

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.

This issue	Item 1	What's in the news
	Item 2	Drug Safety Update- MHRA and Drug deletions
	Item 3	Local news
	Item 4	QIPP
	Item 5	NICE evidence summaries: unlicensed/off-label medicines
	Item 6	Useful resources

1. What's in the news

[DTB April 2016 Volume 54 issue 4](#)

Nicorandil now second-line in the treatment of stable angina

This follows MHRA advice on the use of nicorandil in the treatment of stable angina, specifying that the drug only be used as second-line treatment due to the risk of ulcer complications

Prescribers should follow local guidance, see the [local cardiovascular chapter of the BNF](#) –appendix 6 page 14 placing nicorandil as third or fourth line.

PPI use linked to raised risk of kidney disease

The DTB reports on a large population-based cohort study which suggests that use of PPIs is also associated with an increased risk of incident chronic kidney disease.

As an observational study a causal relationship cannot be established and all the limitations of this type of study design should be noted. This does though add to the growing concern of PPI use and need for a regular medication review, and step down of therapy or stopping where appropriate

Specify levonorgestrel releasing IUS by brand name

The DTB reminds us of advice already given through the Derbyshire Joint Area Prescribing Committee, to prescribe levonorgestrel releasing IUS by its brand name. Locally **Mirena** (levonorgestrel 20 micrograms/24 hours) is the preferred progestogen only IUD and **Jaydess** (levonorgestrel 13.5mg) is commissioned for contraception in line with advice from Public Health both are Green classified. **Levosert** (20 micrograms/24 hours) which is similar to Mirena but not cost-effective is classified as BLACK

Other news.....

Pioglitazone use and risk of bladder cancer: population based cohort study

This population based cohort study included 145,806 patients with type 2 diabetes concluded that the results from this large population indicate that pioglitazone is associated with an increased risk of bladder cancer. The absence of an association with rosiglitazone suggests that the increased risk is drug specific and not a class effect. The risk increases with increasing duration of use and dose

BMJ 2016;352:i1541 | doi: 10.1136/bmj.i1541 Marco Tuccori et al

Antidepressant use and risk of cardiovascular outcomes in people aged 20 to 64: cohort study using primary care database

The aim of this study, using the UK database was to assess associations between different antidepressant treatments and rates of three cardiovascular outcomes in people with depression.

This study found no evidence that selective serotonin reuptake inhibitors are associated with an increased risk of arrhythmia or stroke/transient ischaemic attack in people diagnosed as having depression between the ages of 20 to 64 or that citalopram is associated with a significantly increased risk of arrhythmia. It found some indication of a reduced risk of myocardial infarction with selective serotonin reuptake inhibitors, particularly fluoxetine, and of an increased risk with lofepramine.

Prescribers are reminded of our [local antidepressant guidance](#) produced with and supported by the Derbyshire Healthcare Foundation Trust

BMJ 2016;352:i1350 | doi: 10.1136/bmj.i1350 Carol Coupland et al

Blood Glucose Meters (BGM) and ISO (International Organization for Standardization) 15197:2013 standards

A revised set of quality standards for blood glucose monitoring was published in May 2013 to help ensure accuracy and consistency of results for people with diabetes.

The transition period for the implementation of these standards will end in May 2016. As a result, test strips may be unavailable for non-compliant meter systems. It is vital healthcare professionals (HCPs) ensure their patients are upgraded to compliant meter systems before this date.

There is the potential that patients within Derbyshire are currently using non-ISO 15197:2013 compliant meter systems, and therefore will need to be changed.

The current preferred formulary meters; the AgaMatrix WaveSense JAZZ™ and the Nipro TrueResult™ meters are fully compliant with ISO 15197:2013 and can therefore continue to be used.

The first ISO standard for meter systems was published in 2003 and the latest standards reflect recent advances in technology. The requirements of the ISO 15197: 2013 Standard must be met in order for a meter system to become CE certified compliant.

[Advice concerning the upgrade can be integrated into routine check-ups or new patient assessments.](#)

1. To establish if a non-formulary meter system is compliant, HCPs should consult the website or customer care line of the relevant manufacturer.
2. HCPs should check that their patients are using ISO 15197:2013 Standard compliant meter systems. If they are not, upgrade them to one of the preferred formulary meters or consider another BGM that uses strips under £10 for 50, which meet the patient's needs and of course meet updated ISO standards

Prescription charges

The cost of a NHS prescription in England will increase by 20p to £8.40 with effect from April 2016. The prices for 3 and 12 month pre-payment certificates have remained the same at £29.10 and £104 respectively. For anyone requiring more than 3 items in 3 months or more than 12 in a year these certificates can provide significant savings.

