Midlands and Lancashire Commissioning Support Unit

# Tablets

## Medicines Management News

*Issue 27, June 2016*

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# Current Issues

### LOCAL NEWS

### Denosumab (Prolia®) and testosterone (Nebido®) injection prescribing in Primary Care

The Medicines Management Team has received several queries regarding the prescribing of denosumab and testosterone in Primary Care.

**Denosumab (Prolia®)** is used in the treatment of osteoporosis. It is positioned in the Wirral Osteoporosis Guidelines for primary and secondary prevention where the first-, second- (and third for secondary prevention) line treatments are unsuitable or not tolerated, and is used as per NICE TA 204.

Denosumab is listed as an 'AMBER' drug within the current Wirral RAG list, to be initiated on the recommendation of a Secondary Care clinician. The first dose should be administered in Secondary Care. After this, prescribing will occur in Primary Care.

**References**

1. http://mm.wirral.nhs.uk/document_uploads/guidelines/OsteoporosisGuidelines.pdf
2. http://mm.wirral.nhs.uk/document_uploads/shared-care/RAGlistApril2016v12.pdf

**Testosterone (Nebido®) injection**

We have received several enquiries from Practices, concerned that testosterone (Nebido®) ampoules have been discontinued.

Nebido® has been available in two presentations, 1000mg/4ml ampoules and 1000mg/4ml vials, for several years. The overwhelming majority of prescribing locally was for ampoules. In 2015, the manufacturer (Bayer) discontinued the ampoules in favour of the vials. Any patients prescribed the ampoules will need to be switched to the vials.

**References**

1. Nebido® BNF volume70: accessed on 23/5/2016 at https://www.medicinescomplete.com/mc/bnf/current/

# Topic of the Month

## MEN'S HEALTH WEEK

### Men's Health Week, 13th to 19th June 2016

We all know men are the first to complain when it comes to 'man flu,' but when it comes to more serious health problems, men are often too embarrassed to come forward and speak to a GP or other healthcare professional. Men's Health Week is organised by the Men's Health Forum (MHF). This is an independent charity, which aims to help men and boys by tackling inequalities and issues affecting their health.

Throughout Men's Health Week the charity will be holding a variety of events. The MHF want to promote healthy living and wellbeing in men. They will be asking men to focus on their lifestyles, and the campaign is all about healthy living and lifestyles.

To find out more, visit the official Men's Health Week website at: https://www.menshealthforum.org.uk/mhw

### Men's Health Issues

**Erectile dysfunction (ED)**

ED usually responds well to a combination of lifestyle changes and drug treatment. Patients should lose weight (important), stop smoking, reduce alcohol consumption and increase exercise. Before prescribing, assess whether a patient qualifies for an NHS prescription. If not, a private prescription can be issued.

Generic sildenafil (first-line) does not need to be endorsed with 'SLS' (Selected List Scheme). If prescribing vardenafil (Levitra®), which is second-line, tadalafil (Cialis®), which is third-line, or Viagra® on the NHS, endorse with 'SLS'.

Once-daily tadalafil is **not approved** for local use in Wirral. Please interface report any Secondary Care requests.

Wirral ED guidelines can be found at: http://mm.wirral.nhs.uk/guidelines/

**Benign prostatic hyperplasia (BPH)**

BPH is common in men over 50 years of age and is not usually a serious threat to health. If the prostate becomes enlarged, it can place pressure on the bladder and urethra. This can affect how urine is passed and may cause difficulty starting urination, a frequent need to urinate and/or difficulty fully emptying the bladder.
For the treatment of lower urinary tract symptoms (LUTS), drugs include tamsulosin MR 400mcg capsules, one daily, or alfuzosin MR 10mg tablets, one daily.

Wirral Overactive bladder guidelines can be found at: http://mm.wirral.nhs.uk/guidelines/

**Testosterone deficiency**

Replacement therapy with testosterone can be prescribed for male patients with hypogonadism, once testosterone deficiency has been confirmed by clinical symptoms and laboratory analysis. Treatment includes Sustanon 250® IM injection or testosterone 2% gel (Tostran®).

Wirral Urinary Drug Formulary can be found at: http://mm.wirral.nhs.uk/formulary/

**Alopecia in men**
An option for treatment of alopecia in men is finasteride 1 mg tablets (Propecia®). These are not available to prescribe on the NHS but can be prescribed on private prescription.

