

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

### **Metformin in patients with CKD.**

An [analysis](#) of 3 complementary dose-finding studies concludes that provided the dose is adjusted for renal function, metformin treatment appears to be safe and still pharmacologically efficacious in moderate-to-severe CKD.

UKMi comment: This analysis was conducted to define a safe, effective dose regimen for metformin in moderate and severe chronic kidney disease (CKD; stages 3A/3B and 4, respectively), after the lifting of restrictions on metformin use in patients with diabetes with moderate-to-severe CKD.

### **Kyleena IUS launched in the UK**

A new levonorgestrel-releasing intra-uterine system (IUS) has been launched in the UK, joining Mirena, levosert and Jaydess as the fourth IUS contraceptive on the market.

Kyleena is a 5-year IUS containing 19.5mg of levonorgestrel, which continuously releases a low daily dose of levonorgestrel. It is intermediate in dose between jaydess (containing 13.5mg levonorgestrel) and Mirena/Levosert (each containing 52mg levonorgestrel). It is of similar size to Jaydess, but can be used for up to 5 years, whereas Jaydess can only be used for 3 years.

*A clinical and cost effectiveness review of Kyleena will be presented to a future JAPC meeting for local consideration, updates on commissioning position and traffic light status will then be available.*

### **Impact of issuing longer- versus shorter-duration prescriptions: a systematic review**

*(King S, Miani C, Exley J, Larkin J, Kirtley A and Payne RA. Br J Gen Pract 2018; 68 (669): e286-e292).*

Systematic review to examine the impact of longer-duration (2–4 months) versus shorter-duration (28-day) prescriptions. Evidence of moderate quality from nine studies suggested that longer prescriptions are associated with increased medication adherence. Evidence from six studies suggested that longer prescriptions may increase medication waste, but results were not always statistically significant and were of very low quality. The study concluded that there is insufficient evidence relating to the overall impact of differing prescription lengths on clinical and health service outcomes, although studies do suggest medication adherence may improve with longer prescriptions.

### **Deleted products 2018 | MIMS online** for March 2018

|  |                       |
|--|-----------------------|
| Accolate (zafirlukast)                           | MMA/PA Maxamaid       |
| Trimovate (clobetasone/nystatin/oxytetracycline) | MSUD Maxamaid         |
| HCU Maxamaid                                     | TYR Maxamaid          |
| IVA Maxamaid                                     | Zinbryta (daclizumab) |

## 2. **Drug safety update** primarily relating to primary care prescribing

(For more information see [Drug Safety Update](#) ) Volume 10 Issue 4 November 2016

Relevant to primary care

**Esmya (ulipristal acetate) for uterine fibroids: do not initiate or re-start treatment; monitor liver function in current and recent users.**

Temporary safety measures are in place while an WU review investigates the link between cases of serious liver injury and Esmya for uterine fibroids.

*Advice for healthcare professionals:*

- do not initiate new treatment courses of Esmya, including in women who have completed one or more treatment courses previously

- perform liver function tests at least once a month in all women currently taking Esmya and again 2–4 weeks after stopping treatment.
- check transaminase levels immediately in current or recent users of Esmya who present with signs or symptoms suggestive of liver injury (for example nausea, vomiting, malaise, right hypochondrial pain, anorexia, asthenia, or jaundice)
- stop Esmya in any woman who develops transaminase levels more than 2-times the upper limit of normal, closely monitor and refer women for specialist hepatology evaluation as clinically indicated
- advise women using Esmya about the signs and symptoms of liver injury and tell them to seek immediate medical attention if they occur
- report suspected adverse drug reactions without delay to the Yellow Card Scheme

**JAPC has reclassified Esmya (Ulipristal) as BLACK, pending the full MHRA review. Chesterfield and Derby hospitals have provided assurance that they have carried out the necessary testing on all women who have current or recent Esmya prescriptions. Primary care would need to ensure monitoring has been completed on all current or recent patients that they have prescribed Esmya for, and to ensure no future prescribing of Esmya occurs.**

**Head lice eradication products: risk of serious burns if treated hair is exposed to open flames or other sources of ignition, e.g., cigarettes**

