Clinical Snippets December 2024

1. Empagliflozin and ketoacidosis

The December 2024 Prescriber Update includes a reminder on the risk of ketoacidosis associated with use of SGLT2 inhibitors (empagliflozin in NZ) whether or not they are being used for treatment of diabetes. Key messages and prescribing considerations include:

- Patients taking SGLT-2 inhibitors are more likely to develop ketoacidosis when other risk factors are present, including acute illness, infections, surgery, pancreatic disorders, insulin dose reduction, insulin insufficiency, severe dehydration, reduced caloric intake, low carbohydrate diet, heavy alcohol use and a history of ketoacidosis.
- Inform patients taking SGLT-2 inhibitors about ketoacidosis risk factors, signs and symptoms. Blood glucose levels may be normal or only mildly elevated. Symptoms may be non-specific and include nausea, vomiting, malaise, anorexia, abdominal pain, excessive thirst, shortness of breath, dizziness or confusion. Advise patients to seek medical attention immediately if they experience ketoacidosis symptoms, irrespective of blood glucose levels.
- Consider monitoring ketones and temporarily discontinuing SGLT-2 inhibitors in clinical situations known to predispose patients to ketoacidosis. Refer to local clinical guidelines for further advice, including management before surgery/procedures and during acute illness.
- Ketoacidosis may be prolonged in patients with T2DM, despite stopping SGLT-2 inhibitors.

Healthify has excellent resources for users of empagliflozin including a printable information sheet in a variety of languages that covers risks of ketoacidosis.

2. Decision to fund fosfomycin in the community

Pharmac has decided to fund fosfomycin (branded as UroFos) in the community from 1 November 2024. This decision will allow New Zealanders to access funded fosfomycin treatment in the community, reducing the need for people to be treated for urinary tract infections (UTIs) in the hospital. Dose for an adult is 3g as a single dose – comes as a sachet which the patient mixes with water (see NZF). Special authority is required with initial application from any relevant practitioner. Approvals are valid for 2 months for applications meeting the following criteria:

Both:

- Patient has an acute, symptomatic, bacteriologically-proven uncomplicated urinary tract infection (UTI)/cystitis with Escherichia coli; and

Either:

- Microbiological testing confirms the pathogen is resistant to all of: trimethoprim, nitrofurantoin, amoxicillin, cefaclor, cefalexin, amoxicillin with clavulanic acid, and norfloxacin; or
- The patient has a contraindication or intolerance to all of: trimethoprim, nitrofurantoin, amoxicillin, cefaclor, cefalexin, amoxicillin with clavulanic acid, and norfloxacin that the pathogen is susceptible to.

3. Latent autoimmune diabetes

I have received a complaint recently regarding delayed diagnosis of latent autoimmune diabetes of adults (LADA) in a patient in his 40's with history of Graves disease who was diagnosed with type two diabetes and had two years of poor glycaemic control despite metformin and SGLT2 inhibitors before the correct diagnosis was made and insulin therapy commenced. A BPAC article on management of type 2 diabetes notes at least 5-10% of adult-onset diabetes is not type 2 and this can result in suboptimal treatment. LADA occurs when there is progressive autoimmune-mediated destruction of pancreatic beta cells commencing in adulthood, and has feature of both type 1 and type 2 diabetes (sometimes called type 1.5 diabetes). Features that might raise suspicion of the condition include:

- Symptoms of insulin deficiency at diagnosis e.g. polyuria, polydipsia, weight loss
- Rapid deterioration in glucose levels/HbA1c
- Ketoacidosis (NB: Ketoanaemia or ketonuria without acidosis are weak discriminators between the types of diabetes)
- Normal or low BMI at diagnosis
- Personal or family history of autoimmune disease
- Family history of type 1 diabetes

