assessed for their risk of vitamin D deficiency and to ensure stores are sufficient by the third trimester to reduce the risk of low vitamin D levels in the baby (particularly childhood rickets). Women at high risk of pre-eclampsia should also receive a higher dose (1000 units daily) of cholecalciferol. Community midwives will screen for risk of deficiency at the booking in appointment before 12 weeks and, depending on level of risk, either give general advice (e.g. buy OTC or healthy start vitamins) or test levels. **The GP should follow up, receive blood test results and prescribe vitamin D as necessary.**

Key Recommendations

- Vitamin D supplementation should be discussed with all pregnant and breastfeeding women
- All pregnant/breastfeeding women should receive at least 400 units/day cholecalciferol from OTC preparations or "Healthy Start" if eligible.
- Women should be assessed for their risk of vitamin D deficiency at their booking appointment.
- 'At risk' groups for vitamin D deficiency or insufficiency should be started on 1000 units cholecalciferol daily
- Women at moderate or high risk of vitamin D deficiency should be tested with their booking blood tests.
- All pregnant women with Vitamin D deficiency should have their Vitamin D replaced according to the level of insufficiency to ensure it is adequately replaced by the third trimester.
- All babies should have 400 units per day unless fully formula fed.

So what?
GPs should be aware of vitamin D in pregnancy guideline and the prescribing requirements as a result of blood test results

Levonorgestrel Dose Change for Emergency Contraception

The dose of levonorgesterel for emergency contraception has been updated on the online BNF. The advice includes a higher dose to be considered in patients over a certain weight.
Please be aware, the most recent paper BNF (BNF 74 Sept 2017-March 2018) has not been updated.

The updated dosing information is as follows:

Females of childbearing potential: 1.5 mg for 1 dose, taken as soon as possible after coitus, preferably within 12 hours but no later than after 72 hours, alternatively 3 mg for 1 dose, taken as soon as possible after coitus, preferably within 12 hours but no later than after 72 hours. Higher dose should be considered for patients with body-weight over 70 kg or BMI over 26 kg/m^2.
Unlicensed Use: The dose for emergency contraception in patients with body-weight over 70 kg or BMI over 26 kg/m^2 differs from product license.

So What?
Ensure the most recent dosing information is being used and patient weight is taken into account

FreeStyle Libre

A reminder that prescribers in primary care are requested not to prescribe Freestyle Libre® glucose monitoring sensors on an NHS prescription until the Freestyle Libre® device has been evaluated and approved for use in Oxfordshire. Please see the updated statement here. Queries to OCCG.medicines@nhs.net .

Shared Care Protocols

Locally agreed Shared Care Protocols are available on the OCCG website here: http://www.oxfordshireccg.nhs.uk/professional-resources/shared-care-protocols.htm

The majority of protocols are an agreement between patients, specialists and GPs. However, some may also involve other health care professionals such as community pharmacists. For example, the lithium shared care protocol contains a section on pharmacist responsibilities.

Antimicrobial Prescribing Update

Trimethoprim Patient Group Direction (PGD)

In July 2016, OCCG initiated a small pilot whereby 14 community pharmacies in Oxfordshire could use a PGD to treat simple UTIs in women with trimethoprim. Due to the success of this pilot, the service has been offered to all community pharmacies in Oxfordshire. The pharmacies are able to start providing the service as of 27th November 2017. We have a range of pharmacies signed up currently, and do expect the availability to increase over the next few months.

Please speak to your local community pharmacists to find out if they are providing the service in their store.

The aim of the service is to reduce pressure on GP practices and Out of Hours services by diverting patients with uncomplicated UTIs to a pharmacy. The pharmacist is able to provide advice and treatment with trimethoprim (200mg BD for 3 days) to appropriate patients. Patients exempt from prescription charges will receive the treatment for free, and those who are non-exempt will be charged a standard prescription fee. The inclusion criteria for the PGD are:

- Otherwise healthy women, aged 16-65, presenting with an uncomplicated UTI
- Registered at a G.P practice in Oxfordshire

The PGD also contains certain exclusion criteria. For more information on the inclusion and exclusion criteria, there is an information sheet available on the intranet here.
A list of pharmacies providing the service will be added at a later date. Please review the exclusion criteria before sign posting patients to the pharmacy. Patients who do not meet the inclusion criteria will be referred back to the GP or Out of Hours.

