Prescribing Points

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Oxfordshire Cinical Commissioning Group

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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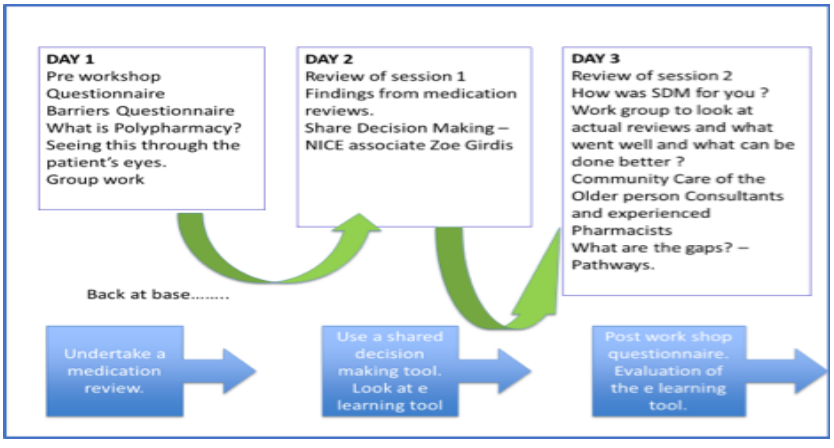
Polypharmacy Action Learning Sets

The Oxford Academic Health Science Network in Partnership with Health Education England are delivering a programme of Action Learning Sets (ALS) for GPs focusing on Polypharmacy. The sets aim to support GPs understand the complex issues surrounding stopping inappropriate medicines safely. In addition, they will help Primary Care Networks (PCNs) deliver the Medicines Optimisation elements of the GP contract. An overview of the programme is shown below.

The programme

The structure of the programme enables a "spiral" learning approach building on learning across the three sessions. Participants will also receive a data pack including their practice's Polypharmacy indicators, published by NHSBSA, and a teaching slide deck to help spread the learning back at practices



The ALSs will be delivered in three half days sessions. There needs to be a commitment to attend all three sessions. As there are limited places it is advisable to book a place as soon as possible. Please see the link here for details for dates and how to book. We have 10 free places available across the CCG and would like to offer places to individual Primary Care Networks. The sets are primarily for GPs however two of these places are available for non-medical prescribers.

So What?

- Please contact Seema Gadhia (seema.gadhia@OXFORDahsn.org) or Ferdinand Manansala (Ferdinand.Manansala@oxfordahsn.org) if you require any further information. Please also let Seema know the person who you have nominated to attend.

Semaglutide Nationwide Audit

Clinical trials with semaglutide suggest that it is more effective than the other GLP-1 receptor agonists. To find out the extent to which the experience in clinical trials translates into the real world, and to investigate the impact of switching from other GLP-1 receptor agonists to semaglutide - the Association of British Clinical Diabetologists (ABCD) has launched a nationwide audit in 2019 to collate this information. For more information about this audit please see the link here.

Prescribers are encouraged to enter patients started on Semaglutide into the National ABCD Semaglutide audit. Data can be collected via the on-line audit tool that is very easy to use, or if preferred paper forms are also available as an option. Please see the link here to register for the audit and for access to the on-line tool on the ABCD website.

Our local GLP-1 Receptor Agonist Guidelines can be found here.

Updates to South Central Antimicrobial Network Guidelines for Antibiotic Prescribing in the Community

SCAN (South Central Antimicrobial Network) guidelines for antimicrobial prescribing were approved for use across Oxfordshire in July 2018. These are regionally produced guidelines which are maintained by the SCAN members. It is available on Clinox here and at www.nhsantibioticguidelines.org.uk.