Minoxidil (Regaine®) solution is not available to prescribe on the NHS. However, it can be purchased over the counter, or can be obtained on private prescription.

Further information can be found at: http://cks.nice.org.uk/alopecia-androgenetic-male#!prescribinginfosub

# Query Corner

## TRANSGENDER HORMONE THERAPY

### General Practitioners on their role and responsibilities in prescribing hormone therapy for transgender and non-binary adults

In March 2016 the General Medical Council (GMC) published Guidance for Doctors Treating Transgender Patients. This guidance reiterates the advice previously set out by NHS England and also explains the legal protection against discrimination and harassment given to trans people by The Equality Act 2010 and Gender Recognition Act 2004. NHS England is the responsible commissioner for the specialised element of the gender dysphoria pathway, which in England is delivered through seven specialist Gender Identity Clinics.

Transgender and non-binary people will spend a relatively short time under the care of a specialist Gender Identity Clinic. General Practitioners therefore have an important role in the on-going care of patients when they no longer have a need for specialised gender identity services. The prescribing and monitoring of hormone therapy can be carried out safely in Primary Care without specialist input, though Gender Identity Clinics are encouraged to provide support to individual General Practitioners when this is requested.

Typical drugs recommended by Gender Identity Clinics include oestradiol preparations (e.g. transdermal oestradiol gels and patches, and oral oestradiol preparations), testosterone preparations (e.g. gels, and Sustanon® and Nebido® injection), gonadotropin-releasing hormone analogues and depilatory agents (e.g. Vaniqa®); this list is not exhaustive. Apart from Sustanon®, there are no licensed products with an approved indication for the treatment of gender dysphoria.

Once the patient has been discharged by a Gender Identity Clinic or gender specialist, the prescribing and monitoring of hormone therapy can be carried out successfully in primary care without further specialist input. From the patient's perspective, management in Primary Care is far easier, and there is no specific expertise necessary to prescribe for and monitor patients on hormone therapy.

General Practitioners are expected to co-operate with Gender Identity Clinics in patient safety monitoring, by providing basic physical examinations (within the competence of General Practitioners) and blood tests and diagnostic tests recommended by the Gender Identity Clinic. Hormone therapy should be monitored at least 6-monthly in the first 3 years, and yearly thereafter, dependent on clinical need.

Guidance published by the General Medical Council in March 2016 advises General Practitioners that they may prescribe 'unlicensed medicines' where this is necessary to meet the specific needs of the patient and where there is no suitably licensed medicine that will meet the patient's need. This advice reiterates existing General Medical Council guidance, 'Good Practice in Prescribing and Managing Medicines and Devices' (2013), which says:

'Prescribing unlicensed medicines may be necessary where there is no suitably licensed medicine that will meet the patient's need, for example, where:

- There is no licensed medicine applicable to the particular patient. For example, if the patient is a child and a medicine licensed only for adult patients would meet the needs of the child; or

- A medicine licensed to treat a condition or symptom in children would nonetheless not meet the specific assessed needs of the particular child, but a medicine licensed for the same condition or symptom in adults would do so; or

- The dosage specified for a licensed medicine would not meet the patient's need; or

- The patient needs a medicine in a formulation that is not specified in an applicable license.'

**Further information:**

Please contact: Steve Hamer, Accountable Commissioner for Gender Identity Services, NHS England
Steve.Hamer1@nhs.net

**Further reading:**

Good Practice Guidelines for the Assessment and Treatment of Adults with Gender Dysphoria (Royal College of Psychiatrists, 2013)

**Reference:** NHS England. Specialised Services Circular. Primary Care Responsibilities in Prescribing and Monitoring Hormone Therapy for Transgender and Non-Binary Adults (updated) April 2016

# NICE

## NEW OR UPDATED PUBLISHED NICE GUIDANCE, APRIL 2016

### Depression in adults: recognition and management clinical guideline

The guideline covers identification and management of depression in adults aged 18 years and older, in Primary and Secondary Care. It aims to improve care for people with depression by promoting improved recognition and treatment. This guideline was updated to contain a link to the guidance on repetitive transcranial magnetic stimulation for depression: https://www.nice.org.uk/guidance/cg90