Most cases of LADA are associated with positive anti-GAD antibodies and reduced C-peptide levels. HealthPathways recommends if both are anti-GAD and anti-IA2 antibodies are negative and you still suspect a type 1 diabetes picture, seek specialist diabetes advice about arranging anti-ZnT8 antibodies. Management principles are similar to that for general diabetes management although use of sulfonylureas is thought to accelerate beta cell loss and earlier progression to insulin therapy. The linked reference notes *the main challenge is to distinguish patients with LADA from those with T2DM. By definition, patients with T2DM have absent autoantibodies to islet cell antigens, normal or elevated fasting, and stimulated C-peptide and usually do not require insulin for an extended period. Clinicians should consider screening for LADA in patients with T2DM who do not achieve adequate glycemic control within a reasonable period after compliance with therapy. This is particularly true if they are not obese, lack the features of the MetS, or they, or their first-degree relatives, have other autoimmune disorders, including Hashimoto thyroiditis, Graves disease, celiac disease, rheumatoid arthritis, or pernicious anemia.*

4. HINTS Test for vertigo

One reasonably common are of complaints I see is missed or delayed diagnosis of posterior circulation stroke, with a contributing factor being assessment of central vertigo as peripheral. While most vertebrobasilar strokes are also accompanied by other signs (such as diplopia, dysarthria, dysphagia, motor and sensory deficits) a proportion of cerebellar strokes present only with vertigo and subtle incoordination on examination. A positive HINTS exam has been reported to have a high sensitivity and specificity for the presence of a central cause of vertigo.

The HINTS exam is only used on a subset of the patients who present with:

- Persistent vertigo over hours or days
- Nystagmus
- A normal full neurological exam

HINTS is comprised of three core components: head impulse test, evaluation of nystagmus, and a test of skew. An excellent 8-minute video that illustrates the tests including abnormal results is available on Youtube.

5. Treating yourself and those close to you

MCNZ has updated their statement on treating yourself and those close to you.

- Allowance made for one-off management of minor ailments
- Accommodating the challenges faced by doctors in rural, remote and under-served communities
- Emergency situations

The statement notes that in those circumstances when treatment is provided, you must inform the patient's general practitioner (with the patient's consent). There are some situations where you must not treat yourself or those close to you:

- Issuing medical certificates, death certificates and conducting third party medical assessments
- Providing psychotherapy
- Providing recurring treatment or ongoing management of an illness or condition
- Performing complex procedures
- Performing sensitive examinations
- Prescribing medication with a risk of addiction or misuse, controlled drugs, and psychotropic drugs (except in an emergency)

6. ADHD changes

The ADHD landscapes is changing. From 1 December 2024, Pharmac removed the renewal criteria for methylphenidate, dexamfetamine and modafinil, medicines used to treat ADHD and narcolepsy. This means that once an initial special authority approval for stimulant medicines has been granted, a doctor or nurse practitioner can continue to prescribe it. From the same date, lisdexamfetamine will be funded when prescribed for people with ADHD who meet certain eligibility criteria, outlined in the Pharmac information page. The Goodfellow Unit has scheduled a half-day online webinar event on 22 February 2025 that aims to provide an in-depth exploration of ADHD care, from initial assessment to long-term management – you can register here. The Unit also has multiple existing podcasts/webinars on various aspects of ADHD diagnosis and management via their searchable database.

7. Pertussis

A whooping cough epidemic has recently been declared in NZ and it is timely to review our part in supporting pregnant patients/hapu mama to receive pertussis and influenza vaccines during pregnancy. An interactive Geohealth Tool allows you to examine vaccination rates in your region by year, vaccine and ethnicity up to 2021. For Hamilton City in 2021, pertussis vaccination rates for hapu mama were 46% for NZE, 13% for Maori, 27% for Pacifika and 49.4% for Asian ethnicity. IMAC includes the following additional pertussis advice:

- Advise pregnant people of the current increase in pertussis cases and strongly recommend the free Boostrix vaccination with every pregnancy. The vaccine is funded from the second trimester of pregnancy and recommended from 16 weeks. Vaccination during pregnancy is 92% protective against infant death from pertussis.
- Encourage all members of the extended whānau, including infants, children and older people to check they are up to date with all immunisations, especially their pertussis boosters - funded for people aged 4 years (Infanrix-IPV), 11 years, 45 years and 65 years (Boostrix). Some whānau may wish to privately purchase a booster (Adacel/Boostrix) if a newborn baby is expected to join the household.
- Ensure all babies receive on-time 6-week immunisations.
- Ensure pathways are in place to identify, diagnose and notify cases as well as seek public health advice for vaccinating close contacts, as recommended.
- Encourage all staff, including reception, administrative and retail, to ensure they are up to date with immunisations (in particular pertussis and measles). Booster vaccinations of Boostrix every 5 years are recommended for all lead maternity carers and healthcare workers who are in regular contact with infants.
- Notify the Medical Officer of Health as soon as you suspect a case of pertussis.