*Advice to pharmacists*

- some products for the eradication of head lice infestations are combustible/flammable when on the hair and can ignite and cause serious harm in the presence of an open flame or other source of ignition such as when lighting cigarettes
- advise parents, caregivers and the person with head lice, if appropriate, that they should not smoke around treated hair and that it should be kept away from open flames or other sources of ignition, including in the morning after overnight application until hair is washed
- always advise parents and caregivers and the person with head lice to read the instructions that come with treatments to ensure that they are used safely and correctly
- report suspected adverse drug reactions, including burns, to the Yellow Card Scheme

**Confidential prescribing and patient safety reports on key indicators now available free for GPs**

The Royal College of General Practitioners (RCGP) in conjunction with the MHRA's Clinical Practice Research Datalink (CPRD) have developed confidential bespoke practice and patient-level drug prescribing reports, available for free for GP practices contributing to CPRD.

The reports provide a list of pseudonymised patients at the practice so that GPs can re-identify and review their care plans. They also show the practice's prescription rate benchmarked against other participating GP practices.

**New measures to avoid valproate exposure in pregnancy endorsed. EMA March 2018**

New measures taken by CMDh (Medicines regulatory body) include a ban on the use of valproate-containing medicines for migraine or bipolar disorder during pregnancy and a ban on treating epilepsy during pregnancy unless there is no other effective treatment available.

Further the medicines must not be used in any women or girl able to have children unless the conditions of a new pregnancy prevention programme are met.

Further information can be found at the [Drug safety update](#) website.

### **3. Local news and GP/pharmacist queries**

**Query from GP practice:**

A paediatrician requested lansoprazole 6mg od for a 23 week old boy. Can we use the orodispersible form or will we need to use lansoprazole liquid which looks like it may be a special order.

**Answer:**

The BNF for children states: "Child (bodyweight up to 30 kg) 0.5–1 mg/kg once daily (max. per dose 15 mg once daily), doses to be taken in the morning for acid-related dyspepsia or gastro-oesophageal reflux disease". The 6mg dose is correct if the child weighs 6kg.

Lansoprazole orodispersible tablets are licensed for adults for reflux/GORD but not for children. According to its SPC: "The use of lansoprazole is not recommended in children as clinical data are limited. Treatment of small children below one year of age should be avoided as available data have not shown beneficial effects in the treatment of gastroesophageal reflux disease". It is difficult to give a dose of 6mg from a 30mg or 15mg orodispersible tablet. This is especially difficult as it would mean giving a partial dose and there could be micro-granules possibly left in a syringe.

Lansoprazole oral suspension seems a more practical and safer option due to the child's age. All lansoprazole suspension strengths (5mg/5ml, 15mg/5ml, and 30mg/5ml) are unlicensed specials. Using the Drug tariff the most cost effective option is to give Lansoprazole 30mg in 5ml. Additionally the volume is appropriate for the patient as young children and babies may struggle with large volumes. The dose would be 1ml (6mg) OD and a 100ml bottle costs £59.32

### **Crushing melatonin (Circadin) 2mg SR tablet?**

There have been reports of patients told by their pharmacists not to crush their melatonin tablets.

All healthcare professionals are reminded the [Derbyshire A to Z of specials](#), includes a monograph for melatonin:

**First choice:** "Circadin 2mg MR is the only licensed melatonin preparation in the UK and is the preferred prescribing option (off-label). See melatonin information sheet for more information.

NB: Changing between immediate release and modified release preparations is not recommended without discussion with the specialist. "

**Second choice:** "Circadin tablets may be halved using a tablet cutter and maintain slow release properties.

Circadin tablets may be crushed. Modified release characteristics are then lost and it acts like an immediate release preparation.

See information sheet on Derbyshire Medicines Management website for more information."

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

### **Quinine prescribing**

A study in JAMA, 2017 found that the long-term use of quinine for nocturnal leg cramps may increase the risk of mortality.

*(Association Between Long-term Quinine Exposure and All-Cause Mortality. Fardet L, Nazareth I, Petersen I.*

*JAMA. 2017;317(18):1907–1909. doi:10.1001/jama.2017.2332)*

Quinine is included within [deprescribing guidance](#) as one of the top drugs where prescribers should consider a trial without. Prescribers are reminded to review frail, elderly and patients on problematic polypharmacy prescribed quinine and to consider the benefit to harm ratio of medicines.

