

The purpose of the Medicines Management newsletter is to deliver succinct, evidence-based advice and information on primary care prescribing issues. Aimed at busy prescribers wanting to know key messages from the many publications in the previous month.

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1. What's in the news

Articles relevant to primary care

For full access to the DTB articles login via Open Athens those without accounts: [https://openathens.nice.org.uk/DTB Vol 52 No 9 | September 2014](https://openathens.nice.org.uk/DTB%20Vol%2052%20No%209%20September%202014)

1. Modelling the impact of lowering HbA1c (DTB)

It is common practice in the treatment of type 2 diabetes mellitus to correct blood glucose levels. The study investigated how treatment burden affects the benefits of intense versus moderate blood glucose levels. The study used outcomes of QALYs (quality adjusted life years) and micro and macro diabetes complications.

Results showed that treatment that lowered HbA1c level by 1 percentage point provided benefits ranging from 0.77 to 0.91 QALYs for simulated patients who received a diagnosis at age 45 years to 0.08 to 0.10 QALYs for those who received a diagnosis at age 75 years. An increase in treatment burden (0.01, or 3.7 days lost per year) resulted in HbA1c level lowering being associated with more harm than benefit in those aged 75 years. Across all ages, patients who viewed treatment as more burdensome (0.025-0.05 disutility) experienced a net loss in QALYs from treatments to lower HbA1c level

The authors of the review concluded that HbA1c targets below 9% should be individualised and this is in line with our [Type 2 diabetes guideline](#). The substantial benefits of blood glucose control appears more beneficial for younger patients, but for patients older than 50 years with an HbA1c level less than 9% receiving metformin therapy, additional glycaemic treatment usually offers at most modest benefits. Local guidance gives other patient factors to consider in the approach to the [management of hyperglycaemia](#)

JAMA Vijan S et al. "Effect of Patients' Risks and Preferences on Health Gains With Plasma Glucose Level Lowering in Type 2 Diabetes Mellitus JAMA Intern Med 2014; 174: 1227–34.

2. Oxycodone for neuropathic pain and fibromyalgia—little evidence (DTB)

Treating neuropathic pain and fibromyalgia is difficult and conventional analgesics are usually not effective. The studies included in this review although of short duration adds to previous findings that there is no convincing evidence that oxycodone is beneficial in treating painful diabetic neuropathy or post herpetic neuralgia. There is furthermore no evidence of oxycodone for neuropathic pain or fibromyalgia.

[Evidence supporting the use of opioids for neuropathic pain and fibromyalgia is limited and the adverse effects and dependence remains a concern. Clinicians in Derbyshire should follow our local \[neuropathic pain guideline\]\(#\).](#)

Gaskell H et al. Oxycodone for neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev 2014; 6: CD010692.

DOI:10.1002/14651858.CD010692.pub2 [Last assessed as up-to-date 6 November 2013].

Other news:

1. Intensive Blood Pressure Control, Falls, and Fractures in Patients with Type 2 Diabetes: The ACCORD Trial

This study investigated whether or not the control of blood pressure to lower thresholds results in a commonly held belief that there is an increased risk of falls and fractures. The review included a subset of patients from the ACCORD study, type 2 diabetes in the intensive (targeting a systolic blood pressure of < 120 mmHg) and standard (targeting a systolic blood pressure of < 140 mmHg) blood pressure control arms. The adjusted rate of falls did not differ in the intensive and standard groups (62.2/100 person-years vs. 74.1/100 person years, RR=0.84, 95 % CI 0.54–1.29, p=0.43. The risk of non-spine fractures was non-significantly lower in the intensive than in the standard blood pressure group (HR 0.79, 95 % CI 0.62–1.01, p= 0.06).

The authors concluded that intensive antihypertensive treatment that lowered mean systolic blood pressure to below 120 mmHg was not associated with an increased risk of falls or non-spine fractures in patients aged 40 to 79 years with type 2 diabetes.

Karen L. Margolis et al [Journal of General Internal Medicine](#)- 16 Aug 2014

2. **Acclidinium bromide for stable chronic obstructive pulmonary disease** ([The Cochrane Library](#))

A Cochrane review looked at acclidinium bromide (a long-acting muscarinic antagonist (LAMA) classified by JAPC as BROWN third line LAMA choice after tiotropium and glycopyrronium. The difference over tiotropium is its greater selectivity for M3 muscarinic receptors and quicker onset of action. Acclidinium though has a shorter duration of action than for tiotropium.

