

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

[DTB October 2015, Volume 53 Number 10](#)

Melatonin for sleep problems in children with neurodevelopmental disorders

Children with neurodevelopmental disorders are at risk of sleep problems, typically difficulty getting to sleep, sleep/wake rhythm disturbances and reduced duration of sleep (insomnia). This may be associated with abnormally timed or inadequate secretion of melatonin, a naturally-occurring hormone involved in coordinating the body's sleep-wake cycle. The DTB has reviewed the off-label and unlicensed use of melatonin in children with attention-deficit hyperactivity disorder (ADHD) or autism spectrum disorder or related neurodevelopmental disorders. The DTB recommends that sleep hygiene and behavioural interventions are considered before drug treatment. Small, short term clinical trials suggest that the absolute benefit of drug treatment to be small and questions the long term effect in children.

Locally only the licensed melatonin MR preparation (used off label), Circadin) where quality can be assured is classified as **BROWN** after specialist initiation, and its use in disabled children and CAMHs patients. Unlicensed melatonin products are available from special-order manufacturers or specialist importing companies and are considerably more expensive. The cost of a 30 tablet pack of 2mg CR melatonin (Circadin) is £15.39. Costs for unlicensed liquid oral preparations listed in the Drug Tariff range from £78 to £255 for a dose of 5mg per day for 30 days. These unlicensed formulations of melatonin were recently re-classified from amber to **RED**.

Changes to the BNF

From the September 2015 edition of the BNF (number 70), numeric categories will no longer be used in the paper edition, instead referenced by the textual descriptive category to which they belong. It will therefore not be possible to reference the BNF by using these numeric categories. The new look BNF should include fully populated monographs enabling the user to find all the information about a drug in one place. The departure from the previous format is that possible multiple differing uses of a drug will be referenced in the same place, not split across different categories

The information on pharmaceutical preparations is very different in the new versions. Just as an example, the BNF no longer lists morphine MR products by duration but by formulation (tablet/ capsule). It is therefore not possible to know which are 12 hour and which are 24 hour preparations

It has recently come to light that there are issues with the new BNF, UKMi have been working with the BNF to clarify the situation. Please see <http://www.bnf.org/news/>

- Some errors have been noted in the latest BNF publications, particularly in BNFC. However, UKMi have categorised the errors as being of one of three groups: indexing errors, changes in preparation information or formatting of information, and finally actual dosing errors.

If you come across errors please submit these directly to editor@bnf.org

- The paper versions of the text should be distributed as mechanisms are in place to amended serious errors where identified by risk type.
- Digital product use should be encouraged.

Since the discussions/email threads on the BNF for Children 2015-2016 and BNF 70 the BNF has issued a [statement](#) of clarify in the new editions.

NICE Type 1 diabetes NG17

[NICE bites](#) is a useful summary of the august publication [of NICE Type 1 diabetes in adults: diagnosis and management](#) local guidance has been updated to reflect advice on the routine self-monitoring of blood glucose levels for all adults with type 1 diabetes.

Deleted products 2015 | MIMS online for October 2015

Advantage Plus test strips	Antepsin, Antepsin Suspension (sucralfate)	Apresoline, Apresoline Injection (hydralazine)
Cavi-Care	Efcortisol (hydrocortisone)	Erythrocin Injection (erythromycin)
Fenistil (penciclovir)	Milupa PKU 3 Advanta	PhosLo (calcium acetate)
Phytext Paint (borotannic complex/salicylates)	Sorbisterit (calcium polystyrene sulfonate)	Sustiva Oral Solution (efavirenz)

2. Drug safety update relating to primary care prescribing

(For more information see [Drug Safety Update](#)) Volume 9, Issue 3, October 2015

The website that hosts the Drug Safety Update has now been moved. You can subscribe to alerts by using the following [sign up link](#). Headlines-

1. Mirabegron (Betmiga ▼): risk of severe hypertension and associated cerebrovascular and cardiac events: An EU-wide review of the latest safety data on mirabegron (Betmiga ▼), a beta 3-adrenoceptor agonist used in the management of urinary frequency, urgency, and incontinence in overactive bladder syndrome, has led to new measures to help reduce the risks of severe hypertension. It is already known that mirabegron can increase blood pressure. However, cases of severe hypertension have been reported, which include hypertensive crisis associated with reports of cerebrovascular and cardiac events (mainly transient ischaemia attack or stroke)—some with a clear temporal relation to mirabegron use.

