

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. Round up of What's in the news

Association Between Use of Sodium-Glucose Cotransporter 2 Inhibitors, Glucagon-like Peptide 1 Agonists, and Dipeptidyl Peptidase 4 Inhibitors With All-Cause Mortality in Patients With Type 2 Diabetes. A Systematic Review and Meta-analysis. Zheng SL; Roddick AJ, Aghar-Jaffar R, et al. JAMA. 2018; 319(15):1580-1591. doi:10.1001/jama.2018.3024

Systematic review compared the efficacies of sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) agonists and Dipeptidyl peptidase-4 (DPP-4) inhibitors on mortality and cardiovascular end points using a network meta-analysis. Researchers reviewed 236 trials (n=176,310 patients) comparing SGLT-2 inhibitors, GLP-1 agonists, and DPP-4 inhibitors—against each other, a placebo, or no treatment at all.

The results demonstrated that the use of SGLT-2 inhibitors or GLP-1 agonists was associated with lower mortality than DPP-4 inhibitors or placebo or no treatment. Use of DPP-4 inhibitors was not associated with lower mortality than placebo or no treatment.

The local Derbyshire diabetes guidance based on the NICE NG28 contains all 3 classes of antidiabetic medication has recently been updated, with a message for prescriber to consider the emerging evidence of cardiovascular benefit of SGLT2 inhibitors and GLP1 agonists for their patients.

Locally within Derbyshire £1.7m is currently spent on the DPP4 inhibitors, compared to £1.2m on the GLP1 agonists and £692k on SGLT2 inhibitors over the same time period.

GP's are reminded that for continued therapy with DPP4 inhibitors and the SGLT2 inhibitors, the patient must show HbA1c reduction ≥ 5.5 mmol/mol (0.5%) in 6 months, otherwise the treatment should be discontinued. The GLP1 agonists should only be continued if there is a reduction of HbA1c by ≥ 11 mmol/mol (1.0%)] and a weight loss $\geq 3\%$ of initial body weight in 6 months.

Considering the evidence and the local spend on these drugs, it is essential only treatments with proven benefits are continued for type 2 diabetic patients.

Association of Inhaled Corticosteroids and Long-Acting β -Agonists as Controller and Quick Relief Therapy With Exacerbations and Symptom Control in Persistent Asthma: A Systematic Review and Meta-analysis

Krishnan JA, Au DH. JAMA. 2018;319(14):1441-1443. doi:10.1001/jama.2018.2029

UKMI comment:

Meta-analysis (n=22,748) concludes use of single maintenance and reliever therapy (SMART) vs inhaled corticosteroids as the controller therapy (with or without long-acting β -agonist) and short-acting β -agonists as relief therapy was linked to lower risk of asthma exacerbations.

Single maintenance and reliever therapy (SMART) is associated with a lower risk of asthma exacerbations compared with a higher dose of inhaled corticosteroids and LABA as controller therapy, absolute risk difference, -2.8% for the children aged 4-11yrs and -12.0% for those >12yrs.

This systematic review supports the combined use of inhaled corticosteroids and LABA as both the controller and quick relief therapy (SMART) among patients aged 12 years or older compared with using either the same or a higher dose of inhaled corticosteroids alone as the controller therapy or the same or a higher dose of inhaled corticosteroids and LABA as the controller therapy.

Acondro (ethinylestradiol/drospirenone)	Hyabak UD (sodium hyaluronate)	Mission Ketone
Amilamont (amiloride)	Lestramyl 20/150 (ethinylestradiol/desogestrel)	Nacrez (desogestrel)
Co-dantrusate capsules	Lestramyl 30/150 (ethinylestradiol/desogestrel)	Olysio (simeprevir)
Hidrasec (racecadotril)	Macilax (macrogol)	Pregnyl (chorionic gonadotrophin [human])
Hidrasec Children (racecadotril)	Macilax Paediatric (macrogol)	SMA Staydown
Hidrasec Infant (racecadotril)	Mission Glucose	Soltamox (tamoxifen)
		SuperCheck2

2. Drug safety update primarily relating to primary care prescribing
(For more information see [Drug Safety Update](#)) Volume 11 Issue 10 May 2018

Valproate medicines (epilium, Depakote): Pregnancy Prevention Programme material online.

The MHRA has produced a set of online materials (and hard copies arriving over the coming weeks by post) to ensure women and girls of childbearing potential on valproate medicines meet the requirements of the Pregnancy Prevention Programme.

[Patient card](#), [patient guide](#), [guide for healthcare professionals](#) and [risk acknowledgement form](#) are available to support the new valproate Pregnancy Prevention Programme.

Valproate medicines must no longer be used in women or girls of childbearing potential unless a Pregnancy Prevention Programme is in place. The requirement for a Pregnancy Prevention Programme is applicable to all premenopausal female patients unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy.

Braltus (tiotropium): risk of inhalation of capsule if placed in the mouthpiece of the inhaler

Reminder for HCP to train patients prescribed Braltus (tiotropium capsules for chronic obstructive pulmonary disease on inhaler technique. Train patients to place the Braltus capsule in the correct chamber of the Zonda inhaler. The MHRA has received reports of patients who have inhaled a Braltus capsule from the mouthpiece into the back of the throat, resulting in coughing and risking aspiration or airway obstruction.

