

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 main publications in the previous month.

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## 1. What's in the news

### [DTB May 2016 Volume 54 issue 6](#)

#### **EMA reviews the risk of pneumonia with inhaled corticosteroids for COPD**

EMA has completed a review of the known risk of pneumonia in patients who take inhaled corticosteroid (ICS) medicines to treat chronic obstructive pulmonary disease (COPD). The review confirmed the risk of pneumonia with ICS products, which has been known for many years, and that it is common (can affect between 1 and 10 COPD patients in 100 using these medicines). The review did not find any conclusive evidence of differences in this risk for different products.

Overall the benefits of inhaled corticosteroid medicines in treating COPD continue to outweigh their risks and they should be prescribed in line with local guidelines.

Patients need to alert their doctors if they start to get symptoms that suggest they are developing pneumonia, so that it can be identified and treated early. Healthcare professionals should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations.

Our local COPD guidance including formulary choice of inhalers can be found on our Derbyshire medicines management [website](#).

#### **The Centers for Disease Control and Prevention**

The CDC Guideline for Prescribing Opioids for Chronic Pain was published in March 2016 following concern over the widespread use of long-acting and extended-release opioids and an increase in deaths from unintentional drug overdoses in the United States. It provides recommendations about the appropriate prescribing of opioid pain relievers and other treatment options to improve pain management and patient safety.

The [CDC has published](#) a checklist decision aid and a series of fact sheets, which are available online. The CDC advises that opioids should not be considered for first-line or routine therapy for chronic pain. Prescribers of Derbyshire are reminded of [local guidance](#) which similarly gives this advice.

#### **Cardiovascular effects of antidepressants**

A UK based cohort study using QResearch primary care database found no evidence that selective serotonin reuptake inhibitors are associated with an increased risk of arrhythmia or stroke/transient ischaemic attack in people diagnosed as having depression between the ages of 20 to 64 or that citalopram (limited data in patients at high dose  $\geq 40\text{mg/day}$ ) is associated with a significantly increased risk of arrhythmia. It found some indication of a reduced risk of myocardial infarction with selective serotonin reuptake inhibitors, particularly fluoxetine, and of an increased risk with lofepramine. Prescribers are reminded of the MHRA advice on QT interval prolongation with citalopram and escitalopram and [local recommendations](#) in prescribing.

#### **PPIs and dementia**

A large prospective cohort study reports of an increased risk of dementia in older patients taking long term PPIs. A study of this design does not prove causality but these findings add to the list of adverse effects and concerns that are associated with use of PPIs (e.g. fractures, Clostridium difficile infection, pneumonia, chronic kidney disease).

#### **Sacubitril valsartan for heart failure** DTB 2016;54:66-69 doi:10.1136/dtb.2016.6.0405

Sacubitril valsartan is a new drug licensed for the treatment of symptomatic chronic heart failure in adults with reduced ejection fraction. Evidence with encouraging data of preventing deaths from the PARADIGM-HF study, a large multicentre study covering 47 countries. In April 2016 NICE issued a positive [technology appraisal](#) and JAPC classified this drug as RED for hospital use only. The results of this trial are encouraging and show sacubitril valsartan may offer an advantage over treatment with an ACE inhibitor for some patients with heart failure with reduced ejection fraction. However like DTB JAPC believe that there needs to be a managed approach to its introduction in to clinical practice, given some of the limitations of the study. Consultants at both Chesterfield and Derby hospitals have been tasked to agree a patient pathway that may include primary care prescribing. Until the review and then agreement at JAPC GPs should not prescribe this drug.