Following the publication of various NICE guidance on prescribing in urinary tract infections (UTI) and updated Public Health England UTI diagnostic guidance, the UTI section of the SCAN guidance has been reviewed and revised to include the following changes:

- Updated signs and symptoms for under and over 65s (in line with PHE)
- Updated guidance on interpreting dipstick testing (under 65 only) in line with PHE
- Updated guidance on interpreting lab results in line with PHE
- Updated 'low resistance risk' information in line with NICE
- Removal of option to use trimethoprim in pregnancy in line with NICE
- Updated specific guidance on interpreting a positive lab report with a catheter UTI in line with NICE
- Specific guidance on catheter UTI in pregnancy in line with NICE
- Updated information on recurrent UTI infections, specifically topical oestrogen for post-menopausal women, self-care measures (including D-mannose at OTC purchase)
- Updated options of standby and prophylactic antibiotics for recurrent infections removing the option of ciprofloxacin (following MHRA alert on use of quinolones)
- Updated referral advice for pyelonephritis in line with PHE
- Pyelonephritis treatment options updated in line with NICE

The paediatric section has also been updated. Following feedback from across the region, in some sections, the guidance now gives a choice of either using reduced dosing frequencies (e.g. BD amoxicillin) **or** following the BNF recommendations (previously only the reduced dosing frequencies were given where relevant). The guidance still suggests to aim to use an antibiotic that minimises dosing frequency and is palatable (if suspension prescribed) to optimise adherence.

This version of the guidance is an interim update as the full SCAN guidance is shortly to be transferred to the app Microguide (which will also available on a web viewer). The pdf version will continue to be available until the app is launched.

Liothyronine

OCCG guidance on the prescribing of Liothyronine has been updated in line with the recent RMOC Liothyronine guidance.

NHS England guidance states that prescribers in primary care should not initiate liothyronine (L-T3) for any new patient, and those individuals currently prescribed liothyronine should be reviewed by a consultant NHS endocrinologist with consideration given to switching to levothyroxine (L-T4) where clinically appropriate. Prescriptions for individuals receiving liothyronine should continue until that review has taken place. The majority of patients suffering from hypothyroidism can be treated effectively with levothyroxine alone, but liothyronine is perceived to be an important medicine for a small proportion of patients in order to maintain health and wellbeing. The prescribing of liothyronine is only supported if initiated by, or considered appropriate following a review by, an NHS consultant endocrinologist. The withdrawal or adjustment of liothyronine treatment should also only be undertaken by, or with the oversight of, an NHS consultant endocrinologist. Where GPs are involved in such treatment changes this should be with NHS consultant endocrinologist support. This advice applies to both liothyronine monotherapy and combination therapy with levothyroxine.

There is work underway to develop a shared care protocol, so key areas of responsibility are defined and a letter for patients who have had liothyronine started by a private endocrinologist but prescribed on NHS saying you can either have this privately prescribed or need to have a review by an NHS endocrinologist, who may or may not decide to continue this drug.

So What?

• In the meantime if you have any question regarding the prescribing of liothyronine you can contact the OUH endocrinology team at oxon.endocrinologyadvice@nhs.net for advice and support.

Changes to Thickeners Scoop Sizes

Recent audit work of the prescribing of thickeners in primary care in Oxfordshire showed that 47.8% of patients did not have an IDDSI (International Dysphagia Diet Standardisation Initiative) descriptor recorded on their EMIS record (592 patients in 43 practices audited between April and December 2019). 79% of patients were on a gum based formula (Resource® ThickenUp® Clear) which is OCCG first line thickener.

- The labelling on products and scoop sizes have changed in order to use the IDDSI descriptors.
- An editable letter is available for GPs to send to their patients informing them of the changes. Informing patients will ensure patients use the correct scoop size and number of scoops, as recommended by their Speech and

Language Therapist. This will reduce the risk of aspiration in patients with dysphagia with the change to the IDDSI descriptors.

