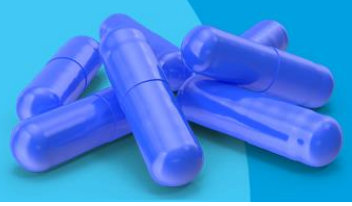
Medicines Management newsletter

Issue 13– December 2018

NHS
Halton Clinical Commissioning Group



Area Prescribing Committee

RECOMMENDATIONS SPECIFICALLY RELEVANT TO PRIMARY CARE

BLACK CO-PROXAMOL tablets

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of CO-PROXAMOL tablets.

- Prescribers may wish to use the NHS England Patient Information Leaflet available to support their discussions with patients.
- Co-proxamol is an unlicensed analgesic, containing paracetamol 325mg and dextroproxyphene 32.5mg. It was withdrawn from the UK market on the advice of the Committee on Safety of Medicines amid serious safety concerns in January 2005.
- In 2009, the European Medicines Agency's Committee for Medicinal Products for Human Use concluded that the benefits of dextropropoxyphene do not outweigh its risks and recommended that all marketing authorisations should be withdrawn throughout the European Union.
- New clinical data in 2011 from the USA showed that dextropropoxyphene can have serious effects on the electrical activity of the heart (resulting in prolongation of the P-R and Q-T intervals, and widened QRS complexes), even at normal therapeutic doses.
- Death from co-proxamol overdose can occur rapidly, even before hospital treatment can be received. The risk of dying after co-proxamol overdose is 2.3 times greater than for tricyclic antidepressants and 28.1 times greater than for paracetamol. The lethal dose of co-proxamol is relatively low and can be potentiated by alcohol and other central nerve depressants.
- The cost of prescribing co-proxamol as an unlicensed 'special' is significantly higher than the licensed cost-effective alternatives. The average cost per item in Pan Mersey is £132.61.

BLACK OXYCODONE with NALOXONE modified release tablets (Targinact®) for adults with chronic pain

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of OXYCODONE with NALOXONE modified release tablets (Targinact®) for adults with chronic pain.

- Prescribers may wish to use the NHS England Patient Information Leaflet available at to support their discussions with patients.

- There are several potential switch/review options for Targinact® products (although clinicians may choose other options according to the clinical need of their patient).
- The use of oxycodone first line over morphine sulfate as a strong opioid is rarely justified as there is a lack of evidence to suggest oxycodone has any clinical advantages over morphine sulfate and the cost of oxycodone is significantly higher than morphine sulfate.
- Oxycodone and morphine are both strong opioids with similar efficacy and side effect profiles.
- It is difficult to determine a precise equivalent dose for oxycodone to morphine as reported equi-analgesic dose ratios vary widely. When converting from one opioid to another, regular assessment and reassessment of efficacy and adverse effects is essential because of the lack of evidence on equi-analgesic doses and inter-individual variation.

GREY Cannabis-based products for medicinal use

The Pan Mersey Area Prescribing Committee does not currently recommend the prescribing of CANNABIS-BASED products for medicinal use. More information will be added to this statement as it emerges nationally.

FORMULARY

GREY DOXYLAMINE/PYRIDOXINE tablets (Xonvea®▼) for Nausea and Vomiting in Pregnancy

The Pan Mersey Area Prescribing Committee does not currently recommend the prescribing of DOXYLAMINE/ PYRIDOXINE tablets (Xonvea®▼) for the treatment of nausea and vomiting in pregnancy.

AMBER RECOMMENDED Midazolam buccal solution (Epistatus® brand)

Seizures - Additional option to Buccolam brand (Epistatus smaller volume, more viscous to aid administration). £46 compared to £23 per dose, but minimal cost implication anticipated as low volume use and available as single pack rather than multi-pack.

GREEN Buprenorphine 3-day transdermal patches

Pain - Removal of 3-day duration patches to avoid confusion with 4-day duration patches. Cost neutral.

