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. What's in the news

DTB July 2015,Volume 53 Number 7
Articles relevant to primary care
For full access to the DTB articles login via Open Athens. Those without accounts: https://openathens.nice.org.uk/

Revised recommendations on administering live vaccines

Public Health England has issued revised recommendations for the administration of more than one live vaccine since the introduction of the live attenuated nasal influenza vaccine and oral rotavirus vaccine. In February 2014 the JCVI agreed that the guidance to either administer the vaccines on the same day or at the 4 week interval period was not generalizable to all live vaccines. All currently used live vaccinescan be given at any time before or after each other except for the following combinations: Yellow Fever and MMR, Varicella (and zoster) vaccine and MMR and Tuberculin skin testing (Mantoux) and MMR.

Review of treatments for hirsutism

The DTB reports on a Cochrane review of interventions for hirsutism. The review states the overall quality of the evidence is rated as moderate to very low with reasons of un-blinded studies, or studies with a small sample size. The authors concluded 'For mild hirsutism there is evidence of limited quality that oral contraceptive pills are effective. Flutamide 250 mg twice daily and spironolactone 100 mg daily appeared to be effective and safe, albeit the evidence was low to very low quality.... Finasteride 5 mg daily showed inconsistent results in different comparisons, therefore no firm conclusions can be made….There was low quality evidence that metformin was ineffective for hirsutism and although GnRH analogues showed inconsistent results in reducing hirsutism they do have significant side effects."

Primary care clinicians are likely to promote cosmetic measures for mild hirsutism such as shaving, waxing, bleaching, electrolysis and laser which are not usually available on the NHS, before considering combined oral contraceptives such as co-cyprindiol. The recommendations for flutamide and finasteride are likely to come from specialist centres when referral is considered appropriate.

Umeclidinium: another LAMA for COPD

Umeclidinium is a once-daily inhaled long-acting antimuscarinic (LAMA) licensed for maintenance treatment of adult patients with COPD. The DTB like JAPC consider that there is currently insufficient evidence to recommend it over the other long-acting antimuscarinics, Prescribers in Derbyshire are reminded to follow JAPC's COPD guideline that recommends tiotropium as 1st line LAMA with second line choices based primarily on patient factors and cost.

Amitriptyline for neuropathic pain in adults Cochrane Database Syst Rev. 2015 Jul 6;7:CD008242

An updated Cochrane review included 2 further studies from the one undertaken in 2015. The review looked at the efficacy of amitriptyline for the relief of chronic neuropathic pain, and the adverse events associated with its use in clinical trials. Overall the study quality was modest and most studies were at high risk of bias due to small size. The authors concluded that 'amitriptyline has been a first-line treatment for neuropathic pain for many years. The fact that there is no supportive unbiased evidence for a beneficial effect is disappointing, but has to be balanced against decades of successful treatment in many people with neuropathic pain. There is no good evidence of a lack of effect; rather our concern should be of overestimation of treatment effect. Amitriptyline should continue to be used as part of the treatment of neuropathic pain, but only a minority of people will achieve satisfactory pain relief. Limited information suggests that failure with one antidepressant does not mean failure with all.' Prescribers should continue to the Derbyshire neuropathic pain guideline which is based on NICE CG 173 and has local pain consultant endorsement. Amitriptyline remains our first line effective treatment choice for treating neuropathic pain and especially when sedation is preferred. It is important to set realistic expectations and treatment goals. Achieving pain free status is not always achievable. Reduction in pain by 50% is a commonly used endpoint in clinical trials

Deleted products 2015 | MIMS online for July 2015

Allevyn Thin	Dozic (haloperidol)	Panadol OA (paracetamol)
Infasoy	PKU 2 Prima	Telfa Max
Ventmax SR (salbutamol)		

2. Drug safety update relating to primary care prescribing

(For more information see Drug Safety Update) Volume 8, Issue 12, July 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. Patient reminder cards about the risk of osteonecrosis of the jaw are being introduced; denosumab 120 mg is now contraindicated in patients with unhealed lesions from dental or oral surgery. The use of denosumab 60mg is covered by a locally agreed shared care agreement but not for the 120mg which has been classified locally as RED.
2. Latanoprost (Xalatan): increased reporting of eye irritation since reformulation
   Xalatan is an eye-drop formulation of latanoprost. It is licensed for the reduction of intraocular pressure in adults and children with ocular hypertension and open angle glaucoma. In 2013, the Xalatan pH was reduced from 6.7 to 6.0 to allow for long-term storage at room temperature. Following this reformulation there has been an increase in the number of reports of eye irritation from across the EU. This advice does not extend to generic prescribing of latanoprost.
3. A new smartphone app for reporting side effects to the Yellow Card Scheme has now launched.

3. Local news and GP/pharmacist queries

GP query

Creon shortage- There is a Creon 40,000 capsule manufacturing problem until 2016 and I have patients that require long term treatment please could you advise on how I can manage these patients?