Binovum (ethinylestradiol/norethisterone)	Diovan Tablets (valsartan)	Diovan Capsules (valsartan)
Sorbion Silver Flex	Versiva XC	

**2. Drug safety update** primarily relating to primary care prescribing  
(For more information see [Drug Safety Update](#) ) Volume 9, Issue 11 June 2016

1. Canagliflozin (Invokana▼, Vokanamet▼): signal of increased risk of lower extremity amputations observed in trial in high cardiovascular risk patients See MHRA advice for healthcare professionals, which may include stopping treatment if a patient develops a significant lower limb complication (eg, skin ulcer, osteomyelitis, or gangrene)
2. Nexplanon (etonogestrel) contraceptive implants: reports of device in vasculature and lung - rare reports of Nexplanon implants having reached the lung via the pulmonary artery. Advice includes immediately after insertion, to verify the presence of the implant by palpation
3. Topical miconazole, including oral gel: reminder of potential for serious interactions with warfarin. MHRA is considering whether further measures are required to minimise the risk of potentially serious interactions between miconazole and warfarin following a coroner's report of a death.

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**Local safety update**

**Miconazole Oral Gel & Warfarin interaction – local incidents**

We have recently had reported to us two local incidents relating to the prescribing and use of miconazole (Daktarin®) oral gel in patients on treatment with warfarin. Concomitant use of these drugs can lead to an enhanced anticoagulant effect of Warfarin and if/when used together, the patient and their INR levels should be monitored closely. Both SystmOne and EMIS e-prescribing systems highlight this drug interaction, as an alert, when a patient on Warfarin is prescribed miconazole oral gel. In the case of both of these incidents this drug interaction was not identified prior to prescribing, dispensing and supplying to the patient. NB nystatin does not interact with warfarin and may have been a suitable alternative.

**Details of the incidents**

Incident no.1 = During the course of combined use of miconazole oral gel and Warfarin, the patient experienced bleeding from ears and nose – admitted to hospital and INR level found to be 11.5.

Incident no.2 = Combined use led to a patient being hospitalised for 3 days, found to have INR of 24.1; given Vitamin K and Octaplex to reverse the anticoagulant effects of warfarin.

NRLS and MHRA Yellow card forms were completed to inform national patient/medications safety teams of these incidents.

These incidents further highlight the important messages as highlighted in the June edition of the MHRA Drug Safety update regarding the use of Topical miconazole in patients on treatment with warfarin.

**Improving safety of Opioid Prescribing in SystmOne**

The following information highlights to all prescribers using SystmOne the importance of setting themselves up for Safer Drug selection following a recent incident whereby Zomorph 100mg was inadvertently prescribed instead of the 10mg strength:

**Learning from a serious medication incident that has occurred locally**

*Following an investigation into a serious incident whereby Zomorph 100mg was inadvertently prescribed instead of the intended dose of 10mg, it was discovered that the prescribers SystmOne settings had contributed to the risk of this error occurring, by causing the 100mg strength of Zomorph to appear above all other, lower strengths of Zomorph.*

**Action required by all prescribers to reduce the risk of further incidents**

*The medicines management team advise that ALL prescribers using SystmOne have their prescribing settings set to display medicines in ascending strength order in the picking list. This will reduce the risk of high strengths being accidentally selected.*

***Instructions on how to do this are attached. This should be done for each individual prescriber and all new prescribers that join your practice in the future.***

See Appendix at the end of this newsletter of the instructions on how to carry this out within SystmOne:

The Medicines Management Team is available to assist you if you have any difficulties.

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

#### Query from GP practice:

If a patient is starting on rivaroxaban for AF, but is currently taking aspirin following a previous MI, what action should be taken?

#### Answer

General advice for any patient starting a Novel Oral Anticoagulant (NOAC) is that they should have baseline blood tests including; full blood count (FBC), renal function, liver function tests (LFTs) and a clotting screen before initiation. Renal function should be calculated using Cockcroft Gault equation and dose adjusted if necessary according to their creatinine clearance (CrCl). Compliance, adverse effects and symptoms related to thromboembolic events should be checked every three months and renal function and LFTs should be repeated at least annually and more frequently if the patient has reduced CrCl. Patient information [booklet](#) and [other resources](#) are available on the medicines management website. Rivaroxaban should always be taken with food as absorption is significantly reduced if taken on an empty stomach.