- When changing patients from a starch based to a gum based thickener the quantity prescribed needs to be reduced as less gum based thickener is needed to achieve the same level of thickness as a starch based thickener - the scoop size for Resource Thicken Up is 4.5g and the scoop size for Resource Thicken Up Clear is 1.2g.
- The number of scoops of **Resource® ThickenUp®** (starch based) required to achieve the levels of thickness are summarised below:

IDDSI framework	Level 1 Slightly thick	Level 2 Midly thick	Level 3 Moderately thick	Level 4 Extremely thick
200ml Liquids (water, juice, tea, coffee)	1½ Scoops	2 Scoops	2½ Scoops	3 Scoops
1 scoop = approx. 4.5 g It is the responsibility of the person administering **Resource® ThickenUp®** to ensure that the liquid is mixed to the appropriate consistency. For food, add **Resource® ThickenUp®** as needed to achieve the appropriate consistency.				

- The number of scoops of **Resource® ThickenUp® Clear** (gum based) required to achieve the levels of thickness are summarised below:

IDDSI FRAMEWORK	200ml liquids (water, juice, tea, coffee)	200ml oral nutritional supplements
LEVEL 1/SLIGHTLY THICK	1 scoop/sachet	-
LEVEL 2/MILDLY THICK	2 scoops/sachets	0.5-1 scoop/sachet
LEVEL 3/MODERATELY THICK	4 scoops/sachets	1-2 scoops/sachets
LEVEL 4/EXTREMELY THICK	6 scoops/sachets*	-

NB The recommended dosage for IDDSI level 4 in Resource® ThickenUp® Clear has been revised from 8 to 6 scoops/sachets by the manufacturer. For scoop size and number of scoops required for other products, see individual product packaging. For more information on IDDSI see https://iddsi.org/.

So What?

• If patients change from a starch based to a gum based thickener, check quantity prescribed – it should be less than the quantity of starch based thickener previously prescribed.

• Send letter to Patients/Carers informing them of the changes in descriptors used for levels of thickness.

Update to MAP Guidelines

Cow's Milk Allergy (CMA) affects less than 2% of the UK infant population and yet there have been rapidly increasing sales of specialist infant formulas. Since the introduction of The Milk Allergy in Primary Care (MAP) Guidelines (2013 - 2018(revised)) there has been a plateauing of sales of these products and in 2018 there was a slow decline in sales.
MAP Guidelines have been updated in October 2019 which includes updated algorithms and an information leaflet to support breastfeeding. The overall aim of the update was to make the guidelines closer to its original aim of facilitating early and accurate diagnosis of CMA, whilst minimising, as far as possible, any concerns around over diagnosis or a risk to breastfeeding rates.

In 2018 the iMAP/MAP Guidelines were criticised for 3 reasons:

- The iMAP Guidelines promote over diagnosis of CMA by suggesting that a large range of common and non-specific symptoms could represent mild to moderate non-IgE mediated CMA.
- There is a risk that the guideline may negatively impact breastfeeding rates.
- There is a possibility that industry could have influence on the guidelines.

The iMAP Guidelines have clear algorithms for the presentation and management of Cow's Milk Allergy to support GPs and other health care staff involved in the care of babies (Healthcare Professional Factsheet - on the use of iMAP guideline).

So What?

- Exclusive breast feeding is recommended in the UK for the first 6 months of life. Mothers should be offered the support of local NHS breast feeding support services and signposted to further support. Please refer to iMAP patient information leaflet on supporting breast feeding.
- Beware of misdiagnosis: The 2019 Guidelines states "The symptoms above are very common in otherwise well infants or those with other diagnoses, so clinical judgement is required. Trial exclusion diets must only be considered if history and examination strongly suggests CMA, especially in exclusively breastfed infants, where measures to support continued breastfeeding must be taken."
- Home reintroduction of cow's milk should be undertaken where there has been clear improvement in both exclusively breastfed infants and in formula fed or mixed fed infants, where the infant has shown a mild to moderate non-IgE reaction to cow's milk:

Exclusively breast fed infants	**Formula fed or Mixed fed (formula and breast fed) infants**
After an elimination trial of cow's milk by the mother for up to 4 weeks, with a minimum of 2 weeks)	After between 2-4 weeks of starting Elimination trial – see iMAP reintroduction leaflet

NB If there is no clear improvement, home reintroduction should not be undertaken - see algorithm for next steps.