Answer

The manufacturer has recommended using the nearest equivalent of the 25,000 capsules to lower the capsule "burden" for patients (rather than using the 10,000 capsules).
For example, they advise:
Current Creon 40,000 dose: 1 x 40,000 (40,000 lipase units)
Proposed 25,000 dose: 2 x 25,000 (50,000 lipase units)

Current Creon 40,000 dose: 2 x 40,000 (80,000 lipase units)
Proposed 25,000 dose: 3 x 25,000 (75,000 lipase units)

For further information see Abbott letter: http://www.leedsformulary.nhs.uk/docs/1.9.4creonavailability.pdf

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

Medicines optimisation:
The Derbyshire medicines management guideline group has updated Chapter 7 of the formulary chapter which includes the most cost effective prescribing options.
For example the combined hormonal contraceptives preferred are:

Category	Preferred option
Ethinyloestradiol 20mcg	Loestrin 20
Ethinyloestradiol 30 micrograms	Levest
Ethinyloestradiol 35micrograms	Ovysmen

And for emergency contraception as levonorgestrel 1.5mg prescribe as Upostelle. N.B. we recommend practices liaise with their local pharmacies to ensure stock availability of Upostelle which will be required by patients as soon as possible.

The complete routine immunisation schedule
Public Health England has updated a user friendly summary schedule includes the new meningococcal B and ACWY vaccines, available from summer 2015

Desmopressin- reminder of prescribing advice

- Nasal formulations of desmopressin should not be used for treatment of primary nocturnal enuresis (PNE)
- All patients with PNE should start oral desmopressin at the lowest recommended dose, which should be increased only if necessary to achieve control of symptoms
- Healthcare professionals and patients should follow closely the advice on fluid intake in the Summary of Product Characteristics and the Patient Information Leaflet to avoid hyponatraemia

Hyponatraemic convulsions after the use of vasopressin spray have been reported to the Committee on Safety of Medicines.

They recommend that the risk of this rare side effect is minimised by:
avoid concomitant use of drugs that may increase endogenous vasopressin e.g. tricyclics

- follow the recommended starting doses for vasopressin
- warn against excessive fluid intake:

Fluid intake should be "limited" from 1 hour before until 8 hours after administration... in addition, the child should avoid ingesting water while swimming.

- if vomiting or diarrhoea occurs then temporarily stop vasopressin

The risk of hyponatraemic convulsions can also be minimised by keeping to the recommended starting doses and by avoiding concomitant use of drugs which increase vasopressin secretion, e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, carbamazepine and chlorpromazine.

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

Type 2 diabetes: dulaglutide

Summary-For reducing HbA1c levels in people with type 2 diabetes, dulaglutide once weekly, when added to metformin, was statistically superior to exenatide twice daily (both in combination with pioglitazone), statistically superior to sitagliptin and statistically non-inferior to liraglutide 1.8 mg daily. As with the other glucagon-like peptide-1 (GLP-1) receptor agonists there are limited data from randomised controlled trials (RCTs) on the effect of dulaglutide on patient-oriented outcomes, such as rates of macrovascular or microvascular events, or on long-term safety

Derbyshire guidance already includes the three other licensed GLP-1 receptor agonists exenatide, liraglutide and lixisenatide and also includes the weekly exenatide pre-filled pen (if tolerability and compliance remains a major issue). Dulaglutide is available as a 4-pre-filled pen pack (4 weeks supply) in two strengths at a cost of £90.95 per pack. The annual cost of dulaglutide 0.75 mg or 1.5 mg once weekly is £1182.35 whereas the annual costs for other GLP-1 receptor agonists range from £705.75 to £941.76. Exenatide once weekly GLP-1 analogue is £818.88 per person per year.
(Prices are excluding VAT; prices taken from MIMS, May 2015).

Type 2 diabetes: insulin degludec/liraglutide (Xultophy) (ESNM60)

Summary- in people who are insulin-naïve, insulin degludec/liraglutide (Xultophy) the first fixed-ratio combination basal insulin and glucagon-like peptide-1 [GLP-1] receptor agonist preparation to be licensed in the UK, was non-inferior to insulin degludec alone and superior to liraglutide alone for reductions in HbA1c (with a difference of 0.64% compared with liraglutide). In people previously treated with basal insulin, insulin degludec/liraglutide was superior to insulin degludec alone for reducing HbA1c with a difference of 1.1%. The safety profile and long-term safety concerns of insulin degludec/liraglutide are broadly in line with those of the 2 included components.

Prescribers are reminded to follow our local diabetes guidance where the combination of GLP1s and basal insulin is currently not recommended and aligned to current NICE recommendations. Local guidance will be reviewed following NICE's update which is expected soon. It is further worth remembering that Managing a person with type 2 diabetes is complex and involves individualising a multifactorial approach, addressing blood pressure, blood lipids and lifestyle issues, as well as blood glucose. With the controlling of blood glucose a careful balance between the intensity of the treatment regimen and avoiding hypoglycaemia is required.

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&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