Deleted products 2016 | MIMS online for April 2016

Decubal Clinic	Filnarine (morphine sulfate)	Kepivance (palifermin)
Lopresor SR (metoprolol)	Recivit (fentanyl)	Seprtin (co-trimoxazole)
Seprtin Adult Susp. (co-trimoxazole)	Seprtin Paed. Susp. (co-trimoxazole)	Ucerax syrup (hydroxyzine)

2. Drug safety update primarily relating to primary care prescribing

(For more information see [Drug Safety Update](#)) Volume 9, Issue 9, April 2016

1. SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis. This endorses the preliminary advice given by the MHRA in June 2015. Noting the importance of discussing with patients the risk factors for, and signs and symptoms of, diabetic ketoacidosis. Prescribers are further reminded that SGLT2 inhibitors should not be used in patients with type 1 diabetes.
2. Natalizumab (Tysabri ▼): progressive multifocal leukoencephalopathy— updated advice to support early detection
3. Dimethyl fumarate (Tecfidera): updated advice on risk of progressive multifocal leukoencephalopathy
4. Fingolimod (Gilenya ▼): risks of progressive multifocal leukoencephalopathy, basal-cell carcinoma, and opportunistic infections
5. Apomorphine with domperidone: minimising risk of cardiac side effects (risk of QT-prolongation). Apomorphine is currently under a [local shared care agreement](#) which is being updated. Patient responsibilities are included to inform their doctor of any changes that could increase their risk of arrhythmia, such as:
 - symptoms of cardiac or hepatic disorders
 - conditions that could cause electrolyte disturbances (e.g. gastroenteritis or starting a diuretic)
 - starting any other medicines
6. Aflibercept (Zaltrap ▼): minimising the risk of osteonecrosis of the jaw in patients treated for cancer.
7. Live attenuated vaccines: avoid use in those who are clinically immunosuppressed. Note-A minor immunodeficiency may not necessarily contraindicate vaccination. The Summary of Product Characteristics* for a particular vaccine will explain specific contraindications and warnings. The [Green Book](#) (Immunisation against infectious disease) [and local shared care guidelines](#) should also be consulted
8. Meprobamate: licence to be cancelled
9. Paraffin-based skin emollients on dressings or clothing: fire risk. Update to previous advice in June 2008. For r resources see [NPSA](#)

Other safety news....

[MHRA information on TPP and QRISK2](#)

The Medicines and Healthcare products Regulatory Agency (MHRA) is investigating an issue involving a digital calculator used by some GPs to assess the potential risk of heart disease in patients.

The QRISK®2 Calculator is a predictive algorithm used to support medical practitioners, mainly in GP practices, to help assess the potential risk of cardiovascular disease in patients, as part of their overall evaluation. The issue has resulted in incorrect results being produced for a limited number of patients. The MHRA is working with TPP, the software provider, as a matter of urgency, to make sure the identified issue is resolved and that any affected patients are identified

Buprenorphine patches – please prescribe by brand name.

A number of incidents have recently been reported involving the generic prescribing of buprenorphine patches, which also reveals a misunderstanding of the different frequencies of patch application available. One incident revealed that a patient prescribed a generically prescribed buprenorphine 35mcg/hr patch with directions for applying one patch every 3 days (supply 10 patches), was dispensed the Transtec® brand by the Community Pharmacy, which should be changed every 4 days. The patient was not harmed in anyway and had their prescription changed to reflect directions as for the Transtec® brand i.e. change every 4 days. A further check was carried out by a member of the Medicines Management Team (MMT) for other patients prescribed Buprenorphine patches in the GP practice, which highlighted other patches prescribed generically (patch to be changed every 4 days) – these were changed over to the Transtec® brand to ensure clarity.

Did you know?.....there are 3 different brands of Buprenorphine patch all with different frequencies for application/patch change.

The brands are not interchangeable as they deliver different amounts of buprenorphine (Butrans® is weaker than Hapoctasin® and Transtec®) and the time each patch is applied is different; see table below (information taken from BNF edition 70):

<i>Brand of Buprenorphine patch</i>	<i>Frequency of application/patch change</i>	<i>Strengths of patch available</i>
Hapoctasin®	72 hours (3 days)	35, 52.5 & 70 micrograms/hr
Transtec®	96 hours (4 days)	35, 52.5 & 70 micrograms/hr
Butrans® or Butec®	7 days	5, 10 & 20 micrograms/hr

The Medicines Management Team (MMT) will be sharing this information with GP practices and highlighting the availability of a ['local detailing aid' for Buprenorphine patches on the Derbyshire Medicines Management website.](#)

The MMT can provide support to help identify patients prescribed buprenorphine generically and ensure prescribing is changed to the appropriate brand. Please speak to your MMT technician or pharmacist

Plain vs. Modified release preparation of drugs – getting it right at the Primary & Secondary care interface

The Medicines Management Team are being informed of errors occurring when patients are discharged from hospital and discharge prescriptions are processed for addition to the GP prescribing systems. These errors appear to involve a potential misunderstanding or picking error when dealing with medicines that are available as plain and modified release preparations. In particular, these errors are being seen for the drug venlafaxine, whereby plain tablets are prescribed on the discharge prescription by the hospital, but these are then being added as the significantly more expensive 'modified release' preparation in error to the GP prescribing systems.

Example of venlafaxine error:

Discharge prescription for 'Venlafaxine 225mg each morning & 150mg at night'.