So What?
GP practices are encouraged to signpost appropriate patients to this service. A poster has been sent to your practice which you can display in your waiting area.

Shorter penicillin courses for sore throats

The September 2017 update to the Public Health England (PHE) infection guideline includes a slight change to the recommended duration of first-line antibiotics (*where antibiotic treatment is indicated*) for acute sore throat in adults, from a 10-day course of phenoxymethylpenicillin (penicillin V) to a **5 to 10** day course. It also recommends considering immediate antibiotics if symptoms are severe, or possibly a short (48 hrs) delayed prescribing strategy, where the FeverPAIN score is ≥ 4.

This option for a shorter course was informed by a new analysis of a large UK cohort of adults presenting to primary care with sore throat, which found little difference in the re-consultation rates and symptomatic outcomes between patients receiving shorter and longer courses of antibiotics.

Acute sore throat (including pharyngitis and tonsillitis) is self-limiting and usually triggered by a viral infection of the upper respiratory tract. Symptoms can last for around 1 week and most people will get better within this time without treatment, regardless of whether their illness is caused by a bacteria or a virus. For decades, phenoxymethylpenicillin has been the preferred treatment option if antibiotics are required, due to its proven efficacy, safety, narrow spectrum and low cost, with a 10-day course often recommended as standard care due to concerns about serious complications of sore throat. However, the incidence of serious complications arising from sore throats (including rheumatic fever and glomerulonephritis) is now very low in developed countries, and there is a need for more evidence on the appropriate duration of treatment in the modern era where the effective use of antimicrobials is a priority.

Possible advantages of a shorter antibiotic course include:

- Better adherence to treatment
- Reduced risk of adverse events
- Reduced likelihood of antimicrobial resistance
- Cost savings

Limitations of this study include its observational design and thus the potential for residual confounding. A randomised controlled trial (RCT) would strengthen the conclusions of this study, and in fact Swedish RCT is underway to compare 5 and 10 days of phenoxymethylpenicillin.

So What?

- For patients presenting with acute sore throat, only prescribe immediate antibiotics, or possibly consider a short (48 hrs) delayed prescribing strategy, if symptoms are severe and where the FeverPAIN score is ≥ 4.
- If antibiotic is needed consider prescribing shorter (**5 to 10** day)course of phenoxymethylpenicillin (penicillin V) as recommended in Public Health England (PHE) infection guideline
- Local guidance will be updated shortly to reflect this new recommendation

English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report 2017

The 2017 ESPAUR report is now available here. ESPAUR state the year-on-year increased burden (in terms of the number of individuals) of antibiotic-resistant Gram Negative Blood Stream Infections (GNBSIs) and Urinary Tract Infections (UTIs), though encouragingly the proportion of GNBSIs that are resistant to key antibiotics has remained broadly stable over the last 5 years. This is in contrast to many other countries globally and most likely reflects good antimicrobial stewardship and rare use of cephalosporins and quinolones in the community settings in England.
The report highlighted that in 2016, the commonest cause of blood stream infections was Escherichia coli; of these, 41% were resistant to the commonest antibiotic used to treat infections in hospitals (co-amoxiclav) and almost one in five of these bacteria were resistant to at least one of other key antibiotics, though multi-drug resistance (resistance to three antibiotics) remained uncommon (<5%).
ESPAUR noted that trimethoprim resistance is very common in laboratory processed urine samples (34%) but that the current recommended first line treatment, nitrofurantoin is currently effective (3%). This supports the PHE infections guidelines to switch from trimethoprim to nitrofurantoin as empiric treatment for UTI before laboratory results are available. This has been reflected in the local OCCG antimicrobial guidelines found here.
The report noted the number of antibiotic prescriptions dispensed in the GP setting decreased by 13% between 2012 and 2016 (-2% from 2015 to 2016), largely driven by reductions in use of penicillins.