Further the MHRA recommend that GPs prescribing quinine for nocturnal leg cramps should exercise particular care in patients with conditions that predispose to QT prolongation.

When used for nocturnal leg cramps, prescribers are reminded a reduction in frequency of leg cramps may take up to 4 weeks to become apparent. Patients should be monitored closely during the early stages of treatment for adverse effects. After an initial trial of 4 weeks, treatment should be **stopped if there is no benefit**. **Treatment should be interrupted at approximately three monthly intervals to assess the need for continuation of treatment with quinine.**

### **Trimovate**

Trimovate has been discontinued, and is now available as an Unlicensed product and has increased in price to £14.95 (May also attract additional charges e.g. out of pocket expenses)

An alternative to trimovate could be Timodine, although not a like for like swap.

| Name      | Steroid             | Antifungal | Antibiotic           | Cost                         |
|-----------|---------------------|------------|----------------------|------------------------------|
| Trimovate | Clobetasone 0.05%   | Nystatin   | Oxytetracycline      | £14.95 (+additional charges) |
| Timodine  | Hydrocortisone 0.5% | Nystatin   | Benzalkonium Chlorid | £3.37                        |

### **March – 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 |
|------------------------------|-----------|------------------|-------------------|
| Aripiprazole 5mg tablets     | 28        | £3.11            | £1.12             |
| Aripiprazole 10mg tablets    | 28        | £3.00            | £1.18             |
| Aripiprazole 15mg tablets    | 28        | £3.75            | £1.29             |
| Amiloride 5mg tablets        | 28        | £2.87            | £1.26             |
| Anastrozole 1mg tablets      | 28        | £4.70            | £3.07             |
| Bicalutamide 50mg tablets    | 28        | £18.00           | £1.67             |
| Bicalutamide 150mg tablets   | 28        | £21.00           | £3.75             |
| Bisacodyl 5mg tablets        | 60        | £3.60            | £1.73             |
| Digoxin 125mcg tablets       | 28        | £1.61            | £1.35             |
| Chlorpromazine 100mg tablets | 28        | £32.01           | £10.20            |
| Chlorpromazine 25mg tablets  | 28        | £31.74           | £15.97            |
| Chlorpromazine 50mg tablets  | 28        | £32.47           | £7.38             |
| Citalopram 40mg tablets      | 28        | £1.56            | £1.34             |
| Digoxin 250mcg tablets       | 28        | £1.60            | £1.35             |

