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 March 2015, Volume 53, Number 3
Articles relevant to primary care
For full access to the DTB articles login via Open Athens. Those without accounts: https://openathens.nice.org.uk/

Shorter courses of corticosteroids for COPD exacerbations

NICE and BNF both recommend systemic corticosteroid treatment with prednisolone for 7-14 days for the management of COPD exacerbations. The DTB reports on a Cochrane review which suggests that the likelihood is low that shorter courses of systemic corticosteroids (of around five days) lead to worse outcomes than are seen with longer (10 to 14 days) courses. The eight studies with 582 participants included in this review were generally well designed, and the quality of the evidence rated as moderate because of imprecision in results; more research, especially involving people with less severe COPD, is needed.
Shorter courses may reduce adverse outocmes associated with corticosteroids on events such as osteoporosis, hyperglycaemia and muscle weakness. The five day course of prednsiolone 40mg per day is also recommended by GOLD (Global Initiative for Chronic Obstructive Lung Disease) but acknowledging that further data is needed to conclude on an optimal duration.

Increased risk of diabetes with statin treatment is associated with impaired insulin sensitivity and insulin secretion: a 6 year follow-up study of the METSIM cohort

Diabetologia DOI 10.1007/s00125-015-3528-5. Henna Cederberg et al
A study of 8,749 non-diabetic men were followed up for 5.9 years. Results showed that those taking a statin were associated with a 46% increase in the risk of type 2 diabetes. The effect was due to decreased insulin sensitivity and secretion. However, experts commenting on the findings have pointed out various flaws and weakness of this research. The study uses observational data and is not designed as a clinical trial so there is a risk of bias.
The study adds to what is already known about the risk of developing diabetes with statins. The cardiovascular benefit of statins still heavily outweighs any diabetogenic risk in patients with moderate and elevated cardiovascular risk. Prescribers should continue to follow our local lipid modification guideline

Deleted products 2015 | MIMS online for March 2015

Novasource GI Forte	Penbritin syrup	Resource Protein
Rienso (ferumoxytol)		

2. Drug safety update relating to primary care prescribing

(For more information see Drug Safety Update - GOV.UK) Volume 8, Issue 8, March 2015

The website that hosts the Drug Safety Update has now been moved. You can subscribe to alerts by using the following link https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/email-signup

Dimethyl fumarate (Tecfidera): fatal PML in an MS patient with severe, prolonged lymphopenia
Reminder to check full blood counts before prescribing dimethyl fumarate and then every 6 to 12 months. Stop treatment immediately if you suspect progressive multifocal leukoencephalopathy. N.B. classified as RED in Derbyshire

Corticosteroids e-learning module launched
New online learning modules about corticosteroids to help clinicians understand how to identify, manage and avoid the important side effects of these valuable and widely prescribed medicines.

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Report misleading medicines advertisements
If you are concerned about advertising you see for a medicine, please report it to the MHRA or industry self-regulatory body

NHS England Patient Safety Alert (Alert reference number: NHS/PSA/W/2015/002)
Risk of death from asphyxiation by accidental ingestion of fluid/food thickening powder
NHS England has received details of an incident where a care home resident died following the accidental ingestion of the thickening powder that had been left within their reach. Appropriate storage and administration of thickening powder needs to be embedded within the wider context of protocols, bedside documentation, training programmes and access to expert advice required to safely manage all aspects of the care of individuals with dysphagia

3. Local news and GP/pharmacist queries

GP/pharmacist query
I recently read a BMJ article titled "Tumour necrosis factor inhibitors versus combination intensive therapy with conventional disease modifying anti-rheumatic drugs in established rheumatoid arthritis: TACIT non-inferiority randomised controlled trial" written by David L Scott et al (BMJ 2015;350:h1046 doi: 10.1136/bmj.h1046)
In discussions the authors said it could be interpreted for patients with rheumatoid arthritis, a strategy of treatment with synthetic disease modifying drugs achieved non-inferior outcomes to the NICE approved strategy of treatment with tumour necrosis factor inhibitor over 12 months and at a lower cost.

Answer (from a local consultant rheumatologist)
Our current approach to new patients with rheumatoid arthritis acknowledges the efficacy of combination conventional DMARDS. Those with active disease are given methotrexate and hydroxychloroquine with intramuscular steroid at treatment initiation and sulfasalazine added at 16 weeks if they still have active disease. Where patients don't tolerate methotrexate up to 20mg orally they are switched to the subcutaneous formulation. This means that patients will have had at least quadruple therapy by 24 weeks before being offered biological treatment. GPs should continue to follow the shared care agreements which are in place across Derbyshire, noting that combination treatments of immunomodulating drugs may be intentional in certain cohorts of patients

Audit of memantine by the DHcFT
The DHcFT has undertaken an audit of patients taking memantine using standards measured against the Derbyshire wide shared care guideline. Following the results of the audit they made the following recommendations some of which apply to primary care clinicians.