Mirabegron is now contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥ 180 mm Hg or diastolic blood pressure ≥ 110 mm Hg, or both). Regular monitoring of blood pressure is important, especially in patients with pre-existing hypertension—

3. Local news and GP/pharmacist queries

GP query

Our local pharmacy informs me that there is a shortage of nefopam, please could you check the availability

Answer

Branded Acupan was discontinued at the beginning of October, but a generic has been launched. However, the generic is much higher in price than branded Acupan.

Acupan (and current drug tariff price) is £10.59/ 90

Current generic acquisition cost is higher than the concessionary price (granted temporarily by the DoH for the month of November) of £25.00/ 90

In such an event the usual process would be for the contractor (pharmacy) to apply for a concession which is done via the PSNC.

Stock has been available locally however supply is sporadic, and it appears that local warehouses' stock is currently exhausted, with pharmacies reporting unable to obtain stock.

We advise that given the price increase, concession price and local stock shortages, that patients are reviewed for the need of nefopam and alternative more cost effective choices are considered.

Local news

1. Shortage of haloperidol injection

Haloperidol injection is licensed for the rapid control of the symptoms of hostility, aggression, hyperactivity, disruptive and violent behavior, confusion, emotional withdrawal, hallucinations and delusions associated with acute and chronic schizophrenia, mania, and hypomania, and organic brain syndrome. It is also licensed for the treatment of nausea and vomiting.

Haloperidol injection is commonly used in the palliative care setting for nausea and vomiting and, in the last days of life, agitation /restlessness. It is now widely accepted that this preparation including parallel imports is not now available or difficult to source. Derbyshire palliative care consultants have jointly issued advice on alternative treatments in the event of stocks not being available or obtainable in the form of a position statement (sent to practices or available from the medicines management teams)

2. NHS England North Midlands has published November's [controlled drugs \(CD\) newsletter](#). This newsletter covers: Potential risk of harm with high strength opioids, CD requisitions, the disposal of obsolete and expired CDs, CD registers and lost or mislaid prescriptions.

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

[The Derbyshire medicines management website](#)

The Derbyshire medicines management website is a site that holds useful resources such as local decisions and advice that is valued by our medical and non-medical prescribers. For example:

1. [Clinical guidelines](#). This categorises formulary drugs by BNF chapters along with key prescribing advice and relevant clinical guidelines
2. [Traffic light classification](#). Allows a database search to ascertain the position of a drug locally and the reason
3. [Shared care guidelines](#). These are local policies to enable GPs to pick up the prescribing and monitoring of medicines/treatments in primary care in agreement with the initiating specialist outlining the responsibilities between the two
4. [JAPC bulletin](#). A 10 minute read outline key issues discussed at the Derbyshire Joint Area Prescribing Committee
5. [Inappropriate requests](#). Allows non-formulary inappropriate requests (patient anonymised) to be collected centrally within medicines management to challenge the provider trust and consultant in a co-ordinated way.
6. [Other useful guidelines](#)- Includes the document "Guidance on Prescribing in Primary Care". Often GP non-medical queries are answered from this section of the website e.g. advice on issuing prescriptions for overseas patients, patients following a private consultation etc
7. [Specials](#)- Useful resource available to practices to manage high cost specials being prescribed.
8. [Patient information leaflets](#)- Signposts to nationally available leaflets and locally agreed.
9. [Patient group directions](#)- National and locally agreed PGDs
10. Signposting to [further resources](#)- to signpost prescribers to evidence base and approved websites.

[Vaccination requirement for adults and children with incomplete or uncertain immunisation status](#)

Public Health England has published a [one page vaccination summary](#) document for those with incomplete or uncertain immunisation status.

[Further useful resources](#) around vaccination information to patients include: "immunisations for young people about the HPV, Td/IPV and MenACWY vaccinations given [between 11 and 19 years of age](#) (school years 7 to 13) Your questions answered" and "A quick guide to childhood immunisations for the parents of [premature babies](#)."

NICE undertook an unlicensed [review of Excessive daytime sleepiness in Parkinson's disease: modafinil](#)

It summarised that there is limited evidence from 4 small, short duration randomised controlled trials (RCTs; total n=89) that found a statistically significant reduction in daytime sleepiness with modafinil treatment in people with Parkinson's disease (PD) in 3 of these studies compared to placebo.