|  |        |        |        |
|--|--------|--------|--------|
| Digoxin 62.5mcg tablets                            | 28     | £1.62  | £1.32  |
| Duloxetine 20mg capsules                           | 28     | £7.49  | £3.16  |
| Duloxetine 40mg capsules                           | 56     | £8.80  | £5.45  |
| Duloxetine 30mg capsules                           | 28     | £4.27  | £2.76  |
| Duloxetine 60mg gastro-resistant capsules          | 28     | £5.86  | £3.73  |
| Eplerenone 25mg tablets                            | 28     | £13.22 | £4.51  |
| Eplerenone 50mg tablets                            | 28     | £8.47  | £5.88  |
| Fexofenadine 120mg tablets                         | 30     | £1.78  | £1.53  |
| Fexofenadine 180mg tablets                         | 30     | £2.35  | £2.15  |
| Gabapentin 400mg capsules                          | 100    | £4.94  | £3.26  |
| Glimepiride 1mg tablets                            | 30     | £2.85  | £0.86  |
| Glimepiride 4mg tablets                            | 30     | £7.81  | £0.90  |
| Glimepiride 2mg tablets                            | 30     | £4.00  | £0.69  |
| Glimepiride 3mg tablets                            | 30     | £4.47  | £0.88  |
| Hydroxychloroquine 200mg tablets                   | 60     | £5.04  | £4.17  |
| Irbesartan 150mg tablets                           | 28     | £5.00  | £1.10  |
| Irbesartan 300mg tablets                           | 28     | £7.00  | £1.66  |
| Irbesartan 75mg tablets                            | 28     | £2.32  | £0.84  |
| Lacidipine 2mg tablets                             | 28     | £2.95  | £1.58  |
| Lacidipine 4mg tablets                             | 28     | £3.25  | £1.74  |
| Lansoprazole 15mg orodispersible tablets           | 28     | £2.98  | £1.88  |
| Lansoprazole 30mg orodispersible tablets           | 28     | £4.39  | £3.26  |
| Levetiracetam 100mg/ml Solution SF                 | 300ml  | £7.35  | £5.63  |
| Losartan 100mg tablets                             | 28     | £1.20  | £1.02  |
| Mebeverine 135mg tablets                           | 100    | £4.59  | £4.39  |
| Mefenamic Acid 500mg tablets                       | 28     | £28.99 | £27.54 |
| Oxazepam 10mg tablets                              | 28     | £11.12 | £10.17 |
| Oxazepam 15mg tablets                              | 28     | £10.55 | £9.08  |
| Perindopril 2mg tablets                            | 30     | £5.00  | £0.84  |
| Perindopril 4mg tablets                            | 30     | £4.90  | £0.96  |
| Perindopril 8 mg tablets                           | 30     | £6.95  | £1.11  |
| Phenoxymethylpenicillin 125mg/5ml oral solution    | 100    | £7.50  | £1.93  |
| Phenoxymethylpenicillin 250mg/5ml oral solution    | 100    | £7.00  | £2.96  |
| Phenoxymethylpenicillin 125mg/5ml oral solution SF | 100ml  | £7.82  | £4.97  |
| Phenoxymethylpenicillin 250mg/5ml oral solution SF | 100ml  | £8.35  | £5.74  |
| Pioglitazone 15mg tablets                          | 28     | £3.32  | £0.73  |
| Pioglitazone 30mg tablets                          | 28     | £4.50  | £0.80  |
| Pioglitazone 45mg tablets                          | 28     | £4.71  | £0.89  |
| Pregabalin 150mg capsules                          | 56     | £3.33  | £2.87  |
| Pregabalin 200mg capsules                          | 84     | £4.72  | £4.43  |
| Pregabalin 50mg capsules                           | 84     | £4.74  | £4.10  |
| Rasagiline 1mg tablets                             | 28     | £3.52  | £2.55  |
| Sodium Cromoglycate 2% Eye Drops                   | 13.5ml | £7.56  | £6.71  |
| Tolterodine 1mg tablets                            | 56     | £2.01  | £1.55  |
| Tolterodine 2mg tablets                            | 56     | £3.50  | £2.17  |
| Topiramate 25mg tablets                            | 60     | £6.00  | £1.34  |
| Topiramate 50mg tablets                            | 60     | £11.89 | £1.71  |
| Topiramate 100mg tablets                           | 60     | £17.67 | £2.25  |
| Tramadol 50mg capsules                             | 30     | £0.75  | £0.66  |
| Tranexamic Acid 500mg tablets                      | 60     | £11.29 | £10.59 |
| Trimethoprim 50mg/5ml oral suspension SF           | 100ml  | £3.52  | £2.22  |

|                             |    |       |       |
|-----------------------------|----|-------|-------|
| Venlafaxine 75mg tablets    | 56 | £5.57 | £1.87 |
| Venlafaxine 37.5mg tablets  | 56 | £3.79 | £1.82 |
| Vitamin B Co Strong tablets | 28 | £3.37 | £2.52 |

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

March 2018

### **NG91 - Otitis media (acute): antimicrobial prescribing.**

This guideline sets out an antimicrobial prescribing strategy for acute otitis media (ear infection). It aims to limit antibiotic use and reduce antimicrobial resistance. Acute otitis media can be caused by viruses or bacteria. It lasts for about a week, and most children get better in 3 days without antibiotics. The guidance states symptoms such as pain can be managed with self-care – through use of paracetamol and ibuprofen. Antibiotic management if needed is also included with the guidance. Serious complications are rare. A useful summary of the guidance for primary care can be found on the NICE website: <https://www.nice.org.uk/guidance/ng91/resources/visual-summary-pdf-4787282702>

## 6. Useful resources

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