- When initiating memantine the clinician should clearly document the indication and rationale (cognitive assessment by using for example MMSE)
- Memantine to be used as monotherapy in line with NICE evidence (co-prescribing of cholinesterase inhibitors is not recommended)
- Review by memory services and the requirement for specialist annual review

Current shared care requires under consultant responsibilities to perform an annual memory service monitoring/comprehensive global assessment. The audit infers that since NICE's publication the value of such a service is questionable. JAPC is aware of these issues. A review of the service model between commissioners and providers has been prompted but until that assessment current shared care agreements for memantine and AChEI should be followed

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

COPD: withdrawal of inhaled corticosteroids and effect on exacerbations
A recent NICE Medicines Evidence Commentary reports on a study that evaluated a stepwise withdrawal of inhaled corticosteroids (ICS) in people with COPD receiving triple therapy (tiotropium, salmeterol and fluticasone propionate). The role of triple therapy in local guidance is by exception and restricted. The study reviewed by NICE was first published in N Engl J Med (2014; 371:1285-1294October 2, 2014DOI: 10.1056/NEJMoa1407154). NICE Summarised the findings that ICS withdrawal was non-inferior to continuing ICS for the time to first moderate or severe exacerbation over 12 months. Despite some limitations, this study gives reassurance to clinicians considering withdrawing ICS treatment in people with COPD. The potential benefit of ICS in people with COPD needs to be balanced against the risk of side-effects (non-fatal pneumonia, systemic side effects including adrenal suppression, reduced bone mineral density, glaucoma and cataracts). Prescribers should note though that there may be subgroups of patients who respond better to ICS and exercise caution in withdrawal, particularly with those in whom the possibility of asthma remains).

Reminder- Feverish illness in children
In May 2013 NICE published CG 160 "Feverish illness in children: assessment and initial management in children younger than 5 years".
This guidance includes a traffic light system of signs and symptoms of serious illness, categorised as: 'green' for low risk of serious illness; 'amber' for intermediate risk of serious illness; and 'red' for high risk of serious illness. The traffic light system should be used in conjunction with the recommendations on investigations and initial management in children with fever.

	Green – low risk	Amber – intermediate risk	Red – high risk
Colour (of skin, lips or tongue)	• Normal colour	• Pallor reported by parent/carer	• Pale/mottled/ashen/blue
Activity	• Responds normally to social cues • Content/smiles • Stays awake or awakens quickly • Strong normal cry/not crying	• Not responding normally to social cues • No smile • Wakes only with prolonged stimulation • Decreased activity	• No response to social cues • Appears ill to a healthcare professional • Does not wake or if roused does not stay awake • Weak, high-pitched or continuous cry
Respiratory		• Nasal flaring • Tachypnoea: respiratory rate: - >50 breaths/minute, age 6-12 months; - >40 breaths/minute, age >12 months • Oxygen saturation ≤95% in air • Crackles in the chest	• Grunting • Tachypnoea: respiratory rate: - >60 breaths/minute • Moderate or severe chest indrawing
Circulation and hydration	• Normal skin and eyes • Moist mucous membranes	• Tachycardia: - >160 beats/minute, age <12 months - >150 beats/minute, age 12-24 months - >140 beats/minute, age 2-5 years • Capillary refill time ≥3 seconds • Dry mucous membranes • Poor feeding in infants • Reduced urine output	• Reduced skin turgor
Other	• None of the amber or red symptoms or signs	• Age 3-6 months, temperature ≥39°C • Fever for ≥5 days • Rigors • Swelling of a limb or joint • Non-weight bearing limb/not using an extremity	• Age <3 months, temperature ≥38°C • Non-blanching rash • Bulging fontanelle • Neck stiffness • Status epilepticus • Focal neurological signs • Focal seizures

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

Glaucoma: brinzolamide/brimonidine combination eye drops ESMN 54

Summary of 2 RCTs:

- Brinzolamide/brimonidine combination eye drops were statistically significantly superior to either constituent drug administered alone as monotherapy in reducing intraocular pressure at 3 months.
- The combination eye drops were non- inferior to brinzolamide plus brimonidine administered concomitantly.

Most reported adverse events were mild to moderate and localised, but these were higher in number with the combination eye drops compared with the individual constituent drugs.

There are no published studies comparing brinzolamide/brimonidine combination eye drops with other drug treatments for managing glaucoma and ocular hypertension. Brinzolamide/brimonidine may be an alternative treatment option for some people, for whom prostaglandin analogues and beta-blockers are unsuitable

Clinicians should continue to follow our local glaucoma guideline.

Asthma: tiotropium (Spiriva Respimat) ESMN 55

Summary of 2 RCTs:

Two RCTs evaluated tiotropium (Spiriva Respimat) in adults with poorly controlled asthma and persistent airflow obstruction who were already treated with an inhaled corticosteroid (ICS) and a long-acting beta-2 agonist (LABA).

- Tiotropium improved peak and trough forced expired volume in 1 second (FEV1) and lengthened the time to first severe exacerbation compared with placebo.
- Differences between add-on therapy with tiotropium and placebo in patient-assessed asthma control and quality of life were small and did not meet the threshold for the minimal clinically important difference.
- There are no RCTs comparing tiotropium with other active treatments or in people with asthma without persistent airflow obstruction

Tiotropium has been classified as BROWN after consultant or specialist initiation for asthma in patients assessed at step 4 of the BTS guidance and with a demonstrated airflow obstruction.

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