### Controlled drugs: safe use and management guideline

The guideline covers systems and processes for using and managing controlled drugs safely in all NHS settings except care homes. It aims to improve working practices to comply with legislation and have robust governance arrangements. It also aims to reduce the safety risks associated with controlled drugs:
https://www.nice.org.uk/guidance/ng46

# Safety

## DRUG SAFETY UPDATE APRIL 2016

### Canagliflozin and risk of lower limb amputation

The manufacturer of **canagliflozin** has written to healthcare professionals, in agreement with the European Medicines Agency (EMA), advising of an **increased risk of lower limb amputations** seen in the CANVAS study. **Canagliflozin** (*Invokana*®, *Vokanamet*®) is licensed for the treatment of adults with **type 2 diabetes mellitus** to improve glycaemic control. Adverse event monitoring in the CANVAS study has observed a **two-fold increase** in the risk of a **lower limb amputation**, primarily the **toe**. (The CANVAS study is an on-going long-term study investigating cardiovascular outcomes).

The **risk rate** in study participants taking canagliflozin is **6 lower limb amputations per 1,000 patient years** compared to a risk of 3 per 1,000 patient years in patients taking placebo. No dose response had been noted. The issue is under

investigation and any mechanism behind the events is as yet unknown. However, dehydration and volume depletion might play a role in the development of events.

Healthcare professionals are advised that:

- Routine preventative foot care management remains important.
- Patients with other risk factors for amputation, such as peripheral vascular disease or peripheral neuropathy, should be carefully monitored.
- Early treatment for foot problems should be initiated including, but not limited to, ulceration, infection, new pain or tenderness.
- Consideration should be given to suspending treatment in patients who develop significant lower limb complications such as ulcers, osteomyelitis or gangrene.
- Patients should be advised to maintain adequate hydration and be monitored for signs or symptoms of volume depletion, especially those who are also taking diuretics.

Regulatory agencies will continue to monitor and investigate this issue.

**Reference:** https://www.gov.uk/drug-safety-update/letters-sent-to-healthcare-professionals-in-april-2016

## DRUG SAFETY UPDATE MAY 2016

### BCR-ABL tyrosine kinase inhibitors (imatinib, dasatinib, nilotinib, bosutinib, ponatinib) and the risk of hepatitis B reactivation

In agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA), the manufacturers of imatinib, dasatinib, nilotinib, bosutinib and ponatinib have recently written to healthcare professionals about cases of reactivation of hepatitis B virus (HBV), which have occurred in patients who are chronic carriers of HBV after they received BCR-ABL tyrosine kinase inhibitors (TKIs).
Some cases of HBV reactivation resulted in acute hepatic failure or fulminant hepatitis leading to liver transplantation or death.

They have made the following recommendations:

- Patients should be tested for HBV infection before initiating treatment with BCR-ABL TKIs.
- Consult experts in liver disease and in the treatment of HBV before starting treatment in patients with positive HBV serology (including those with active disease) and for patients who test positive for infection during treatment.
- Closely monitor patients who are carriers of HBV requiring treatment with BCR-ABL TKIs for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.

https://www.gov.uk/drug-safety-update/bcr-abl-tyrosine-kinase-inhibitors-risk-of-hepatitis-b-reactivation

### The manufacturer of pomalidomide (Imnovid®) has issued new important advice that hepatitis B virus status should be established before initiating treatment with pomalidomide

**Summary**

- Reactivation of the hepatitis B virus (HBV) has been reported rarely following treatment with pomalidomide plus dexamethasone in patients previously infected with HBV.
- Some of these cases have progressed to acute hepatic failure and resulted in discontinuation of pomalidomide.
- HBV status should be established before initiating treatment with pomalidomide.
- For patients who test positive for HBV infection, consultation with a physician with expertise in the treatment of hepatitis B is recommended.

- Caution should be exercised when using pomalidomide in combination with dexamethasone in patients previously infected with HBV, including patients who are anti-HBs positive but HBsAg negative.
- Previously infected patients should be closely monitored for signs and symptoms of active HBV infection throughout therapy.

https://www.gov.uk/drug-safety-update/pomalidomide-imnovid-risk-of-hepatitis-b-reactivation

## Retigabine (Trobalt®): risk of acquired vitelliform maculopathy

A macular abnormality with features of vitelliform maculopathy (AVM), usually diagnosed through macular optical coherence tomography (OCT), has been identified in some patients taking retigabine. The new adverse drug reaction of AVM has, therefore, been included in the prescribing information for retigabine. This is in addition to the risk of pigmentation (discolouration} of ocular tissue, including the retina, previously identified for retigabine.