GREEN Desmopressin lyophilisate (Noqdirna® brand)

Nocturia - Brand specifically licensed in >65 years of age. Cost neutral.

GREEN Levonorgestrel intrauterine device (Kyleena® brand)

Contraception - Additional option to maximise patient choice.
Less expensive: £76 / 5 years compared to £69 / 3 years (for Jaydess® brand)

GREEN Pramipexole, ropinirole, rotigotine

Restless legs syndrome - Change of RAG designation from amber recommended as suitable for initiation in primary care for this indication (remain amber recommended in Parkinson's disease). Minimal cost implication anticipated.

GREEN Tiotropium

Asthma - Routine update of current statement. RAG status changed from Amber Recommended following updated NICE and BTS guidance. Minimal cost implication anticipated.

Medicines Management Work Plan 2018/19

During **December 2018 and January 2019** the NHS Halton CCG Medicines Management Team will be doing the following pieces of work:

- **Salmeterol and Serevent® 25mcg Inhalers** – Switch of generically written salmeterol 25mcg CFC free inhalers and Serevent® 25mcg Evohaler to branded generic Soltel® 25mcg CFC free Inhalers. Patients with an allergy to nut or soya will be excluded from the switch as contra-indicated for Soltel® brand. This review will also include highlighting any patients using a long acting beta2 agonist (LABA) without a corticosteroid for referral to the GP/nurse for review for safety purposes.
- **Gluten Free (GF) Blacklisting** – From the 4th December 2018 the Drug Tariff 'Borderline Substances list' (Part XV) has been amended to exclude all GF products in the categories of biscuits, cereals, cooking aids, grains/flours, and pasta. However, a limited number of GF breads and GF mixes are retained in the ACBS list and will remain available on prescription in primary care. A table giving details of the specific available products is included in the PSNC briefing available at https://psnc.org.uk/dispensing-supply/psnc-briefings-dispensing-and-supply/psnc-briefing-061-18-changes-to-the-availability-of-gluten-free-foods-on-nhs-prescription-november-2018/. Patients who have had an item prescribed in the last 6 months that is now blacklisted and no longer available for NHS prescribing in line with Department of Health recommendations will be identified. With GP practice agreement, the identified patients will be sent a letter informing them that this is a national decision and will include a list of items the patient has had which can no longer be prescribed and some Frequently Asked Questions regarding the national consultation.
- **Vitamin D Deficiency** – Launch of NHS Halton CCG Vitamin D Deficiency in Adults Prescribing Guidance with accompanying patient leaflet and practice review. The guidance will include the recommendation for prescribing by brand. The first line brand formulary choices for NHS Halton CCG will be as follows:
    - Invita® D3 50,000unit and 800unit capsules.
    - Invita® D3 50,000units/ml solution.
    - Aviticol® 20,000unit capsules

The review will include switching patients on generic and branded vitamin D formulations, where appropriate, to formulary choices.

Hot Topic - Falls risk and Medication in older adults

The aetiology of falls is multifactorial, related to patient characteristics and external factors. Physiological changes associated with age, sensory deficits, chronic diseases, substance abuse and environmental hazards have all been identified as falls risk factors. Patients may have a loss of strength and balance related to changes in muscle mass, the presence of a degenerative joint, gait or vestibular disorders. Changes in vision and cognition, such as those occurring with dementia and Alzheimer's disease, may increase the risk of falls by decreasing patients' awareness of their surroundings and their ability to recognise potential trip/fall hazards in their environment.

It is difficult to overstate the contribution that drugs make as a risk factor for falls. A variety of commonly used drug groups are associated with an increased likelihood of falls. Indeed there are few, if any, drug groups that don't have

some potential to increase falls risk. That said, drugs/drug groups can be stratified according to the level of risk (e.g. high risk and medium risk).

How medicines can cause falls

In theory any medicine that causes one of the following effects can increase the risk of falling.

