Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch Monthly Summary August 2017

Monthly News Update

Welcome to the KINES Monthly News Update for August 2017. Other recent KINES Updates have discussed:

- cardiovascular (CV) outcomes data for canagliflozin. This is the second sodium-glucose co-transporter 2 inhibitor to be associated with CV benefits, raising the possibility of a class effect. In this analysis canagliflozin was associated with an approximately doubled relative risk of lower limb amputation.
- a large randomised controlled trial (RCT) that failed to find benefit for monthly high-dose vitamin D supplements in reducing the risk of falls and fractures.
- an observational study reporting that people with Alzheimer's disease who received benzodiazepines were around 30% more likely to develop pneumonia compared with those not taking benzodiazepines.

Update from NICE:

- New guidance has been issued by NICE on the use of bisphosphonates for osteoporosis. Based on cost-effectiveness analyses that reflect falling treatment costs, the population eligible for treatment has been expanded, with oral bisphosphonates now recommended as an option for those people eligible for a risk assessment (*see comment below*) who have a 10-year fracture risk of **1% or higher** (as measured by FRAX or QFracture tools). Intravenous bisphosphonates are recommended if fracture risk is ≥10%, or ≥1% where oral bisphosphonates cannot be taken, are contraindicated or not tolerated. Choice of treatment should be made after discussions about the advantages and disadvantages, and if generic products are available, NICE states that treatment should be started with the least expensive formulation. These recommendations apply to both men and women.

  Keele's comment: Notably, these recommendations are applicable only to patients who are **eligible** for fracture risk assessment. This is defined by NICE in CG146 as:
  - women aged 65 years and over; men aged 75 years and over
  - patients under these ages who have a risk factor (e.g. previous fragility fracture; current/frequent use of glucocorticoids; history of falls; family history of hip fracture; other causes of secondary osteoporosis; BMI < 18.5 kg/m^{2}; smoking; > 14 units/week alcohol (women) or > 21 unit's/week (men).
  - **Routine assessment should not be undertaken in people <50 years**, except in the case of major risk factors (e.g. glucocorticoids, untreated premature menopause; previous fragility fracture).

  The treatment thresholds differ from those in the recently updated National Osteoporosis Guideline Group (NOGG) guideline. The NICE guideline committee acknowledge that the thresholds in the NOGG guideline may be used to determine when to offer treatment in clinical practice, but that cost effectiveness had not been taken into account by NOGG.

  We have looked at resources available to support treatment discussions with patients, particularly as lower risk patients may want to understand potential benefits and risks. Decision aids have not been produced by NICE, and are not available in the RightCare decision aid library. Some 'numbers needed to treat' (NNTs) have been included in the review for the guideline committee (*NNTs ranged from 697 to 2222 for the prevention of 1 fracture occurring in the first 6 months after starting treatment*), but these are not linked to fracture risk scores. Outside the UK, decision aids linked to FRAX scores have been published by the Mayo Clinic. The Cochrane Library also has some decision aids for individual bisphosphonates.

  Regarding treatment costs, alendronic acid (70 mg once weekly) is the lowest cost oral treatment.
- NICE has now published final guidance on roflumilast (Daxas), recommending it as an option in **severe** chronic obstructive pulmonary disease (COPD), where post-bronchodilator forced expiratory volume in 1 second (FEV_1) is below 50% and only if the patient has had at least 2 exacerbations in the last year despite use of triple inhaled therapy. Treatment should be started by a specialist.
- An evidence summary has been published on the use of adjuvant bisphosphonates in early breast cancer. The strengths and limitations are considered of the 2015 meta-analysis that reported reductions in breast cancer mortality, bone recurrence and all-cause mortality for postmenopausal women treated with bisphosphonates. Benefits were not observed in premenopausal women.

Regulatory agency safety update:

- New MHRA advice has been issued on adrenaline/epinephrine auto-injectors. It is recommended that 2 injectors are prescribed which patients should carry at all times. Healthcare professionals are also asked to ensure patients/carers

receive training for their specific device, and encourage them to obtain training devices, which are available from manufacturers' websites. A new patient advice sheet has also been produced.

- Patients prescribed corticosteroid treatments should be advised to report any blurred vision or visual disturbances. This new MHRA advice follows reports of the retinal disorder central serous chorioretinopathy, which has previously been linked with systemic corticosteroids, after local administration of corticosteroids, e.g. via inhaled and intranasal, epidural, intra-articular, topical dermal, and periocular routes. The risk is considered rare. Consider referral to an ophthalmologist for evaluation of possible causes if a patient presents with vision problems.

