Derbyshire Medicines Management Newsletter

www.derbyshiremedicinesmanagement.nhs.uk

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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.

1. Medicines Digest and what's in the news

DTB | Vol 52 | No 5 | May 2014 - *Key primary care headlines of DTB relevant to primary care*

For full access to the DTB articles login via Open Athens those without accounts: https://openathens.nice.org.uk/

Tight versus conventional blood-glucose control in type 1 diabetes: (http://dtb.bmj.com/content/52/5/50.full#sec-4)

A Cochrane review, mainly from studies in younger patients at early stages of the disease, has concluded that tight blood sugar control reduces the risk of developing microvascular diabetes complications. The benefit is weak in young patients already with complications and the evidence in the elderly is lacking.

DTB 2014;**52**:50-53 doi:10.1136/dtb.2014.5.0251

Changes to Controlled Drug Legislation (MIMS online; accessed June 2014)

The Home Office has updated the legal classification of tramadol, lisdexamfetamine, zopiclone and zaleplon. Summary of changes:

	Lisdexamfetamine	Tramadol	Zopiclone	Zaleplon
Designation (from 10th June 2014)	Schedule 2 (CD POM)	Schedule 3 (CD No Reg POM)	Schedule 4 (Part I)	Schedule 4 (Part I)
CD prescription requirements	Yes	Yes	No	No
Prescription valid for	28 days	28 days	28 days	28 days
Prescription is repeatable	No	No	Yes	Yes
Safe custody regulations apply	Yes	No	No	No

NICE guidance for managing medicines in care homes (NICE; accessed June 2014)

NICE has published a good practice guide to "Managing medicines in care homes" with advice on systems and processes for managing medicines in care homes.

Comment: This guideline considers prescribing, handling and administering medicines to residents living in care homes and the provision of care or services relating to medicines in care homes.

Change in schedule from three to two doses in the HPV vaccination programme (link)

NHS England has written out to healthcare professionals informing them of the change to the HPV vaccination programme due to take place in September. In March 2014, the Joint Committee on Vaccination and Immunisation (JCVI) revised its existing recommendation to change from a three to a two dose schedule.

- The first dose can be given at any time during school year 8
- The minimum time between the first and second dose should be six months where the priming dose is received at less than 15 years of age
- The maximum time between the first and second dose is 24 months
- For operational purposes PHE recommends around a 12-month gap between the two doses which would reduce the number of HPV vaccination sessions. However, local needs should be considered when planning the programme
- Girls who have not had their first dose of HPV vaccine by the time they are 15 years old should be offered the three

dose schedule. This is because the antibody response in older girls is not quite as good

- Both Gardasil and Cervarix have been approved for use in a two dose schedule-The patient information leaflet (PIL) included in the packaging may still refer to a three dose schedule, or give different recommended timings between doses. The PIL will be updated by the vaccine manufacturer as soon as possible. Only Gardasil is part of the national programme in England.
- An updated Q&A for health professionals will be available in mid-June to reflect the programme changes
- A revised information leaflet is being developed to reflect the changes which can be used as part of the consent process

Recent research shows that antibody response to the 2 dose schedule in adolescent girls is equivalent to the response that correlated with protection against persistent infection and precancerous lesions in the initial vaccine trials

The HPV Patient Group Direction (PGD) is currently being updated by the Area Team, and will be available on the medicines management website soon.

St John's wort reduces effectiveness of contraceptive implants (http://dtb.bmj.com/content/52/5/50.full#sec-2)

St Johns wort and herbal products that contain it should not be taken by women using hormonal contraception (including implants) to prevent pregnancy.

2. Drug Safety Update relating to primary care prescribing

(For more information see Drug Safety Update : MHRA) Volume 7, Issue 10, May 2014

Domperidone: risks of serious side effects- indication restricted to nausea and vomiting, new contra-indications, and reduced dose and duration of use

Domperidone is associated with a small increased risk of serious cardiac side effects. Its use is now restricted to the relief of nausea and vomiting and the dosage and duration of use have been reduced. It should no longer be used for the treatment of bloating and heartburn. Domperidone is now contraindicated in those with underlying cardiac conditions and other risk factors (see below). Patients with these conditions and patients receiving long-term treatment with domperidone should be reassessed at a routine appointment, in light of the new advice.