8. Medical Aspects of Fitness to Drive

On 25 November 2024, Waka Kotahi published the 2024 edition of MAFTD. A summary of changes is available and worth reviewing (15 pages). Legal and other obligations to which the health practitioner undertaking the driver's examination and completing certification are subject to include:

- To use the guide when doing a medical examination
- To give NZTA medical reports as soon as practicable of persons unfit to drive, or who should only drive subject to conditions, and are likely to continue to drive after being advised not to. Delays in sending or not giving enough information can create a road safety risk.
- When issuing a medical certificate, to give NZTA written notice as soon as practicable that the applicant isn't medically fit to drive. Delays in sending or not giving enough information can create a road safety risk.
- Always advise your patient about the impact their medical condition, disability or treatment, may have on their ability to drive. Give this advice to them in writing as well as verbally.
- Recommend any temporary driving restrictions to the patient where appropriate. This could be not driving for a specific amount of time or not driving at night.
- Discuss with your patients any recommendations you'll make to NZTA around their fitness to drive, including licence conditions, potential suspension, or revocation of their licence.
- Advise patients on their responsibility to report their condition to NZTA if their long-term or permanent injury or illness may affect their ability to drive safely.
- Include ongoing consideration of their fitness to drive while you treat, monitor, and manage the patient's medical condition.

9. Unexpected weight loss

Issue 247 of GP Research Review included a recently published paper in the BMJ looking at the predictive value that unexpected weight loss had for cancer, according to patient age, sex and clinical

features. The study population included 326,240 adults who presented to primary care with unexpected weight loss in England, between 2000-19. Within 6 months of presentation, 4.8% of all patients were diagnosed with cancer, of whom 98.9% were aged ≥40 years, and 96.3% ≥50 years. The most common malignancies were lung cancer (22.8%), bowel cancer (15.6%) and gastro-oesophageal cancer (12.4%). It was concluded that for men aged ≥50 years and women aged ≥60 years, the presence of unexpected weight loss alone warrants referral for invasive investigation, as the positive predictive values for cancer were above the recommended NICE threshold of 3%. Invasive investigation was also recommended for younger patients who presented with unexpected weight loss and concurrent clinical features (various symptoms and signs listed in the paper). Some of the concurrent clinical features with strongest associations with malignancy were bloating, dysphagia, chest signs, abdominal or rectal mass, VTE, pelvic mass (women) and iron deficiency anaemia (men). The blood test results associated with cancer included raised platelets (positive likelihood ratio 3.48), low albumin (3.24), raised CRP (3.13) and raised total white cell count (3.01). Reviewer's comment: It is the doctor's dilemma! A patient presents with unexplained weight loss, a few non-specific blood results just outside normal parameters, and nothing else. How often do we as GPs see that?

10. Quickies

- A recent Medscape article looked at evidence for pharmacological agents used in post-Covid syndrome and listed the most promising (with cited references) as: low dose naltrexone; SSRIs; modafinil; antihistamines.
- Goodfellow Unit has a learning module on Doxy-PEP to reduce chlamydia and syphilis risk, completion of which is eligible for professional development points.
- A reminder from Medsafe (Prescriber Update) that aciclovir and valaciclovir can accumulate in the presence of renal impairment and cause neurotoxicity (confusion, agitation, hallucinations or seizure. NZ Formulary gives specific dosing instructions for various eGFR ranges.
- The October issue of GP Voice included links to a one-page summary regarding management of patient with possible MS relapse. The MS Health Pathways section has more comprehensive advice including links to patient resources. Both refer to use of methylprednisolone, **not** prednisone, if treatment of a relapse is required with dose recommendation differing between the two resources. New Zealand Formulary recommends a dose of 1000mg once daily for three days or 500mg once daily for five days. Tablets are available in 100mg strength.