Our AF guideline states that for stable CV disease (i.e. at least 12 months since an acute event) aspirin should be discontinued if a patient is commenced on anticoagulation. For warfarin this should be when the patient's INR reaches therapeutic range. Rivaroxaban should reach full therapeutic effect within 2-4 hours so the patient should be advised to start rivaroxaban on the day following the last dose of aspirin at a similar time.

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

#### Continence appliances

Derbyshire prescribers are reminded of our [continence guidance](#) for cost effective choices in patients, written and agreed with provider and commissioner organisations following a long consultation process. The top [10 tips](#) include also guidance on the producing issuing of prescriptions which can reduce waste.

- Include full details of product required to ensure the correct size, type, quantity and gender (for catheters).
- The brand and manufacturer should be stated to ensure continuity of supply.
- DO NOT prescribe generically because of the differences between individual products.
- Avoid the term 'original pack' (OP). Pack sizes differ between products and patients may receive inappropriate amounts if the quantity is not stated.
- When new products are being tried, the smallest amount required should be prescribed to minimise wastage.

#### Average quantities to prescribe for ONE month are:

Product	Type	Monthly quantity
Catheters	Indwelling Foley	ONE (plus ONE spare)
	Single use PVC or self-lubricating Nelaton catheters for ISC	125-130 (5-6 packs of 25)
Sheaths	All	THIRTY (1 box)
Leg bags	Drainable	FIVE (preferable to supply one complete box (10) on a prescription so a box should last 2 months)
Night bags	Drainable	FIVE (preferable to supply one complete box (10) on a prescription so a box should last 2 months)
	Non-drainable	THIRTY (3 boxes of 10 )

#### Generic shortages (NCSO and 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.

#### June 2016

Drug	Pack size	Current months Drug tariff price	Price concession
Bumetanide 1mg tablets	28	£1.37	£2.50
Celiprolol 400mg tablets	28	£36.37	£39.69
Cimetidine 400mg tablets	60	£15.18	£20.24
Desmopressin 10micrograms/dose nasal spray	60 dose	£21.66	£24.00
Flecainide 50mg tablets	60	£3.39	£10.80
Flecainide 100mg tablets	60	£4.24	£10.80
Isosorbide mononitrate 10mg tablets	56	£1.50	£3.31
Isosorbide mononitrate 20mg tablets	56	£1.19	£4.85

Lamotrigine 5mg dispersible tablets sugar free	28	£5.58	£7.45
Lamotrigine 100mg dispersible tablets sugar free	56	£4.28	£3.60
Losartan 12.5mg tablets	28	£26.66	£8.09
Mefenamic acid 500mg tablets	28	£7.22	£9.25
Nitrofurantoin 100mg tablets	28	£2.46	£13.99
Nitrofurantoin 50mg tablets	28	£7.50	£13.20
Procyclidine 5mg tablets	28	£12.65	£12.20
Ropinirole 1mg tablets (new)	84	£1.80	£56.71
Trazodone 100mg capsules (new)	56	£42.54	£36.50
Trazodone 150mg tablets (new)	28	£33.88	£28.50
Trazodone 50mg capsules (new)	84	£30.16	£30.50

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

1. [Visual impairment due to myopic choroidal neovascularisation: aflibercept](#) – related to secondary care setting
2. [Complicated urinary tract infections: ceftolozane/tazobactam](#) - related to secondary care setting (IV formulation)
3. [Moderate to severe acute post-operative pain: fentanyl transdermal system](#) - related to secondary care setting
4. [Complicated intra-abdominal infections: ceftolozane/tazobactam](#) - related to secondary care setting (IV formulation)