Advice for healthcare professionals:

Indication

- Domperidone is now restricted to use in the relief of nausea and vomiting
- It should be used at the lowest effective dose for the shortest possible time

Contraindications

- Domperidone is now contraindicated in people:
  - With conditions where cardiac conduction is, or could be, impaired
  - With underlying cardiac diseases such as congestive heart failure
  - Receiving other medications know to prolong QT interval or potent CYP3A4 inhibitors
  - With severe hepatic impairment
- Patients with these conditions should have their treatment reviewed at their next routine appointment and be offered alternative treatment if required

Posology

Oral formulations

- For adults and adolescents over 12 years of age and weighing 35 kg or more, the recommended maximum dose in 24 hours is 30 milligrams (dose interval: 10 milligrams up to three times a day)
- In children under 12 years of age and weighing less than 35 kg, the recommended maximum dose in 24 hours is 0.75mg/kg body weight (dose interval: 0.25 mg/kg body weight up to three times a day)

Suppository formulation

- Suppositories should only be used in adults and adolescents weighing 35 kg or more, the recommended maximum daily dose in 24 hours is 60 milligrams (dose interval: 30 milligrams twice a day)

Duration of treatment

- The maximum treatment duration should not usually exceed one week
- Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change, or cessation

Administration of liquid formulations

- Oral liquid formulations of domperidone should only be given via appropriately designed, graduated measuring devices (eg. oral syringes for children and cups for adults and adolescents) to ensure dose accuracy

Comment: There is a position statement that has been agreed across Derbyshire to support the use of domepridone for long term use in gastroparesis. See MHRA Drug Safety Update

Adrenaline auto-injector advice for patients: after every use, an ambulance should be called even if symptoms are improving, the individual should lie down with legs raised and, if at all possible, should not be left alone

People who have been prescribed an adrenaline auto-injector because of the risk of anaphylaxis should carry two with them at all times for emergency, on-the-spot-use. After every use of an adrenaline auto-injector, an ambulance should be called (even if symptoms are improving), the individual should lie down with their legs raised and, if all possible, should not be left alone.

Advice for healthcare professionals:

- Ensure that people with allergies and their carers have been trained to use the particular auto-injector that they have been prescribed. Injection technique varies between injectors.
- Encourage people with allergies and their carers to obtain and practise using a trainer device (available for free from the manufacturers' websites).

Advice to give to people with allergies and their carers:

- Carry two adrenaline auto-injectors at all times. This is particularly important for people who also have allergic asthma as they are at increased risk of a severe anaphylactic reaction.
- Use the adrenaline auto-injector at the first signs of a severe allergic reaction.
- Take the following actions immediately after every use of an adrenaline auto-injector:
  1. Call 999, ask for an ambulance and state "anaphylaxis", even if symptoms are improving.
  2. Lie flat with the legs raised in order to maintain blood flow. If you have breathing difficulties sit up to make breathing easier.
  3. Seek help immediately after using the auto-injector and if all possible stay with the person while waiting for the ambulance.
  4. If the person does not start to feel better, the second auto-injector should be used 5 to 15 minutes after the first.
- Check the expiry date of the adrenaline auto-injectors and obtain replacements before they expire. Expired injectors will be less effective.

Statins benefits and risks

Statins (HMG-CoA reductase inhibitors) are widely used medicines for patients with lipid disorders and in the primary and secondary prevention of heart attack and stroke.

Muscle-related side effects of statins

All effective medicines can cause side effects in some patients and a small proportion of patients taking statins will inevitably experience side effects. Although they may be distressing to the individual concerned and limit that individual's willingness or ability to tolerate statin use, statin-related side effects are generally mild and not medically serious.

Muscle-related problems are the most frequently reported side effect of statins. The following statin side effect incidences have been estimated based on randomised trial data, cohort studies, published case reports and spontaneous reports:

- Mild muscle pain:190 cases per 100,000 patient years
- Myopathy: 5 cases per 100,000 patient years
- Rhabdomyolysis: 1.6 cases per 100,000 patient years

Things to consider when prescribing statins

Advise patients to seek prompt medical attention if they experience muscle problems while taking statins. Myopathy may not be clinically serious to start with, but can rarely progress to potentially fatal rhabdomyolysis. Review statin treatment if muscle problems occur. For some patients, stopping statin treatment may be appropriate. If statin treatment must be continued despite muscle problems, consider using a lower statin dose or switching to a different statin. Take into account the severity of the myopathy, the degree of hypercholesterolaemia, and the patient's medical history.

