Clinical Snippets July 2024

1. Heart Foundation resources

New home blood pressure resources - The Heart Foundation has created some handy guidance for patients using a blood pressure monitor at home. There's a step-by-step guide and a video on how to take accurate blood pressure readings at home, along with a logbook for recording readings. There are a number pf phone apps available for logging home blood pressure data eg. Blood Pressure Diary.

2. Atrial fibrillation and anticoagulation

I have recently reviewed a case where a patient with AF and a mechanical heart valve was swapped from warfarin to rivaroxaban and suffered a stroke several weeks later. BPAC have published an updated article on atrial fibrillation management. With respect to anticoagulation in AF:

- The need for anticoagulant treatment to reduce this risk should therefore be considered immediately following diagnosis. In primary care, this decision can be guided by balancing the patient's CHA_2DS_2-VASc score (stroke risk) against their HAS-BLED score (bleeding risk), although there are no specific cut-offs in the HAS-BLED score to identify patients who should not be initiated on an anticoagulant, particularly as the consequences of a stroke are typically more severe than the consequences of a bleed ie. an elevated bleeding risk alone does not automatically make patients ineligible for oral anticoagulant use.

- ACC/AHA 2023 AF guidelines outline that stroke scoring tools such as ATRIA and GARFIELD-AF potentially improve the accuracy of stroke risk assessment compared with CHA2DS2-VASc scoring, and the GARFIELD-AF scoring includes mortality and bleeding risk assessment. However, the guidelines also note that the calibration and performance of ATRIA and GARFIELD-AF has not been as robustly evaluated as CHA2DS2-VASc.

- Direct oral anticoagulants (DOACs) are typically preferred over warfarin as they are superior for reducing the risk of stroke and all-cause mortality, reduce the risk of intracranial bleeding and have a comparable risk of major bleeding. However, there are some situations in which DOACs are contraindicated (e.g. mechanical heart valves) or there is insufficient evidence to support their use (e.g. moderate-to-severe mitral stenosis, severe liver or renal dysfunction), and warfarin should be used instead.

- Oral anticoagulants are superior to aspirin and/or clopidogrel for the prevention of stroke, systemic embolism and myocardial infarction in patients with AF, and are associated with a lower risk of major bleeding and intracranial haemorrhage. Long-term antiplatelet medicine use alone is therefore no longer recommended in patients with AF, even if they are at very low risk of stroke (i.e. CHA2DS2-VASc score of 1 for females or 0 for males). NB Post acute MI situation – confirm intended duration of antiplatelet therapy if unclear.

- The decision to stop anticoagulant medicines should be based on a continued evaluation of the patient's stroke and bleeding risk (e.g. determined by CHA_2DS_2-VASc and HAS-BLED scores) and not because AF has reverted to sinus rhythm or symptom resolution.

- With respect to diagnosis of AF, the positive predictive values for AF reported in studies involving wearable devices using photoplethysmography and AF algorithms range from 84 – 98%, suggesting that these alerts are of clinical significance. However, this does not replace the need for usual diagnostic investigations for AF, i.e. pulse palpation and ECG

3. Pharmac supply updates

(i) **Liquid morphine**: The latest Pharmac update re liquid morphine supplies - It appears RA-Morph 1 mg per ml is now back in stock. The supplier has shipped stock to wholesalers in the week beginning 3 June 2024 but there may be some delay in pharmacies replenishing stock. Pharmac listed Oramorph CDC (2mg/mL) from 9 May 2024. It is not Medsafe approved so must be prescribed and dispensed as a section 29 medicine.

Important differences from the RA-Morph brand:

- **Labelled 10 mg per 5 ml** (equivalent to 2 mg per ml)
- Different morphine salt (sulphate instead of hydrochloride)
- Contains alcohol (ethanol) 10%v/v as a preservative. The alcohol content in 5 ml of Oramorph is equivalent to 10 ml beer or 4 ml wine.
- Colourless to pale yellow

(ii) **Liraglutide and dulaglutide**: A reminder that from 1 May 2024, Pharmac is limiting funded access to dulaglutide and liraglutide to people already taking these diabetes medicines. The suppliers of dulaglutide (Eli Lilly) and liraglutide (Novo Nordisk) in New Zealand have advised Pharmac that stock of both medicines for 2024 and 2025 is only enough to meet current demand.