The authors concluded that acclidinium is associated with improved quality of life and reduced hospitalisations due to severe exacerbations in patients with moderate to severe stable COPD compared to placebo, but overall, did not significantly reduce mortality, serious adverse events or exacerbations requiring oral steroids or antibiotics, or both.

[Comparative trials of efficacy and safety with tiotropium are lacking or limited. Clinicians in Derbyshire should continue to follow local preferred formulary choices and COPD guideline](#)

2. **Drug Safety Update** relating to primary care prescribing

(For more information see [Drug Safety Update: MHRA Volume 8, Issue 2 Sept 2014](#))

Denosumab: minimising the risk of osteonecrosis of the jaw; monitoring for hypocalcaemia—updated recommendations

Advice for healthcare professionals on osteonecrosis of the jaw (ONJ) and risk of hypocalcaemia. The MHRA advises the following when denosumab 60mg is used for osteoporosis:

- Check for ONJ risk factors before starting denosumab 60 mg for osteoporosis. A dental examination and appropriate preventive dentistry are now recommended for patients with risk factors.
- Tell all patients to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain, or swelling to a doctor and dentist.
- *Check calcium levels:*
 - before each dose
 - within two weeks after the initial dose in patients with risk factors for hypocalcaemia (e.g., severe renal impairment, creatinine clearance <30 ml/min)
 - If suspected symptoms of hypocalcaemia occur
- Tell all patients to report symptoms of hypocalcaemia to their doctor (e.g., muscle spasms, twitches, or cramps; numbness or tingling in the fingers, toes, or around the mouth).

[Prescribers should continue to follow our local Shared Care Guideline for denosumab 60 mg for the treatment of osteoporosis.](#)

Nitrofurantoin now contraindicated in most patients with an estimated glomerular filtration rate (eGFR) of less than 45 ml/min (previously contra-indicated if creatinine clearance <60ml/min)

Advice for healthcare professionals:

- Nitrofurantoin is contraindicated in patients with an estimated glomerular filtration rate (eGFR) of less than 45 ml/min.
- Nitrofurantoin should not be used to treat sepsis syndrome secondary to urinary tract infection or suspected upper urinary tract infections
- A short course (3 to 7 days) may be used with caution in certain patients with an eGFR of 30 to 44 ml/min. Only prescribe to such patients to treat lower urinary tract infection with suspected or proven multidrug resistant pathogens when the benefits of nitrofurantoin are considered to outweigh the risks of side effects.
- Consider checking renal function when choosing to treat with nitrofurantoin, especially in the elderly.
- Closely monitor for signs of pulmonary, hepatic, neurological, haematological, and gastrointestinal side effects during treatment, as previously advised in the summary of product characteristics.
- Consult official guidance on the appropriate use of antibiotics when prescribing nitrofurantoin.

[This change allows nitrofurantoin to be used in patients previously for whom it was not recommended. Prescribers should continue to follow our local guidelines which will be updated following the advice from our specialist antimicrobial pharmacist.](#)

3. **Local News and GP queries**

GP query

Should we prescribe fluoride toothpastes on the recommendation of a dentist?

Answer

[Issuing a prescription for fluoride toothpaste should only be prescribed after carrying out a full oral health assessment including advice and any necessary tests such as radiographs. These types of assessments are typically carried out by a dentist. The dentist has clinical responsibility for the patient and prescribing should remain with the dentist.](#)

Local News

Atrial fibrillation – The Derbyshire guideline on [Management of non-valvular atrial fibrillation](#) which is reflective of [NICE CG 180](#) is now available. Primary care clinicians will find additional resources within the document to support primary care prescribing. Useful examples include practical differences between the new oral anticoagulants, what to do with existing patients on treatment outside NICE guidelines and prescribing recommendations after patients are discharged from secondary care.