Clinicians are advised to:

- Carry out a macular optical coherence tomography (OCT) test as part of the routine eye monitoring at baseline and at least every six months for patients taking retigabine.
- Review the updated physician's guide (including the section on 'points to discuss with your patients') for further guidance (please visit the electronic Medicines Compendium (eMC): https://www.medicines.org.uk/emc/medicine/24527. If you would like to obtain hard copies, these can be requested from GlaxoSmithkline's Medical Information department, by telephoning 0800 221441 option 2, or emailing ukmedo@gsk.com.
- Continue to report all suspected side effects to retigabine or any other medicine to the Medicines and Healthcare products Regulatory Agency (MHRA) through the Yellow Card scheme at: https://yellowcard.mhra.gov.uk/.

https://assets.digital.cabinet-office.gov.uk/media/572cb12b40f0b60374000004/Trobalt_DHCP_sent_April_2016.pdf

## Idelalisib (Zydelig®): for chronic lymphocytic leukaemia and follicular lymphoma

The manufacturers of idelalisib have issued new interim treatment recommendations in light of new findings from clinical trials outside its currently authorised drug combinations or indicated populations.

**Indications**

**Chronic lymphocytic leukaemia**

- Do not start as first-line treatment in patients who have 17p chromosome deletion or P53 mutation.
- For patients who have a 17p deletion or P53 mutation, who are already receiving idelalisib first-line, clinicians should carefully consider the balance of benefits and risks for the individual (see below), and should decide whether to continue treatment.
- Idelalisib combined with rituximab can be started or continued in patients who have received at least one previous line of therapy.

**Follicular lymphoma**

- Idelalisib monotherapy can be started or continued in adults with disease refractory to two previous lines of treatment.

**New measures to minimise risk for all patients**

- Inform patients of the risk of serious and fatal infections (see below).
- Do not start treatment in patients with any evidence of ongoing systemic bacterial, fungal or viral infection.
- All patients should receive prophylactic treatment for *Pneumocystis jirovecii* pneumonia throughout idelalisib treatment.
- There should be regular clinical and laboratory screening for cytomegalovirus infection. Stop treatment in patients with evidence of infection or viraemia.

- Monitor patients for signs and symptoms of respiratory disease throughout treatment and advise them to promptly report any new respiratory symptoms.
- Monitor absolute neutrophil counts in all patients at least every 2 weeks for the first 6 months of treatment, and at least weekly in those with a count fewer than 1000 per $mm^3$ (further guidance is provided in a table in the letter, which was sent to healthcare professionals)

https://www.gov.uk/drug-safety-update/idelalisib-zydelig-interim-measures-following-signal-of-serious-infection-and-deaths-related-to-infection-found-in-clinical-trials

# Drug Tariff

## PRICE CHANGES

### Top 10 monthly price reductions

Atomoxetine 4mg/1ml oral solution sugar free [1 x 300] £85.00 (-£15.00)
Atomoxetine 100mg capsules [1 x 28] £70.79 (-£12.49)
Atomoxetine 80mg capsules [1 x 28] £70.79 (-£12.49)
Atomoxetine 10mg capsules [1 x 28] £53.09 (-£9.37)
Atomoxetine 18mg capsules [1 x 28] £53.09 (-£9.37)
Atomoxetine 25mg capsules [1 x 28] £53.09 (-£9.37)
Atomoxetine 40mg capsules [1 x 28] £53.09 (-£9.37)
Atomoxetine 60mg capsules [1 x 28] £53.09 (-£9.37)
Aripiprazole 10mg orodispersible tablets sugar free [1 x 28] £89.30 (-£4.57)
Aripiprazole 15mg orodispersible tablets sugar free [1 x 28] £89.30 (-£4.57)

### Top 10 monthly price increases

Alimemazine 7.5mg/5ml oral solution [1 x 100] £103.95 (+£20.79)
Trimipramine 50mg capsules [1 x 28] £130.00 (+£20.00)
Primidone 250mg tablets [1 x 100] £109.70 (+£12.25)
Rifampicin 300mg capsules [1 x 100] £86.04 (+£11.46)
Alimemazine 10mg tablets [1 x 28] £56.51 (+£11.30)
Primidone 50mg tablets [1 x 100] £101.16 (+£11.21)
Selegiline 5mg tablets [1 x 60] £26.50 (+£11.13)
Alimemazine 30mg/5ml oral solution [1 x 100] £164.67 (+£8.62)
Penicillamine 250mg tablets [1 x 56] £82.50 (+£7.50)
Sulfadiazine 500mg tablets [1 x 56] £78.43 (+£7.12)