Prescribers should consider clinically appropriate alternative medications, including SGLT2 inhibitors.

(iii) **Oestrogen patches:** Supply of all oestradiol patches remains very limited with Pharmac stating this situation will continue through 2024 and likely for some time into 2025. The current supply status of each brand and strength of patches is available on the Pharmac website. As at 13 June 2024 the 25 mcg patches are out of stock in all brands. Stock of the 50, 75 and 100 mcg strengths is arriving but may not be available at your pharmacy.

- Update on 3 July 2024, a new funded brand (Lyllana) is becoming available. 25 mcg patches will be available from late July and 50 mcg Lyllana patches to be available in late August/early September. Monthly deliveries of all strengths of Lyllana patches until the end of the year to start in late September.

- These patches are not Medsafe approved so will need to be prescribed and dispensed in line with section 29 of the Medicines Act. Pharmac has encouraged the supplier to apply for Medsafe approval.

- Dr Samantha Newman of the FemaleGP Clinic has produced a very helpful resource for patients and GPs with respect to management options in light of the patch shortage. This is available from the FemaleGP website (bottom of Home page under 'Files for Healthcare Professionals' - When there are no patches (v2).)

4. Prescriber Update

The June 2024 Prescriber Update is now available on the Medsafe website. Brief highlights include:

(i) **Potassium in dietary supplements** may lead to hyperkalaemia. In patients with hyperkalaemia or signs and symptoms suggestive of hyperkalaemia, remember to ask about dietary supplement use. Hyperkalaemia-inducing medicines include angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), non-steroidal anti-inflammatory drugs (NSAIDs), spironolactone, potassium supplements, beta blockers, digoxin and trimethoprim. Some herbal ingredients in supplements contain potassium, including (but not limited to) stinging nettle, evening primrose, turmeric, dandelion. Other supplements may contain potassium as an ingredient or excipient, for example, glucosamine sulfate–potassium chloride complex.

(ii) **Medicine-induced hyponatraemia**: increased risks in older people. Hyponatraemia signs and symptoms range from mild and nonspecific (such as weakness or nausea) to severe and life-threatening (such as seizures or coma). Hyponatraemia may also be asymptomatic. In older people, hyponatraemia can be associated with cognitive impairment, gait disturbances and falls and fractures. The most frequently reported suspect medicines for people >65 years were bendroflumethazide, omeprazole, citalopram, fluoxetine and cholecalciferol but the list of potential culprits is long!

(iii) With **pseudoephedrine** now available again there is a reminder that the drug must not be used in people with uncontrolled hypertension or severe coronary artery disease, concomitantly with monoamine oxidase inhibitors (MAOIs), or in people with hypersensitivity to pseudoephedrine. Do not use in children aged under 12 years. Use pseudoephedrine with caution in patients with hepatic or renal impairment, severe hepatic or renal dysfunction, controlled hypertension, hyperthyroidism, diabetes mellitus, coronary or ischaemic heart disease, glaucoma and enlarged prostate. Additionally, pseudoephedrine is included on the World Anti-Doping Agency (WADA) in-competition prohibited list. Athletes must stop taking pseudoephedrine at least 24 hours before competition.

5. Prescribing to competitive athletes subject to drug testing

A recent NZ Doctor article reported the case of a competitive archer banned from the sport for two years after failing a drug test. The archer tested positive for metoprolol after winning an event at the North Island Senior Target Archery Championships in April. The competitor stated he had been using the substance on the advice of his doctor. All beta-blockers are banned in and out of competition for the sports of archery, shooting and underwater sports. In addition, they are banned in-competition for some automobile sports, billiards, darts, golf and mini-golf, some ski and snowboarding events

An earlier NZ Doctor article on prescribing for competitive athletes subject to drug testing included the following points:

- Athletes must take utmost care in ensuring they do not take any prohibited substances – they cannot rely on doctors and trainers.
- Before prescribing to a competitive athlete, check whether they are subject to doping testing.
- Advise athletes to check any medications you prescribe with their medical team.
- Use an online tool (eg, globaldro.com) to check whether medications and ingredients of supplements are prohibited or permitted.