- **Sedation, drowsiness**
- **Impaired postural stability**
- **Hypoglycaemia**
- **Hypothermia**
- **Confusion**
- **Dehydration**
- **Vestibular damage (tinnitus, deafness)**
- **Visual impairment (blurred vision, dry eyes)**
- **Orthostatic hypotension**
- **Drug induced Parkinsonism**

There are two classes of drugs that have the highest propensity to cause falls, those acting on the brain and those acting on the heart and circulation.

Drugs acting on the brain (psychotropic drugs)

There is good evidence that stopping psychotropic drugs can reduce falls.

Taking a psychotropic medicine approximately doubles the risk of falling. There is no data on the effect of taking two or more psychotropic medicines at the same time.

High risk drugs include Benzodiazepines, Z-drugs and tricyclic antidepressants (TCAs) all of which cause drowsiness, impair reactions and balance.

Sedatives, antipsychotics and sedating antidepressants cause drowsiness and slow reaction times. Some antidepressants and antipsychotics also cause orthostatic hypotension.

Drugs with CNS activity, whether for therapeutic effect or as a side effect, usually carry a high or moderate risk.

CNS active drugs which pose a moderate risk of falls include SSRIs. Several population studies have shown that SSRIs are consistently associated with an increased rate of falls and fractures, but there are no prospective trials and the mechanism is not known. They can cause orthostatic hypotension and bradycardia but only rarely as an idiosyncratic side effect. They do not normally sedate but can impair sleep quality.

Drugs acting on the heart and circulation

Maintaining consciousness and an upright posture requires adequate blood flow to the brain. This requires an adequate pulse and blood pressure. In older people a systolic blood pressure of 110mmHg or below is associated with an increased risk of falls. Any drug that reduces the blood pressure or slows the heart can cause falls (or feeling faint or loss of consciousness or “legs giving way”). In some patients the cause is clear – they may be hypotensive, or have a systolic drop on standing. Others may have a normal blood pressure lying and standing, but have syncope or pre-syncope from carotid sinus hypersensitivity or vasovagal syndrome. Stopping cardiovascular medication reduces syncope and falls by 50%, and reduces the prevalence of these four syndromes.

Drugs which pose a moderate risk include diuretics (both loop and thiazide). Loop diuretics have the potential to cause dehydration which my precipitate hypotension and thiazides may cause orthostatic hypotension. Both may cause hyponatraemia and hypokalaemia which may lead to muscle weakness.

General Considerations

It should be remembered that older patients tend to be more sensitive to the adverse effects of drugs and falls risk is 'additive' with each additional drug and/or morbidity adding to the overall falls risk. However, as with all prescribing the risk/benefit should be considered e.g. Parkinson's' disease carries a high risk of falls, so whilst it's true that many antiparkinsonian drugs increase the risk of falls, when optimally titrated, the benefits of drug treatment outweigh the falls risk from the drugs themselves.

This poses the question 'Is polypharmacy always hazardous? Polypharmacy has often been regarded as a surrogate indicator of poor prescribing quality, however a retrospective cohort study published in the British Journal of Clinical Pharmacology[3] in 2014 concluded that 'Unplanned hospitalisation is strongly associated with the number of regular medications. However, the effect is reduced in patients with multiple conditions, in whom only the most extreme levels of polypharmacy are associated with increased admissions. Assumptions that polypharmacy is always hazardous and represents poor care should be tempered by clinical assessment of the conditions for which those drugs are being prescribed.'

Given the multifactorial aetiology of falls, an individual patient centred approach is necessary when evaluating the effectiveness and appropriateness of prescribing.