### Top 100 annual price increases

http://www.panmerseyapc.nhs.uk/home/tariff_watch/partviiia_reductions_201605.pdf

### Top 100 annual price reductions

http://www.panmerseyapc.nhs.uk/home/tariff_watch/partviiia_increases_201605.pdf

## DRUG AVAILABILITY

### Medication supply issues

The following generic drugs have supply issues and hence are incurring increased costs; they have been given a NCSO (NO CHEAPER STOCK OBTAINABLE) status for May 2016. Please consider the costs of the following drugs before prescribing:

| Product | Quantity | Price Concession |
|---|---|---|
| Bumetanide 1mg tablets | 28 | £2.05 |
| Celiprolol 400mg tablets | 28 | £39.65 |
| Cimetidine 400mg tablets | 60 | £19.99 |
| Desmopressin 10micrograms/dose nasal spray | 60 dose | £24.00 |
| Flecainide 100mg tablets | 60 | £10.73 |
| Flecainide 50mg tablets | 60 | £7.50 |
| Isosorbide mononitrate 10mg tablets (new) | 56 | £16.05 |
| Isosorbide mononitrate 20mg tablets (new) | 56 | £10.50 |
| Lamotrigine 5mg dispersible tablets, sugar-free | 28 | £7.50 |
| Lamotrigine 100mg dispersible tablets, sugar-free | 56 | £3.60 |
| Mefenamic acid 500mg tablets | 28 | £9.50 |
| Nitrofurantoin 100mg tablets | 28 | £12.25 |
| Nitrofurantoin 50mg tablets | 28 | £11.50 |

### Other drugs with long-term supply issues

The following drugs have long-term supply issues. The table below shows the reason for the supply issue, where known and possible return to stock dates.

| Item | Status | More Information |
|---|---|---|
| **Aveeno® cream x 100ml** | Supplier unable to confirm | Alternatives include Zerocream® and Zeroderm® |
| **Cardura® XL 8mg tablets** | Supplier unable to confirm | Prescribe as immediate release doxazosin 4mg tablets |
| **Cavilon® Durable Barrier cream x 92g** | No availability date | |
| **Erythroped® A 500mg tablets** | Due August 2016 | Prescribe as erythromycin 250mg tablets |
| **Isosorbide mononitrate 10mg, 20mg, 40mg tablets** | Due July 2016 | ISMO® brand is available but slightly more expensive |
| **Kwells® (12), Kwells Junior® tablets** | Long term out of stock | |
| **Nozinan® Ampoules 25mg/ml 1ml x 10** | Due July 2016 | If used as an anti-emetic in palliative care haloperidol 5mg/1ml injection is an alternative |
| **Selsun ® shampoo x 150ml** | No availability date | 100ml size available |
| **Sno Tears® x 10ml** | Supplier unable to confirm | Liquifilm® Tears 1.4% drops is an alternative |
| **Sorbaderm® Non-Sting cream x 92g** | Supplier unable to confirm | |

| | | |
|---|---|---|
| **Univer® capsules 120mg and 240mg** | Due July 2016 | Alternatives include Half Securon SR® and Securon SR® Tablets |
| **Xailin® gel 0.2%** | No availability date | |
| **Zomig® nasal spray 5mg, 2 x 3** | No availability date | Prescribe generically as sumatriptan 10mg/dose nasal spray. |

### Licensed equivalents now available

Morphine sulfate 1mg/1ml solution for injection ampoules have recently been licensed by Torbay Pharmaceuticals and should ideally be dispensed in preference to morphine sulfate 1mg/1ml solution for injection ampoules (Special Order). The Special Order product has now been discontinued.
There is a licensed preparation available of nitrazepam 2.5mg/5ml suspension, which is made by Essential Pharma Ltd and replaces nitrazepam 2.5mg/5ml suspension sugar-free (Special Order) which is unlicensed.

**Reference**: NHSBSA Hints and Tips bulletin issue 23

# Medicines Management Team contacts

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