#### 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: 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 <a href="http://www.thelancet.com/content/register">http://www.thelancet.com/content/register</a> . Print copies of The Lancet are available at DCGH library.	<a href="http://www.library.nhs.uk">www.library.nhs.uk</a>  or <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: NB: It is recommended that you register on a Trust (NHS) PC for speedy confirmation of your username and 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  Nathnac NHS evidence Electronic medicines compendium Clinical Knowledge Summaries Medicines Prescribing Centre (Formerly NPC) Medicines for children (patient information leaflets)  Drugs in lactation	<a href="http://www.ukmi.nhs.uk/">http://www.ukmi.nhs.uk/</a> <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> <a href="http://www.nathnac.org/">http://www.nathnac.org/</a> <a href="http://www.evidence.nhs.uk/">http://www.evidence.nhs.uk/</a> <a href="http://www.medicines.org.uk/emc/">http://www.medicines.org.uk/emc/</a> <a href="http://www.cks.nhs.uk">www.cks.nhs.uk</a> <a href="http://www.nice.org.uk/mpc/">http://www.nice.org.uk/mpc/</a> <a href="http://www.medicinesforchildren.org.uk/">http://www.medicinesforchildren.org.uk/</a>  <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>

# Appendix 1

## SystemOne Settings for Safer Drug Selection

Using the recommended settings ensures that lower strength medicines appear higher up the picking list than higher strengths. This reduces the risk of picking a higher strength than intended. See Zomorph example below:

**Without recommended settings**  
Zomorph 100mg appears above 10mg strength

Search results for ZOMORPH	
ⓧ Morphine 10mg modified-release capsules	£3.47CD
ⓧ morphine sulfate 12 hour modified release capsules 100mg	£0.00CD
ⓧ morphine sulfate 12 hour modified release capsules 200mg	£51.30CD
ⓧ morphine sulfate 12 hour modified release capsules 30mg	£8.30CD
ⓧ morphine sulfate 12 hour modified release capsules 60mg	£16.20CD
ⓧ Zomorph 100mg modified-release capsules (ProStrakan Ltd)	£21.80CD
ⓧ Zomorph 10mg modified-release capsules (ProStrakan Ltd)	£3.47CD
ⓧ Zomorph 200mg modified-release capsules (ProStrakan Ltd)	£43.60CD
ⓧ Zomorph 30mg modified-release capsules (ProStrakan Ltd)	£8.30CD
ⓧ Zomorph 60mg modified-release capsules (ProStrakan Ltd)	£16.20CD

**With recommended settings**

Search results for ZOMORPH	
ⓧ Morphine 10mg modified-release capsules	£3.47CD
ⓧ morphine sulfate 12 hour modified release capsules 30mg	£8.30CD
ⓧ morphine sulfate 12 hour modified release capsules 60mg	£16.20CD
ⓧ morphine sulfate 12 hour modified release capsules 100mg	£0.00CD
ⓧ morphine sulfate 12 hour modified release capsules 200mg	£51.30CD
ⓧ Zomorph 10mg modified-release capsules (ProStrakan Ltd)	£3.47CD
ⓧ Zomorph 30mg modified-release capsules (ProStrakan Ltd)	£8.30CD
ⓧ Zomorph 60mg modified-release capsules (ProStrakan Ltd)	£16.20CD
ⓧ Zomorph 100mg modified-release capsules (ProStrakan Ltd)	£21.80CD
ⓧ Zomorph 200mg modified-release capsules (ProStrakan Ltd)	£43.60CD

### Instructions:

Check prescribers settings for ‘tree sorting’ is set to FDB Picklist. Setting it to Alphabetical means that drugs do not appear in strength order.

This must be done for each individual prescriber .

1. Whilst in a patient record (or preferably a test patient) go to the prescribing screen.
2. When the “Select Drug or Appliance” box pops up select the Settings tab along the top.
3. Make sure that the “tree sorting” is set to “FDB Picklist, grouping by form”.
4. In addition, to make sure that formulary products are listed first, select the “Drug & Appliance Browser” tab and ensure that the formulary entries box is ticked and not the frequently used box.
5. Close the “Select Drug or Appliance” window and your settings will be remembered from now onwards.