Prescribed on GP system as 'Venlafaxine 225mg MR each morning & 150mg MR at night'.

However, should have been prescribed on GP system as 'Venlafaxine 75mg tablets; take three tablets each morning & two tablets at night'

There are many other drugs that are available as plain and modified release preparations (e.g. metformin, doxazosin, sodium valproate, carbamazepine, isosorbide mononitrate, Co-careldopa) & therefore, there is potential for an error to occur with any of these drugs too.

Key messages:

- When adding to or amending medicines in GP prescribing system using information from a hospital discharge or clinic letter, please be vigilant when picking the drug formulations on the GP prescribing system. It is good practice to self-check your own work and what you have added to the GP prescribing system to ensure no errors have been made during the transcription process.
- The medicines management teams would recommend that only clinical staff (GPs, nurses, pharmacists or technicians) add prescriptions to a patients record to reduce the risk of error.
- 'Modified release' preparations may be abbreviated as 'MR'. Some medicines may instead be called 'sustained release' (abbreviated as 'SR') or controlled release' (abbreviated as 'CR'), which are different versions of modified release preparations, but the principles of slower drug delivery are the same.
- For further information, training & support for receptionists/prescription clerks, please contact your Medicines Management Team.

3. Local news and GP/pharmacist queries

Query from GP practice:

Triiodothyronine in mental health

A Patient has been discharged on triiodothyroxine 50microg daily. Please advise on thyroxine prescribing for mental health problems as I believe it to be unlicensed.

Answer:

Tri-iodothyronine is the same as Liothyronine. Orally it is only licensed for hypothyroidism.

The CCG class liothyronine as AMBER: Shared care for depression.

This requires specialist assessment to enable patient selection and initiation of treatment It also requires short or medium term (e.g. 3-6 months) specialist monitoring of efficacy or until the patient is stable.

[Shared care for Liothyronine](#)

The unlicensed special-order tablets are expensive and the cost of the 5mg and 25mg tablets are unknown.

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

TOXBASE app now free for NHS users

[Toxbase](#) in an online clinical toxicology database The app which was re-launched in October 2015 and now allows free access to the full database for NHS/PHE users.

Toxbase also allows access to The United Kingdom Teratology Information Service (UKTIS) a national service commissioned by Public Health England to provide information on all aspects of the toxicity of drugs and chemicals in pregnancy.

New telephone numbers UK National Poisons Information Service 0344 892 0111 and UK Teratology Information Service 0344 892 0909

Neonatal hepatitis B immunisation programme – for babies born to HepB+ mothers

NHS England commissions GP practices to deliver the neonatal hepatitis B immunisation programme. As the numbers of affected babies in Derbyshire are quite low many practices may not realise what care they are contracted to deliver with regards to this programme. A new pathway developed by NHS England has recently been shared with practices that highlight these requirements. In short this means that practices should;

1. On notification of a baby being born to a hepatitis B mother this information should be inputted on to babies record 'mum is Hep B positive'
2. The practice should arrange appointments for vaccination at 1 month, 2 month, 12 months and with the pre-school booster. Any DNA's should be chased as this is a post exposure prophylactic course of vaccinations.
3. A blood test should be arranged at 12 months to ensure that the **child has not become infected with Hep B**. We are not looking for antibodies but infection. This can be via a dried blood spot (DBS) test or through paediatric phlebotomy services. Please ensure the correct test is requested if using phlebotomy services. Practices can contact the Screening and Imms team for support if doing the DBS in the surgery
4. Child Health Records Department should be notified of all vaccinations and of a blood result at 12 months
5. All babies are monitored by the Screening and Immunisation team and any un-vaccinated babies will be followed up

For information about the Meningococcal vaccine schedules, please see [Chapter 22 of the Green Book](#) and in particular pages 13 and 14 regarding Meningitis B vaccinations where it states as a footnote that only children born on or after 1st May 2015 should be offered 4CMenB catch-up vaccinations.

Generic shortages (NCSO and 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.

April 2016

Drug	Pack size	Drug tariff price	Price concession
Bumetanide 1mg tablets	28	£1.30	£2.05
Celiprolol 400mg tablets	28	£32.32	£39.65
Cimetidine 400mg tablets	60	£9.72	£19.99
Desmopressin 10micrograms/dose nasal spray (new)	60 dose	£13.77	£24.00
Flecainide 50mg tablets	60	£3.35	£7.50
Flecainide 100mg tablets	60	£4.32	£6.83
Fludrocortisone 100mcg tablets (new)	100	£5.05	£96.00
Lamotrigine 5mg dispersible tablets sugar free	28	£2.68	£7.50
Mefenamic acid 500mg tablets	28	£8.25	£10.25
Nitrofurantoin 100mg tablets (new)	28	£2.88	£12.50
Nitrofurantoin 50mg tablets (new)	28	£8.23	£11.50
Pioglitazone 15mg tablets	28	£11.23	£19.20
Pioglitazone 30mg tablets	28	£10.99	£24.32

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

Nothing to note

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/
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