- For further information contact occg.dietitian@nhs.net.

Supply Issues and Product Discontinuation

Midazolam (5mg/ml) 50mg in10ml solution for injection ampoules

A supply issue with midazolam (5mg/ml) 50mg in 10ml ampoules has been reported which is anticipated to be resolved by 31st January 2020. Midazolam (5mg/ml) 10mg in 2ml ampoules are currently available. Healthcare professionals are advised to review local protocols and to give consideration to mitigating the risks associated with switching to a different volume of midazolam (5mg/ml) ampoule presentation.

Ranitidine Injections

Ranitidine injection supplies are now available to be ordered from wholesalers and no longer expected to be out of stock. An updated Medicine Supply Notification (MSN/2019/019U) was issued to secondary care on 9th December with further information, which supersedes the clinical and supply management advice for ranitidine injection included in the supply disruption alert (SDA/2019/005-U) issued on 27 November 2019.

Please note there is no change to the supply situation for oral ranitidine and the guidance issued in SDA/2019/005-U should continue to be followed.

Zoton FasTabs (Lansoprazole) 15 and 30mg Dispersible Tablets

Zoton FasTabs 15mg and 30mg dispersible tablets are currently out of stock until 24 January 2020. Generic lansoprazole 15mg and 30mg orodispersible tablets remain available. For patients prescribed Zoton FasTabs by brand who do not have sufficient supplies for the out of stock period, clinicians should consider prescribing the generic product.

Moclobemide 150mg and 300mg Tablets

Mylan has reported that moclobemide 150mg and 300mg tablets are currently out of stock and they expect these to be back in stock in March 2020 and April 2020, respectively. Sandoz is in stock of moclobemide 150mg tablets, however, is out of stock of moclobemide 300mg until January 2020. Unlicensed moclobemide 300mg tablets are available from importers however lead times may vary.

Product Discontinuation: Insuman®

Three presentations of Insuman recombinant human insulin are to be discontinued due to limited capacity at the manufacturing site. This is not due to any safety issue, and Insuman currently on the market can continue to be used.

- No new patients should be started on the below presentations
- Switching of insulins should be done under the supervision of a healthcare professional who can provide training on how to use the new delivery device (pen);
- blood glucose levels should be closely monitored while the patient becomes familiar with their new product

Presentations to be discontinued (and suggested alternatives) are:

Insuman Cartridges

1. Insuman® Comb 15 100 IU/mL- suspension for injection in a cartridge – Subcutaneous use.
Expected End of Supply – June 2020
There is no alternative Insuman Comb 15 presentation available

Insuman Vials

2. Insuman® Basal 100 IU/mL- suspension for injection in a vial - Subcutaneous use.
Expected End of Supply – May 2020
Alternative Insuman® Basal Presentation - Cartridge and Prefilled SoloStar® Pen
3. Insuman® Comb 25 100 IU/mL- suspension for injection in a vial - Subcutaneous use.
Expected End of Supply – June 2020
Alternative Insuman® Comb 25 Presentation - Cartridge and Prefilled SoloStar® Pen

Switching to an alternative human insulin:

Insuman ®	Alternative Human Insulin
Basal Vial	Insuman Basal Cartridge Insuman Basal SoloStar Humulin® I Vial
Comb 25 Vial	Insuman Comb 25 Cartridge Insuman Comb 25 SoloStar Humulin® M3 Vial
Comb 15 Cartridge	Insuman Comb 25 Cartridge Humulin® M3 Cartridge

Switching from Insuman Basal to another basal human insulin may require minimal or no dose adjustment. Switching from Insuman Comb 15 to the alternative insulins will require close medical supervision, as the differences in proportions of the soluble and isophane insulins are likely to be clinically significant and a dose adjustment would be anticipated.

Any switch to insulin analogues should be done under careful medical supervision as the pharmacokinetic and pharmacodynamic profiles of insulin analogues are different from human insulins, as are the international units used for human insulins and the analogue-specific units. As a result, switching patients from Insuman to an insulin analogue may require adjustments in the dose and/or dosing regimen on a case by case basis.