RightCare – is a well-established Derbyshire wide scheme which was designed by Derbyshire Health United (DHU) clinicians to ensure that seamless patient care takes place out of hours, when GP practices are closed. Examples of patients that may benefit from the scheme are those with long term conditions and complex healthcare needs, including

end of life patients. The scheme helps to prevent unnecessary admissions to hospital and attendance at Accident and Emergency (A&E), lowers patient anxiety, provides reassurance and allows patients to access the most appropriate healthcare and advice quickly. For further information see [DHU website](#)

Benzodiazepines – DHcFT Drugs and Therapeutics Group this month discussed reported cases in Derbyshire where GPs are refusing to prescribe benzodiazepines when asked to do so following consultant/specialist advice, and that GPs are attempting benzodiazepine withdrawal programmes in patients still under specialist supervision without communication. [These cases highlight the need for good communication between primary care and the Derbyshire Healthcare Foundation Trust.](#)

4. QiPP

Guidance on infection control in schools and other childcare ([GOV.UK](#))

PHE has updated guidance published in 2010 that provides guidance for schools and other childcare settings, such as nurseries, on infection control issues.

Long-acting reversible contraception (update) [NICE CG 30](#)

NICE makes reference to clinical opinion that LARC methods may have a wider role in contraception and their increased uptake could help to reduce unintended pregnancy. This guideline has been updated noting that the subdermal implant Implanon is no longer available and has been replaced by the implant Nexplanon, which contains the same drug (etonogestrel) and dose, but also contains barium to make it radio-opaque, and has a different insertion technique.

[The appendices provides a useful summary listing key features of progestogen-only subdermal implants to discuss with women, and summarises issues affecting choice for specific groups of women and women with medical conditions.](#)

5. NICE Evidence summaries: New medicines and unlicensed/off-label relating to primary care prescribing

New medicines

COPD beclometasone/formoterol (Fostair) ESNM47

[In April 2014 Fostair's licence was extended to include COPD in addition to asthma. Fostair is included in local guidance for asthma and COPD](#)

In a randomised controlled trial (RCT; n=718), beclometasone/formoterol was non-inferior to budesonide/formoterol in improving pre-dose morning lung function in people with severe COPD over 48 weeks. There was no significant difference between the treatments in the rate of COPD exacerbations/patient per year. The incidence of adverse events was similar between the treatments.

In a second RCT (n=419), beclometasone/formoterol statistically significantly improved the onset of bronchodilation in people with moderate-to-severe COPD compared with fluticasone/salmeterol, although it is unclear whether the improvement is clinically important. The treatments were equivalent in improving dyspnoea over 12 weeks. Serious adverse events were statistically significantly more common with fluticasone/salmeterol

From the published data, beclometasone/formoterol appears to work as well in COPD as the 2 commonly used ICS/LABA combinations, its constituent ingredients have been available for many years so their safety profile is known, it costs less than most alternatives and it can be used with a spacer, which many people with COPD need.

Unlicensed/ off-label reviews

[None for September 2014](#)

6. Useful resources

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| BMJ | www.bmj.com |
| JAMA: The Journal of the American Medical Association | http://jama.ama-assn.org/ |
| The Lancet | www.thelancet.com |
| The New England Journal of Medicine | http://content.nejm.org/ |
| BMJ, JAMA and NEJM can be accessed in full-text directly through your NHS Athens Account via: National Library for Health: search via My Journals MyAthens: via National Library for Health Resources or Local Resources. Current Lancet articles are sometimes available with free registration from http://www.thelancet.com/content/register . Print copies of The Lancet are available at DCGH library. | www.library.nhs.uk or www.athens.ac.uk |
| If you have not already registered for an NHS Athens Account, please register at: NB: It is recommended that you register on a Trust (NHS) PC for speedy confirmation of your username a password. Once registered, your account can be accessed from any computer with online access. | https://register.athensams.net/nhs/nhseng/ |
| UKMI Nathnac NHS evidence Electronic medicines compendium Clinical Knowledge Summaries Medicines Prescribing Centre (Formerly NPC) Medicines for children (patient information leaflets) Drugs in lactation | http://www.ukmi.nhs.uk/ https://www.evidence.nhs.uk/search?om=%5B%7B%22srn%22%3A%5B%22%20ukmi%20%22%5D%7D%5D http://www.nathnac.org/ http://www.evidence.nhs.uk/ http://www.medicines.org.uk/emc/ www.cks.nhs.uk . http://www.nice.org.uk/mpc/ http://www.medicinesforchildren.org.uk/ http://www.midlandsmedicines.nhs.uk/content.asp?section=6&subsection=17&pageldx=1 |
| UK teratology services | http://www.uktis.org/index.html |
| Vaccine update- Vaccination newsletter for health professionals and immunisation practitioners | https://www.gov.uk/government/organisations/public-health-england/series/vaccine-update |