Oxfordshire Study on E.Coli Infections and Antibiotic Susceptibilities

A local study on Trends in Escherichia coli bloodstream infection, urinary tract infections and antibiotic susceptibilities in Oxfordshire has recently been published. Notably, higher co-amoxiclav use in primary care was associated with higher rates of both E.coli UTIs and co-amoxiclav resistant E.coli UTIs, supporting drives to reduce broad spectrum and inappropriate antibiotic use. However, despite substantial increases in co-amoxiclav-resistant E.coli blood stream infections, evidence that patient clinical outcomes are no worse does not support broadening empiric antibiotic prescribing from co-amoxiclav. Increases in the incidence of E. coli bloodstream infections were driven mainly by non-hospital-associated cases; however, neither patients with previous UTIs nor having previously had urine specimens sent from catheters appeared to be driving the increases. Co-amoxiclav-resistant bloodstream infections rose significantly faster than co-amoxiclav-susceptible bloodstream infections, with the greatest number of co-amoxiclav-resistant bloodstream infections in 2016 being in patients discharged more than a month previously (i.e. community-associated)

Sensitivity data for gram-negative infections in Oxfordshire

The most recent sensitivity data also supports the avoidance of prescribing co-amoxiclav empirically to treat UTIs:

June 2016 to May 2017		% resistant to						
	Number of isolates	Co-amox	Cipro	Pip-taz	Temo	Fosfo	Gent	Co-tri
E coli (not ESBL)	20163	27	7	2	27	1	4	25
E coli (ESBL)	1364	100	52	9	45	1	27	56
K pneumo (not ESBL)	1973	17	5	6	11	14	2	15
K pneumo (ESBL)	173	99	39	33	43	24	45	75
E cloacae	659	98	2	11	21	16	7	13
E aerogenes	251	100	2	23	24	11	6	7

So What?

The ESPAUR report 2017 and the Oxfordshire study highlight the increased burden of antibiotic resistant GNBSI and UTIs. The local data particularly supports the drive to reduce inappropriate use of co-amoxiclav in primary care. Prescribers should ensure that local antimicrobial prescribing guidelines are being followed when making a decision to prescribe an antibiotic

Medicines availability update

Shortage of tranexamic acid tablets 500mg (all brands)

There are currently limited supplies of generic tranexamic acid 500mg tablets on the market. This is due to difficulty in manufacturers obtaining raw material. Branded Tranexamic Acid 500mg (Cyklokapron), the over the counter product (Cyklo-f) and some generic tranexamic acid 500mg tablets continue to be remain available; however there may be intermittent supplies issues until at least 2018.

Shortage of hydrocortisone 100 mg/mL or 500mg/5ml Injection

The supplier of hydrocortisone sodium phosphate injection (formerly Efcortesol) is currently out of stock due to an issue with the active pharmaceutical ingredient. Further supplies are not due until late in 2018. The only other licensed hydrocortisone injectable preparation available is Solu-Cortef® (hydrocortisone sodium succinate), each vial of which contains the equivalent of 100 mg hydrocortisone as the sodium succinate powder for reconstitution with 2 ml of sterile water for injection. Great Ormond Street Hospital has produced a patient information leaflet on how to reconstitute Solu-Cortef®.

Discontinued: One Touch Ultra Test Strips

One Touch Ultra test strips were discontinued in June 2017. There is still some stock available; however it is expected that this stock will run out by January 2018. There are still a reasonable number of One Touch Ultra test strips being prescribed in Oxfordshire. If you have any patients still using a meter that requires these strips, consider switching to a meter with cost effective strips e.g. GlucoRx Nexus, One Touch Select Plus or Glucomen Areo strips. For more examples and further information please see our Choosing a Blood Glucose Monitoring Meter Guidelines here.

Epipen availability

We have been informed that Epipen is now back in stock. The manufacturer has advised that pharmacies can now order stock from the wholesaler.

Long term use of Proton Pump Inhibitors

It has been suggested that long-term use of PPIs is associated with a number of adverse effects. These include *Clostridium difficile* infection in patients in hospital, bone fractures, hypomagnesaemia and vitamin B_{12} deficiency. However, causality is difficult to establish and most of the evidence relates to observational data, which are subject to bias and confounding by indication.

Although there is some uncertainty over the incidence of adverse effects associated with long-term use of PPIs, it is recommended these drugs should be initiated only if clearly indicated, and for the shortest possible time at the lowest effective dose. The main indications where the benefits of long-term PPI use outweigh the potential long-term risks include oesophageal stricture, Barrett's oesophagus, a history of a bleeding gastrointestinal ulcer and gastroprotection for concomitant use of a NSAID.

Patients with less severe conditions (e.g. indigestion) should be given advice on lifestyle changes before being offered a PPI. In those taking PPIs for no clear indication, de-prescribing should be considered. A gradual reduction in PPI dose and frequency may be needed.