Product Discontinuation: Slo-Phyllin® (theophylline) capsules

Due to manufacturing issues, Slo-phyllin® 60mg, 125mg and 250mg capsules have been discontinued. Prescribers will need to review and switch all affected patients who still require theophylline, from Slophyllin® to alternative preparations. The respiratory team at the OUH has produced the following advice:

Adult patients:
All healthcare professionals in primary, secondary or specialist healthcare services who prescribe theophylline preparations, should:

- review patients to determine if theophylline is still required as it may be of minimal benefit for that patient and has a significant side effect profile;
- review patients on Slo-Phyllin® preparations and switch to aminophylline tablets (Phyllocontin Continus®/Forte Continus®). When switching patients from theophylline to aminophylline the dose will need to be converted. **(225mg aminophylline ≡ 180mg theophylline)**

More information on aminophylline (Phyllocontin®) can be found in the SmPC here and the usual adult dose is 225mg twice daily which may be titrated to a higher dose if required.

Paediatric patients:
Children on Slo-Phyllin® should have their treatment reviewed, and prescribers should liaise with the paediatric respiratory consultants who will provide recommendations on the best alternative treatment options.

So What?

- Prescribers should review patients on Slo-Phyllin® in accordance to the specialist advice above, either stopping or switching treatments, as clinically appropriate.
- If you have any query please contact occg.medicines@nhs.net.

Product Discontinuation: Haloperidol (Serenace®) 500 mcg Capsules

Teva, supplier of haloperidol (Serenace®) 500 mcg capsules is out of stock for the foreseeable future. Haloperidol 500 mcg tablets remain available from Crescent Pharma Limited.

For patients who require a supply of haloperidol (Serenace®) 500 mmcg capsules consider prescribing haloperidol 500 mcg tablets. If patients are unable to swallow a tablet, consider prescribing haloperidol oral solution as all various strengths that remain available.

Product Discontinuation: Glibenclamide 2.5 and 5mg Tablets

Wockhardt have discontinued glibenclamide 2.5mg and 5mg tablets and there are no other manufacturers in the market. Prescribers are advised to switch patients to other sulfonylureas, as per table below. If it is not considered appropriate to switch patients, unlicensed imports of glibenclamide tablets are available. For more details please see the advice from the SPS.

Sulfonylurea	Daily dose	Dose equivalence to 5mg glibenclamide
Glibenclamide	2.5- 15mg	
Gliclazide	40 to 320mg	80mg
Glipizide	2.5-20mg	5mg
Glimepiride	1-6mg	No data
Tolbutamide	0.5-2g	1g

Safety Alerts

The MHRA has recently urged any GP practices that are not signed-up, to register to receive safety alerts via its central alerting system (CAS), which is replacing local email alerting arrangements. The registration form is available here.

Yellow Fever Vaccine

The Commission on Human Medicines has issued a series of recommendations to strengthen risk minimisation measures for the yellow fever vaccine (Stamaril®). This follows very rare fatal reactions to the vaccine namely viscerotropic disease (YEL-AVD) and neurotropic disease (YEL-AND), which both resemble yellow fever infection. Key recommendations include the revised contraindications and precautions to protect patients with a weakened immune system, which includes people aged 60 years or older. Standardised risk-benefit evaluation procedures have also been sent to vaccination centres to ensure risk assessments are carried out.

So What?

- Only healthcare professionals specifically trained in benefit-risk evaluation of yellow fever vaccine should administer the vaccine, following their individualised assessment of a person's travel itinerary and suitability to receive the vaccine
- Every vaccinee should be advised to seek emergency medical attention if they develop signs or symptoms of very rare neurotropic disease (YEL-AND) or viscerotropic disease (YEL-AVD) and should receive the manufacturer's patient information leaflet as part of the travel consultation
- Report suspected adverse drug reactions to vaccines to the Yellow Card Scheme.