Advice for healthcare professionals:

- train patients in the correct use of their inhaler; a placebo device is available for training purposes (see below) and instructions for patients are provided in the patient information leaflet and on the carton
- tell patients to store capsules in the screw-cap bottle provided (never in the inhaler) and to always check the mouthpiece is clear before inhaling
- pharmacists dispensing Braltus capsules should remind patients to always read the [instructions for use](#) in the package leaflet and that they must never place a capsule directly into the mouthpiece
- please continue to report adverse incidents during use of the inhaler as well as suspected adverse reactions to the medicine on a [Yellow Card](#)

3. Local news and GP/pharmacist queries

Query from GP practice:

Restless legs syndrome (RLS) – what are the treatment options?

Answer:

For patients with mild symptoms, explanation, reassurance and self-help measures should be sufficient. To reduce the severity, good sleep, reduced caffeine/alcohol, stopping smoking and exercise should help. To relieve an episode patients are recommended to try walking/stretching/massaging the limb's, heat pads, hot bath, relaxation and distraction e.g. games/reading.

JAPC recommend that ropinirole, rotigotine and pramipexole (unlicensed), are only prescribed for severe RLS that has a significant impact on the quality of life after self-help measures have been tried as above. These have been classified as BROWN (exceptional use only). Gabapentin and pregabalin are alternative 1st line agents according to CKS. JAPC has not classified them for RLS and their use would be off-label.

See <https://cks.nice.org.uk/restless-legs-syndrome#!scenario> for more details

Derbyshire Medicines Safety Network (DMSN)

A new Derbyshire Medicines Safety Network (DMSN) has been created with accountability to JAPC. The DMSN is a forum to inform and improve medication safety across the Derbyshire health economy through sharing of information and learning from medication safety issues occurring in primary and secondary care.

It also makes recommendations in terms of medicines safety issues which span the interface between primary and secondary care. Representation of the group includes Medication Safety Officers/Pharmacists from various different provider organisations across Derbyshire.

4. **Quality, Innovation, Productivity and Prevention (QIPP)**

Highlighting potential QIPP opportunity

Cost of the combination product of pioglitazone and metformin

- Competact (pioglitazone/Metformin 15/850mg) x 56 = £35.89

Cost of the individual products

- Pioglitazone 15mg x 28 = £2.07
- Metformin 850mg x 56 = £1.28

If the individual drugs are prescribed the total cost = £5.42 for one month's supply; compared to £35.89 for the combination product - competact, delivering £30.47 saving per item prescribed.

JAPC has recently classified competact as BLACK.

NHSE have published the following guide:

[Quick Reference Guide for Healthcare Professionals: Conditions for which over the counter items should not routinely be prescribed in primary care.](#)

May – price concessions

Prescribers should note that the re-imburement price on FP10 may not necessarily reflect the Drug Tariff price as a result of a drug shortage. These concessionary prices are set by the Department of Health to reflect actual market prices.

A concession only lasts until the end of the month in which it was granted. If there is an on-going supply problem, it is possible that a new concession will be granted by the Department of Health the following month, however this is not guaranteed

Drug	Pack size	Price concession	Drug tariff price
Amisulpride 100mg tablets	60	£9.95	£3.24
Amisulpride 200mg tablets	60	£15.95	£5.59
Aripiprazole 10mg tablets	28	£3.27	£1.99
Aripiprazole 15mg tablets	28	£3.12	£2.75
Aripiprazole 5mg tablets	28	£2.77	£2.37
Chlorpromazine 50mg tablets	28	£33.95	£28.09
Glimepiride 3mg tablets	30	£4.79	£3.65
Irbesartan 150mg tablets	28	£5.31	£1.08
Irbesartan 75mg tablets	28	£2.67	£0.80
Levetiracetam 100mg/ml Oral Solution	300ml	£7.05	£6.76
Perindopril erbumine 2mg tablets	30	£3.70	£3.08
Perindopril erbumine 8mg tablets	30	£5.47	£3.82
Phenoxymethylpenicillin 125mg/5ml oral solution	100ml	£5.67	£4.97
Pioglitazone 15mg tablets	28	£10.83	£0.50
Pioglitazone 30mg tablets	28	£14.07	£0.92
Sodium Valproate SF Liquid 200mg/5ml	300ml	£5.94	£4.46
Telmisartan 20mg tablets	28	£0.95	£0.63
Trimethoprim 200mg tablets	6	£0.40	£0.31
Venlafaxine 75mg tablets	56	£5.68	£1.94

5. **NICE summaries: New medicines (relating to primary care prescribing)**

None primary care related

6. **Useful resources**

BMJ	www.thebmj.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/

<p>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.</p>	<p>www.library.nhs.uk</p> <p>or</p> <p>www.athens.ac.uk</p>
<p>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.</p>	<p>https://register.athensams.net/nhs/nhseng/</p>
<p>UKMI Nathnac NHS evidence Electronic medicines compendium Clinical Knowledge Summaries Medicines Prescribing Centre (Formerly NPC) Medicines for children (patient information leaflets)</p> <p>Drugs in lactation</p>	<p>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/</p> <p>http://www.midlandsmedicines.nhs.uk/content.asp?section=6&subsection=17&pageIdx=1</p>
<p>UK teratology services</p>	<p>http://www.uktis.org/index.html</p>
<p>Vaccine update- Vaccination newsletter for health professionals and immunisation practitioners</p>	<p>https://www.gov.uk/government/organisations/public-health-england/series/vaccine-update</p>