MHRA Drug Safety Updates

Rare risk of central serous chorioretinopathy (CSCR) with systemically and locally administered corticosteroids.

CSCR is a retinal disorder that has been linked to the systemic use of corticosteroids. Recently, this has also been reported after local administration of corticosteroids via inhaled and intranasal, epidural, intra-articular, topical dermal, and periocular routes. Symptoms include blurred and distorted vision, typically in one eye. Some may also experience difficulty with bright lights and contrast sensitivity.

So what?
Healthcare professionals are reminded to inform patients to report any vision problems or disturbances during or after corticosteroid treatment. Consider referral to an ophthalmologist for evaluation of possible causes, as blurred vision is a known side effect of steroid treatment and can also be caused by other conditions such as cataract and glaucoma.

Methylprednisolone injectable medicine containing lactose (Solu-Medrone 40 mg): do not use in patients with cows' milk allergy

Solu-Medrone 40 mg uses lactose produced from cows' milk as an excipient and may contain trace amounts of milk proteins; other strengths of Solu-Medrone do not contain lactose. Serious allergic reactions have been reported in patients allergic to cows' milk proteins.

So What?
Healthcare professionals are reminded not use injectable methylprednisolone medicines that contain lactose in patients with a known or suspected allergy to cows' milk. If a patient's symptoms worsen or any new allergic symptoms occur, allergic reaction to cows' milk proteins should be suspected; stop administration of the product and treat the patient's condition accordingly.
Lactose-containing methylprednisolone medicines will be reformulated to remove any trace of milk proteins. Companies have been asked to take steps towards lactose-free formulations by 2019.

MHRA drug alert: Class 4 Medicines Defect Information: BUCCOLAM (midazolam) Oromucosal Solution Pre-filled Syringes

The MHRA has issued a class 4 medicines defect information alert regarding Buccolam (Midazolam) due to reports that the translucent tip-cap sometimes remains on the syringe tip when pulling the red cap off, as shown in the Direct Healthcare Professional Communication (DHCP) diagrams (please see MHRA alert for full details). If this occurs, the translucent tip cap needs to be removed manually to enable administration of BUCCOLAM and to prevent it falling into the patient's mouth upon application of extreme pressure. There have not yet been any reports of the translucent tip-cap falling into a patient's mouth but this cannot theoretically be excluded.
This issue is applicable to all unexpired batches of BUCCOLAM currently in the marketplace.

So What?
As outlined in the DHCP, we ask you share this information with your patients' parents and caregivers, and with age-appropriate patients, during your interactions with them going forward to ensure they are aware of this issue when handling the product.
We suggest to help you in this you should run a search for patients in your practice prescribed this to ensure they are made aware of this issue.

Gabapentin: risk of severe respiratory depression

The MHRA issued a Drug Safety Update on 26 October 2017 as gabapentin has been associated with a rare risk of severe respiratory depression even without concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants, and elderly people might be at higher risk of experiencing severe respiratory depression. Dose adjustments might be necessary in these patients.
Prescribers should also be aware that when prescribing gabapentin in patients who require concomitant treatment with opioid medicines, patients should be carefully observed for signs of CNS depression, such as somnolence, sedation, and respiratory depression, and the dose of either gabapentin or the opioid should be reduced appropriately.

So What?
The MHRA advises healthcare professionals to:
•be aware of the risk of CNS depression, including severe respiratory depression, with gabapentin
•consider whether dose adjustments might be necessary in patients at higher risk of respiratory depression, including elderly people, patients with compromised respiratory function, respiratory or neurological disease, or renal impairment, and patients taking other CNS depressants
•report any suspected adverse reactions on a Yellow Card

Clozapine: reminder of potentially fatal risk of intestinal obstruction, faecal impaction, and paralytic ileus

Clozapine has been associated with varying degrees of impairment of intestinal peristalsis. These adverse events are thought to be due to the anticholinergic properties of clozapine. The effects can range from constipation, which is very common, to intestinal obstruction, faecal impaction, and paralytic ileus, which are very rare. On a few occasions, cases have been fatal.

So What?
Healthcare professionals are reminded to exercise particular care in patients receiving other drugs known to cause constipation (especially those with anticholinergic properties), patients with a history of colonic disease or lower abdominal surgery, and in patients aged 60 years and older. Patients should be advised that if they develop constipation, they should tell their doctor immediately before taking the next dose of clozapine. It is vital that constipation is recognised early and actively treat