NHS England/Department of Health/Public Health England:

- Updated guidance on measles, including recommendations on post-exposure prophylaxis, has been published by Public Health England (PHE). Changes include that infants under 6 months who have had close contact with a likely or confirmed measles case should now be offered immunoglobulin prophylaxis regardless of the mother's immune status. Classification of immunosuppressed groups has also been updated to include people treated with newer immunosuppressive treatments, such as biological therapies.
- PHE has also issued advice on the infection control of *Candida auris* in community care settings. A leaflet is also available for patients and visitors. Covered widely by the press this month, *C. auris* is an emerging fungal pathogen of concern, which is commonly resistant to the first line antifungal agent fluconazole and for which colonisation can be difficult to eradicate.
- PHE is encouraging people to come forward for Hepatitis C (hepC) testing. Specific groups who should be tested are people who:
  - received a blood transfusion before Sept 1991, or a blood product before 1986 in the UK
  - have ever shared needles/other equipment to inject drugs
  - have had medical/dental treatment abroad in unsterile conditions or have had a tattoo/piercing/acupuncture/electrolysis/semi-permanent make up using potentially unsterilized equipment
  - had unprotected sex, or shared a toothbrush or razor, with someone who has/might have hep C.

  This follows a PHE report highlighting the need to find and treat those infected patients to sustain the recent falls seen in deaths from HepC.
- Pharmacists may be interested in first update from NHS England's newly appointed National Pharmacy Adviser for RightCare. The blog includes links to various RightCare medicines optimisation resources.
- A PHE report on malaria has found failure to take chemoprophylaxis is associated with the majority of UK cases. It is suggested that messages about chemoprophylaxis may not be reaching 'at risk' groups, identified as people visiting family in their country of origin, particularly those of Black African heritage and/or born in Africa. Alternatively, these groups may not be acting on messages to obtain chemoprophylaxis. Healthcare professionals providing advice are asked to engage with these groups, including possibly discussing future travel plans outside of travel health consultation, e.g. during new patient checks or childhood immunisation appointments.
- Finally, the latest Vaccine Update is a special edition on flu. The update includes links to various resources to support this year's flu programme.

Drug update:

Launched:

- The first triple inhaler for COPD has been launched. Trimbow, which is a metered dose inhaler (MDI), contains a long-acting beta agonist (LABA) (formoterol fumarate; 6 µg/puff), an inhaled corticosteroid (ICS) (beclometasone dipropionate 100 µg/puff) and a long-acting muscarinic antagonist (LAMA) (glycopyrronium; 10 µg/puff). It is licensed as maintenance treatment in adults with moderate to severe COPD who are not adequately treated by a combination of an ICS and a LABA. The recommended (*and maximum*) dose of Trimbow is two inhalations twice daily.

  Keele's comment: The 2017 update to the GOLD COPD guideline gives triple therapy a very limited place, for selected Group D patients requiring a step-up in therapy from a LABA/LAMA (***which is now the recommended initial therapy for Group D patients***) or a LABA/ICS (*a possible first choice for some patients, such as where there is asthma-COPD overlap*). Group D includes patients who have the greatest symptom burden and risk of exacerbation, defined as ≥2 exacerbations in the past year (or ≥1 leading to a hospital admission), and an mMRC dyspnoea score ≥2 or a COPD Assessment Test [CAT] score ≥10.) **De-escalation in treatment**, i.e. stepping back down from triple therapy to a LABA/LAMA, is also suggested for the first time in GOLD, where there has been resolution of some symptoms. (*See the November 2016 KINES for an overview of GOLD*). NICE guidance on COPD is currently being updated, and is due to be published late next year.
  We note that the licensed indication for Trimbow refers to use in people who are not adequately treated by LABA/ICS combination therapy. Evidence is not available on the benefits stepping up to Trimbow from LABA/LAMA dual bronchodilator therapy, which is being given a greater role in the management of COPD and may be an option to explore first in some patients, ahead of a step-up to triple therapy.

Risk minimisation materials:

- New risk minimisation materials this month include a discussion guide to use when initiating treatment with the multiple sclerosis treatment Aubagio (teriflunomide), a document to clarify differences between the newly launched Kyleena intrauterine device (IUD)(*link to Kyleena SPC*) and Mirena and Jaydess IUDs, and several new resources about the risk of phototoxicity and squamous cell carcinoma with the anti-fungal voriconazole.