The current NICE guideline on PD which was published in 2006 and is currently being updated, recommends that modafinil may be considered for excessive daytime sleepiness in people with PD. Since the guideline was published, it has become apparent that modafinil is associated with serious psychiatric, cardiovascular and skin adverse effects. In 2010 a safety review by the European Medicines Agency (EMA) concluded that the benefits of modafinil outweighed the risks only in the treatment of narcolepsy

[Currently in Derbyshire modafinil is classified as BLACK for fatigue in multiple sclerosis and all other indications except narcolepsy and narcolepsy secondary to Parkinson's disease and GREEN following specialist initiation: to treat narcolepsy and narcolepsy secondary to Parkinson's disease.](#)

[Fusidic acid 1% increase in drug tariff price](#)

Since the discontinuation of *Fucithalmic* the price of fusidic acid 1% eye drops has continued to rise. The cost is now £29.06 for 5g. Prescribers are urged to ensure that where antibiotic treatment of conjunctivitis is considered necessary, chloramphenicol 0.5% eye drops are always considered first line (£1.53 for 10ml).

Clinical features of infective conjunctivitis :

- Most people with infective conjunctivitis get better, without treatment, within 1–2 weeks.
- For most people, use of a topical ocular antibiotic makes little difference to recovery from infective conjunctivitis.
- Up to 10% of people treated with topical ocular antibiotics complain of adverse reactions to treatment.
- The risk of a serious complication from untreated infective conjunctivitis is low.

To consider offering a topical ocular antibiotic to a person with infective conjunctivitis when:

- Infective conjunctivitis is severe, or likely to become severe, providing serious causes of a red eye can be confidently excluded

Chloramphenicol is the first-line for empirical treatment of infective conjunctivitis when a topical ocular antibiotic is considered necessary.

Fusidic acid is an alternative empirical treatment. It is preferred for people who:

- Are pregnant.
- Have a personal or family history of blood dyscrasias, such as aplastic anaemia.
- Are intolerant of chloramphenicol.

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

[Type 1 diabetes mellitus in adults: high-strength insulin glargine 300 units/ml \(Toujeo\) \(ESNM62\)](#)

NICE Summary: High-strength insulin products such as insulin glargine 300 units/ml (Toujeo) have been developed for people with large daily insulin requirements to reduce the number and volume of injections. Toujeo has shown similar efficacy to insulin glargine 100 units/ml (Lantus) in terms of HbA1c reduction, but the basal insulin dose used was higher with Toujeo than with Lantus. There was no benefit of Toujeo over Lantus in terms of reduced hypoglycaemic events. The safety profile of Toujeo is largely similar to that of Lantus. Toujeo is not bioequivalent to Lantus and they are not interchangeable without dose adjustment.

[JAPC had horizon scanned this preparation which was classified this as BLACK on launch.](#)

[Orthostatic hypotension due to autonomic dysfunction: midodrine \(ESNM61\)](#)

Midodrine (Bramox) is the first medicine to receive a UK marketing authorisation for orthostatic hypotension. NICE summarises the results of two randomised controlled trials (RCTs) (n=171 and n=97) which found that midodrine significantly increased standing blood pressure 1 hour post dose compared with placebo in people with symptomatic orthostatic hypotension due to autonomic dysfunction. There was also limited evidence that midodrine improved some symptoms of orthostatic hypotension, such as syncope (fainting) and low energy levels.

However, results for other symptoms such as light-headedness and dizziness were less positive, and the studies did not assess quality of life, falls or ability to carry out daily activities

[Midodrine is currently classified as RED based on the historical rationale that it requires specialist assessment to enable patient selection, initiation and ongoing treatment and at the time of classification was an unlicensed drug. JAPC intends to re-visit this decision based on the NICE review considering also that the licensed preparation is 60% less expensive than the current imported 'specials'.](#)

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:</p> <p>National Library for Health: search via My Journals</p> <p>MyAthens: Via National Library for Health Resources or Local Resources.</p> <p>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:</p> <p>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>	https://register.athensams.net/nhs/nhseng/
<p>UKMI</p> <p>Nathnac</p> <p>NHS evidence</p> <p>Electronic medicines compendium</p> <p>Clinical Knowledge Summaries</p> <p>Medicines Prescribing Centre (Formerly NPC)</p> <p>Medicines for children (patient information leaflets)</p> <p>Drugs in lactation</p>	<p>http://www.ukmi.nhs.uk/</p> <p>https://www.evidence.nhs.uk/search?om=%5B%7B%22srn%22%3A%5B%22%20ukmi%20%22%5D%7D%5D</p> <p>http://www.nathnac.org/</p> <p>http://www.evidence.nhs.uk/</p> <p>http://www.medicines.org.uk/emc/</p> <p>www.cks.nhs.uk.</p> <p>http://www.nice.org.uk/mpc/</p> <p>http://www.medicinesforchildren.org.uk/</p> <p>http://www.midlandsmedicines.nhs.uk/content.asp?section=6&subsection=17&pageldx=1</p>
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