Patients and prescribers should also be aware that other side effects have also been reported in association with statins. These are listed in the summary of product characteristics and patient information leaflet of each statin.

The benefits of using any statin in its licensed indication outweigh the risks in most patients. As with all medicines, the MHRA constantly reviews the safety of statins and will inform prescribers and patients when new important information becomes available. In deciding whether to offer statin therapy, carefully consider both the potential benefits and harms for each patient

Zolpidem: reminder of the risk of impaired driving ability the next day

Zolpidem (Edluar, Stilnoct) is used to treat insomnia. Taking zolpidem is associated with a risk of impaired driving ability the next day. To reduce this risk, advise patients:

- To take 10 milligrams of zolpidem at bedtime and not to take it again the same night
- Not to drive, operate machinery, or work at heights until at least 8 hours after taking zolpidem
- Not to take zolpidem with alcohol, illicit drugs, or other central nervous system suppressants
- Not to drive, operate machinery or work at heights if they are still drowsy after taking zolpidem

People with liver impairment and the elderly should take no more than 5 milligrams of zolpidem a night.

Mims deletions: May 2014 Cutisorb LA, Kelanu XL (alfuzosin), Otosporin (polymyxin B/neomycin/hydrocortisone) Preotact (parathyroid hormone) and Sinepin (doxepin)

3. Local News and GP queries

GP query

I understand a Glucophage (metformin) oral powder sachet is being discontinued – what are the alternatives?

Answer

Merck Serono Limited has confirmed that they are discontinuing Glucophage (metformin) 500 mg and 1000 mg powder for oral solution in sachets due to unforeseen manufacturing issues.

If metformin tablets still cannot be swallowed whole, these are your options-

1. Prescribe as metformin 500mg/5ml oral solution sugar free. This is a licensed alternative and costs £69.90 for 150ml.
2. Alternatively you may wish to consider that metformin immediate-release tablets can be crushed and mixed with water to form a fine suspension that can be given orally or via a feeding tube, if this provides the most appropriate option for a particular patient. This is off-label use of a licensed medicine (this advice should be noted as patient information leaflets may state that the tablets should be swallowed whole and not chewed).

4. QiPP

Using haemoglobin A1c to diagnose type 2 diabetes or to identify people at high risk of diabetes *BMJ 2014;348:g2867 doi: 10.1136/bmj.g2867 (Published 25 April 2014)* http://www.bmj.com/content/348/bmj.g2867

HbA1c has advantages over blood glucose monitoring (less time consuming, less costly, assesses glycaemic control over a longer period and is less inconvenient to patients through fasting).

In 2011 WHO recommended that an HbA1c threshold of 48 mmol/mol (6.5%) or above for the diagnosis of type 2 diabetes but does not advice below this level. A UK expert advisory body has recommended that high risk patients of developing diabetes (HbA1c of 42-47 mmol/mol or HbA1c of 6-6.5%l) should be given intensive lifestyle advice and retested annually.

There are groups of patients where HbA1c is not recommended for diagnosis (e.g. all children and young people) and where caution is advised (e.g. patient is anaemic)

5. NICE Evidence summaries: New medicines and unlicensed/off-label medicines relating to primary care prescribing (NICE evidence summaries can be found here).

New medicines

ESNM 40 Premature ejaculation: dapoxetine

Summary – dapoxetine is a short-acting selective serotonin-reuptake inhibitor (SSRI). It is the first pharmacological treatment for premature ejaculation to be licensed in the UK. In a pooled analysis of 4 randomised controlled trials (RCTs) in men with premature ejaculation there was a statistically significant increase in intravaginal ejaculatory latency time (IELT) with dapoxetine 'on demand' compared with placebo 'on demand', although an increase in IELT was also seen with placebo JAPC has already classified this drug as BLACK not recommended or commissioned recognising established alternative cost effective treatment options that can be used off-label. (See the Derbyshire Medicines Management website for Dapoxetine position statement)

Evidence summaries: unlicensed/off-label medicines

None this month

6. Useful resources

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&pageIdx=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