Emerade 150, 300 and 500 mcg Adrenaline Auto-Injectors

There has been a further safety update from the MHRA on Emerade® adrenaline auto-injectors (AAI). This follows the manufacturer's investigation into the failure of some pens to activate, which, it is now understood, could be exacerbated if pens are exposed to higher temperatures. All Emerade® pens are now being recalled from pharmacies. Emerade® stock currently held by patients is not being recalled, as there are insufficient supplies of alternative brands to cover the replacement of all Emerade® pens already held by patients.

The Department of Health and Social Care (DHSC) issued a Supply Disruption Alert recently and advises of the following:

- Patients who require a replacement for an Emerade® AAI that has expired or been used will need to be prescribed an AAI of an alternative brand (Epipen® /Jext®).
- For those patients who require a single expired AAI to be replaced, owing to the supply situation it is not possible to replace this with two AAIs of a different brand. Therefore, these patients will, for a period of time, be carrying two AAIs of different types. It is important that they and their caregiver are confident in the way each AAI is used and they should decide in advance which type of AAI they feel most confident to administer as the first AAI to be used in an anaphylactic emergency.
- The advice to continue using Emerade® AAIs until the expiry date has been given in order to avoid a serious shortage of AAIs for the wider patient community. The MHRA and DHSC consider that the risk of not having an AAI is much higher than having an AAI that may not activate.
- In the absence of an Emerade® 500 mcg, affected patients should be prescribed a 300 mcg AAI and, as per existing guidance, advised to keep two AAIs with them at all times.

So What?

- Healthcare professionals are being urged to share safety information with Emerade® users, including advice on not exposing pens to temperatures above 25°C and to carry two devices at all times.
- Patients/caregivers should continue to keep their Emerade® devices until their expiry date, at which point alternative products will be supplied.
- Prescribers should prescribe other brands (EpiPen® or Jext®) until this error has been corrected.
- Training on the use of different devices will also need to be provided to patients.

Domperidone for Nausea and Vomiting

Latest data on domperidone has shown that there is a lack of efficacy in the relief of the symptoms of nausea and vomiting in children under 12 years old. Consequently the licensed indication of domperidone has been updated in line with the new evidence. Domperidone is now authorised for the relief of symptoms of nausea and vomiting only in adults and adolescents 12 years of age or older and weighing 35 kg or more. Alternative treatments should be considered in children younger than 12 years of age who need relief of symptoms of nausea and vomiting.

European regulatory studies also showed that some physicians, including in the UK, are not aware of the important precautions for use of domperidone introduced in 2014. The following is the reminders of contraindications:

Domperidone is contraindicated:

- in patients with moderate to severe hepatic impairment
- in patients with known existing prolongation of cardiac conduction intervals (particularly QTc)
- in patients with underlying cardiac diseases such as congestive heart failure,
- in patients with significant electrolyte disturbances,
- during co-administration with QT-prolonging drugs (for more information about considerations with apomorphine (see Drug Safety Update, April 2016)
- during co-administration with potent CYP3A4 inhibitors (regardless of their QT-prolonging effects)
- in patients with hypersensitivity to domperidone
- in patients with a prolactin-releasing pituitary tumour
- in patients in which stimulation of the gastric motility could be harmful (for example, in patients with gastro-intestinal haemorrhage, mechanical obstruction, or perforation)

Reminder of recommendations for dose and treatment duration:

- for adults and adolescents 12 years of age or older and weighing 35 kg or more, the recommended maximum dose in 24 hours is 30 mg (dose interval: 10 mg up to 3 times a day)
- domperidone should be used at the lowest effective dose for the shortest possible duration and maximum treatment duration should not usually exceed 1 week

So What?

- Do not prescribe domperidone for the relief of symptoms of nausea and vomiting in children under the age of 12 years old. Consider other alternative treatments in paediatric population.
- Be aware of the contraindications and report suspected adverse drug reactions associated with domperidone to the Yellow Card Scheme.