References:
1. https://www.sussexpartnership.nhs.uk/sites/default/files/documents/medication_falls_spt_-_final_-_0715_0.pdf
2. Payne, Abel et al. Br J Clin Pharmacol. 2014 Jun; 77(6): 1073–1082.
3. Falls: assessment and prevention of falls in older people. NICE Clinical Guideline 161. June 2013. Available at http://www.nice.org.uk/Guidance/CG161
4. Campbell AJ, Robertson MC, Gardner MM, et al. Psychotropic medication withdrawal and a homebased exercise program to prevent falls: a randomized, controlled trial. J Am Geriatr Soc 1999; 47: 850–3.

Safety

DOUBLE CHECK PATIENTS WITH 'PENICILLIN ALLERGY' TO AVOID INCREASED MRSA RISK

National Institute for Health and Care Excellence | 31 Oct 2018

NICE is urging healthcare staff to be aware of this and ensure that only people with a true allergy to penicillin are documented as such. Incorrectly identifying people as allergic could also contribute to antimicrobial resistance, as these people are likely to instead be given broad-spectrum antibiotics.

https://www.nice.org.uk/news/article/double-check-patients-with-penicillin-allergy-to-avoid-increased-mrsa-risk?utm_medium=email&utm_source=nicenewsletter&utm_campaign=penicillinallergycheck

HYDROCHLOROTHIAZIDE: RISK OF NON-MELANOMA SKIN CANCER, PARTICULARLY IN LONG-TERM USE

This update advises that patients taking hydrochlorothiazide-containing products should be informed of the cumulative, dose dependent risk of non-melanoma skin cancer, particularly in long-term use.

Advice for Healthcare Professionals:

- Inform patients taking hydrochlorothiazide-containing products of the risk of non-melanoma skin cancer, particularly in long-term use, and advise them to regularly check for and report any new or changed skin lesions or moles.
- Reconsider the use of hydrochlorothiazide in patients who have had previous skin cancer.
- Examine all suspicious moles or skin lesions (potentially including histological examination of biopsies).

- Advise patients to limit their exposure to sunlight and UV rays and use adequate protection when exposed to sunlight and UV rays to minimise the risk of skin cancer.

https://www.gov.uk/drug-safety-update/hydrochlorothiazide-risk-of-non-melanoma-skin-cancer-particularly-in-long-term-use

SYSTEMIC AND INHALED FLUOROQUINOLONES: SMALL INCREASED RISK OF AORTIC ANEURYSM AND DISSECTION; ADVICE FOR PRESCRIBING IN HIGH-RISK PATIENTS

Fluoroquinolone medicines available in UK are Ciprofloxacin, Levofloxacin, Moxifloxacin and Ofloxacin. In patients at risk for aortic aneurysm and dissection, fluoroquinolones should only be used after careful assessment of the benefits and risks and after consideration of other therapeutic options.

Advice for Healthcare Professionals:

- Systemic and inhaled fluoroquinolones may be associated with a small increased risk of aortic aneurysm and dissection, particularly in older patients.
- Fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients at risk for aortic aneurysm and dissection.
- Conditions predisposing to aortic aneurysm and dissection include:
    - A family history of aneurysm disease.
    - Diagnosis with pre-existing aortic aneurysm and/or aortic dissection.
    - Other risk factors or conditions predisposing for aortic aneurysm and dissection (for example, Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's disease, hypertension, and known atherosclerosis).
- Advise patients, particularly elderly people and those at risk, about rare events of aortic aneurysm and dissection and of the importance of seeking immediate medical attention in case of sudden-onset severe abdominal, chest or back pain.

https://www.gov.uk/drug-safety-update/systemic-and-inhaled-fluoroquinolones-small-increased-risk-of-aortic-aneurysm-and-dissection-advice-for-prescribing-in-high-risk-patients

CANNABIDIOL OIL – POTENTIAL ADVERSE EFFECTS AND DRUG INTERACTIONS

Due to an increasing popularity of self-administration of over-the-counter bought cannabidiol oil, doctors and pharmacists should be aware of its potential adverse effects and interactions. Available data suggests it interacts with cytochrome p450 enzymes.

https://www.sps.nhs.uk/articles/cannabidiol-oil-potential-adverse-effects-and-drug-interactions/