Drugs may be prohibited out of competition or just in-competition, and some prohibitions are sport specific. In some circumstances, use of a prohibited drug may be allowed but the athlete must apply for a therapeutic use exemption (TUE). Some athletes must apply for a TUE in advance (i.e. before using any banned medications or methods). Others can only apply retroactively (i.e. after a positive test). TUE information and application forms are available on the Drug Free Sport website. The advice provided to athletes is:

- Tell your doctor that you're an athlete and subject to anti-doping rules;
- If prescribed a medication containing a banned ingredient, ask for a permitted alternative;
- Know your TUE status (in-advance or retroactive);
- Keep detailed medical notes for any diagnoses or treatments that involve a banned substance or method;
- In an emergency, always get the treatment you need.

6. Montelukast

A recent news article in the BMJ notes the asthma drug montelukast (Singulair) will carry more prominent warnings in the UK to alert doctors and patients to its potentially serious behavioural and neuropsychiatric side effects. Previously noted side effects associated with the oral treatment include sleep disturbances, depression, and agitation (which may affect up to one in 100 people); disturbances of attention or memory (up to one in 1000); and hallucinations and suicidal ideation (up to one in 10,000). A similar warning was provided to NZ prescriber in a 2017 Prescriber Update which included the recommendations that prescribers should advise patients that neuropsychiatric reactions can occur with montelukast and patients and/or family members should be instructed to contact a healthcare professional should any neuropsychiatric reaction occur.

7. Vitamin D supplementation in pregnancy and infants

With winter upon us it's time to consider local recommendations for Vitamin D supplementation in pregnancy and infants. The Te Whatu Ora publication covers additional aspects such as appropriate risk benefit discussion, when you might test Vitamin D levels and sun safety advice but the basics include:

- Risk factors during pregnancy: naturally dark skin tone; live south of Nelson Marlborough during winter or spring; spend limited time outdoors and/or have minimal sun exposure due to religious, cultural, personal or medical reasons.

- Offer vitamin D supplementation during pregnancy for women with any of the risk factors. Prescribe 400 to 800 IU colecalciferol oral liquid per day (Clinicians Vitamin D brand 10mcg/drop is subsidised – dose 1-2 drops per day). Individuals with all three risk factors in pregnancy may be at higher risk of vitamin D deficiency and blood testing may be considered. Where vitamin D insufficiency or deficiency is confirmed through testing, follow the advice from NZF regarding supplementation doses.

- Advise people at lower risk of vitamin D deficiency during pregnancy that they may benefit (and are unlikely to suffer harm) from vitamin D supplementation of between 400 IU per day (10 micrograms/day) and 800 IU per day (20 micrograms/day) throughout their pregnancy, particularly in the third trimester.

- Risk factors for infants less than 6 months: exclusively breastfed or partially breastfed receiving less than 500 mL of infant formula per day; breastfed over winter/spring months; a sibling diagnosed with rickets or hypocalcaemic seizures; maternal vitamin D deficiency or higher risk of maternal deficiency; preterm infants and infants who weigh less than 2.5 kg at birth; naturally dark skin.

- Offer to prescribe vitamin D supplements to all exclusively or partially breastfed infants as soon as practical, but by 4 weeks until 12 months of age. Prescribe colecalciferol oral liquid (7,500 IU/mL vitamin D drops, one drop per day. The subsidised formulation is Puria Vitamin D. Infant formula is fortified with vitamin D so fully formula fed infants or those receiving formula supplementation of >500mL per day should receive adequate vitamin D and do not require supplementation.

8. Abortion reversal

The RNZCGP has recently released a statement on abortion reversal noting claims that medical abortion can be 'reversed' by a dose of progesterone after a woman has taken the first medical abortion medication are not based on reputable scientific evidence. The College upholds views by other medical Colleges' that the promotion of the term 'abortion reversal is 'unproven and unethical' based on the strength of evidence. Abortion reversal involves administration of high dose progesterone (vaginally, orally or by injection) after the woman has taken mifepristone but prior to administration of misoprostol if she changes her mind about proceeding with medical abortion. A 2024 systematic review concluded that based mostly on poor-quality data, it appears the ongoing pregnancy rate in individuals treated with progesterone after mifepristone is not significantly higher compared to that of individuals receiving mifepristone alone. Despite this, a significant number of states in the USA have enacted medical abortion reversal laws that require patients receive information during pre-abortion counselling, require physicians or physicians' agents to inform patients, instruct patients to contact a health care provider or visit "abortion pill reversal" resources for more information, and require reversal information be posted on state-managed Web sites.