TRANSDERMAL FENTANYL PATCHES: LIFE-THREATENING AND FATAL OPIOID TOXICITY FROM ACCIDENTAL EXPOSURE, PARTICULARLY IN CHILDREN

MHRA continue to receive reports of preventable accidental fatalities and opioid toxicity with fentanyl patches. All Healthcare Professionals, particularly those involved in the prescribing and dispensing of fentanyl patches, should provide clear information to patients and caregivers regarding risk of accidental transfer and ingestion of patches, and need for appropriate disposal of patches.

Advise patients and caregivers to follow closely the instructions on the patch packaging, the carton, and in the accompanying Patient Information Leaflet.

Advice for Healthcare Professionals:

- Always fully inform patients and their caregivers about directions for safe use for fentanyl patches, including the importance of:
    - Not exceeding the prescribed dose.

    - Following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application.
    - Not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower).
    - Ensuring that old patches are removed before applying a new one.
    - Following instructions for safe storage and properly disposing of used patches or those which are not needed.
- Ensure that patients and caregivers are aware of the signs and symptoms of fentanyl overdose and advise them to seek medical attention immediately (by dialing 999 and requesting an ambulance) if overdose is suspected.
- In patients who experience serious adverse events, remove patches immediately and monitor for up to 24 hours after patch removal.
- Advise patients and carers about taking precautions to prevent accidental transfer of the patch to another person e.g. when co-sleeping.

https://www.gov.uk/drug-safety-update/transdermal-fentanyl-patches-life-threatening-and-fatal-opioid-toxicity-from-accidental-exposure-particularly-in-children

The Care Quality Commission (CQC), Safer Management of Controlled Drugs Annual Report 2017 (published July 2018) also highlights the following as on-going administration issues with transdermal opioid preparations:

'Body maps are not always in place when applying transdermal patches. There is also a lack of awareness of the effect of heat, the importance of removing a previous patch and the need to check the patch every day.'

'Application and removal of transdermal patches continues to cause concern, and we expect to see appropriate arrangements in place to ensure that patches are managed safely.'

https://www.cqc.org.uk/sites/default/files/20180718_controlleddrugs2017_report.pdf

ORAL LIDOCAINE-CONTAINING PRODUCTS FOR INFANT TEETHING: ONLY TO BE AVAILABLE UNDER THE SUPERVISION OF A PHARMACIST

Oral lidocaine-containing products for infant teething are only to be available under the supervision of a pharmacist so that parents and caregivers can receive guidance about managing infant teething symptoms. Non-medicinal options such as a teething ring or massaging the gum should be the first line for relieving infant teething symptoms, and lidocaine-containing products should only be used when simple measures have failed to provide sufficient relief. Please follow the link below for more information regarding this alert:

https://www.gov.uk/drug-safety-update/oral-lidocaine-containing-products-for-infant-teething-only-to-be-available-under-the-supervision-of-a-pharmacist

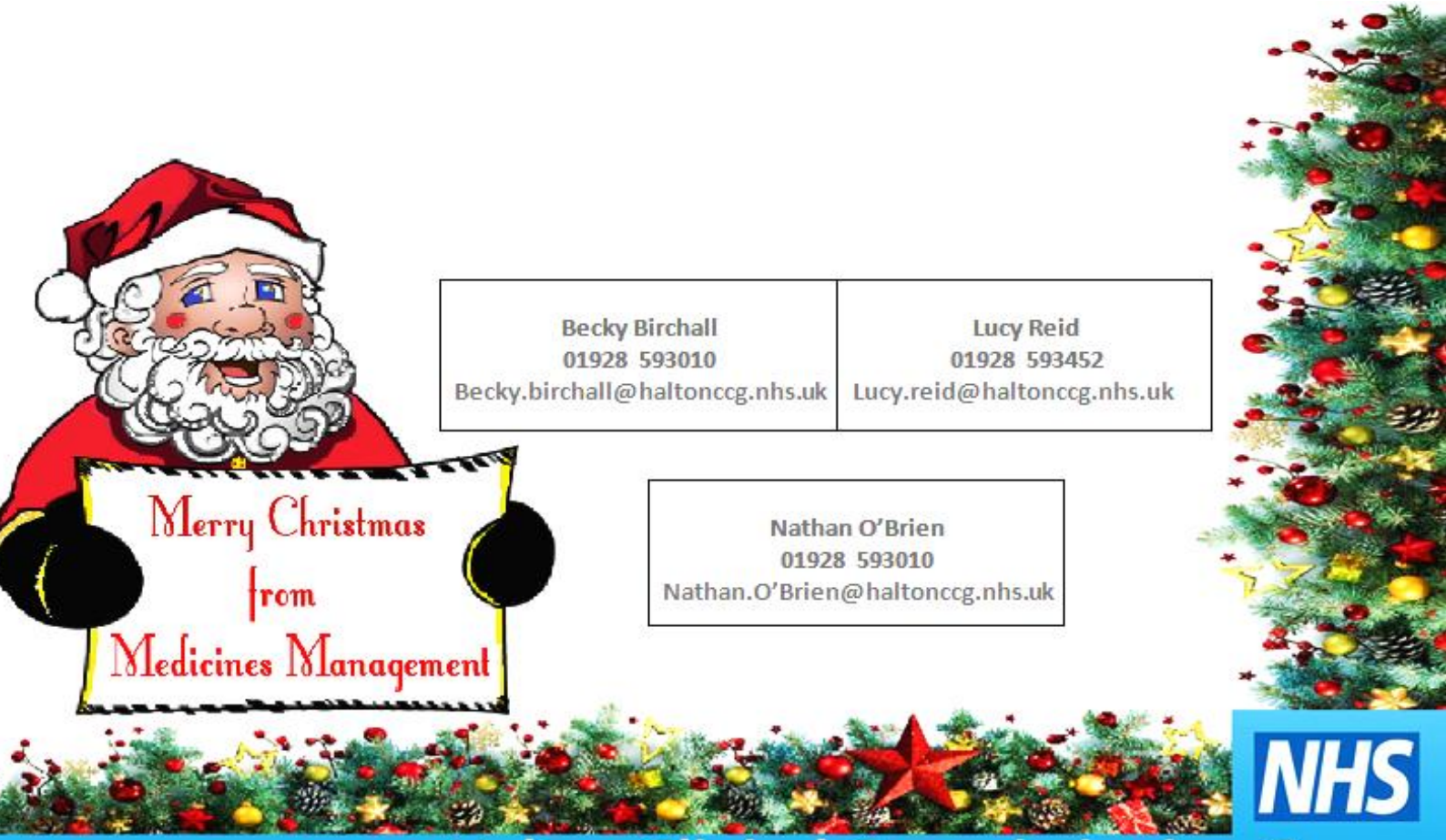
RITONAVIR-CONTAINING PRODUCTS: REPORTS OF INTERACTION WITH LEVOTHYROXINE LEADING TO REDUCED THYROXINE LEVELS

The MHRA advises that thyroid-stimulating hormone should be monitored in patients treated with levothyroxine for at least the first month after starting and ending ritonavir. This interaction has been added to SPCs and PILs for ritonavir-containing medicines and levothyroxine.

https://www.gov.uk/drug-safety-update/ritonavir-containing-products-reports-of-interaction-with-levothyroxine-leading-to-reduced-thyroxine-levels

Medicines Supply Issues Update

Below is a link to the December issue of the 'Supply issues update for primary care'. This report has been produced by the Department of Health and Social Care (DHSC) Medicine Supply team and provides an update on current primary care medicine supplies issues.
http://www.haltonccg.nhs.uk/members-practices/medicines-management/medicines-supply-issues



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