Greater East Midlands Commissioning Support Unit in association with
Lincolnshire Clinical Commissioning Groups, Lincolnshire Community Health Services,
United Lincolnshire Hospitals Trust and Lincolnshire Partnership Foundation Trust

Lincolnshire Prescribing and Clinical Effectiveness Bulletin

Volume 8; Number 7 **April 2014**

HAPPY EASTER TO ALL OUR READERS

What's new this month?

- **The recent death in Lincolnshire of a young man from disseminated tuberculosis has highlighted the potentially fatal link between anti-Tumour Necrosis Factor alpha drugs and infectious diseases like TB. *BNF* guidance on the importance of pre-treatment screening for TB within specialist services and the need for clear communication between specialist services and primary care is emphasized. Primary care clinicians need to remain vigilant and responsive to signs suggestive of tuberculosis in patients receiving anti-TNF therapy. The atypical nature of presenting symptoms in patients taking anti-TNF alpha treatment can make the diagnosis of TB particularly difficult in these patients (see page 2).**
- **Trial evidence suggests that the potential benefits of nalmefene (*Selincro*) in patients with a high drinking risk level are dependent upon initial evaluation using a two week alcohol consumption diary followed by continuous psychosocial support for those that end up on prescribed therapy. As this level of support is only available through specialist alcohol services, nalmefene tablets 18mg (*Selincro*) are only approved for restricted use within the *Lincolnshire Joint Formulary* and are designated RED. There is no requirement for GPs to prescribe this treatment and any requests received from specialist services should be refused (see page 4).**
- **Inactivated quadrivalent influenza vaccine (*Fluarix Tetra*) should only be used in children aged 3 to 18 as defined in the influenza chapter of *Immunisation Against Infectious Disease* (chapter 19). There is no role for the product in older age groups and it should not be prescribed or administered to this group as part of the influenza vaccination programme for 2014/15. The product is designated RED-RED for this indication (see page 7).**
- ***Accu-Chek Active* blood glucose testing meter and strips are confirmed as fully compliant with PACEF evaluation criteria and are designated GREEN; they are approved for inclusion in the *Lincolnshire Joint Formulary* alongside all of the other lower cost products approved for use earlier in the year. The online version of the *PACE Bulletin* evaluating lower cost BGTS (Vol 8 No 2 (February 2014)) has been updated to include this product (see page 8).**
- **A recent audit of patients prescribed lithium therapy that was undertaken within LPFT has identified a number of recurrent problems both with the monitoring of the drug itself and the monitoring of the patients' health and wellbeing. Patients prescribed lithium should have their renal and thyroid function checked before treatment is started and every six months thereafter. Lithium plasma levels should be checked one week after initiation (and after every dose change) and every three months thereafter. The therapeutic range is 0.6 to 0.8mmol/L. All patients taking lithium should be aware of potential side effects and the signs, symptoms and risk factors for lithium toxicity (see page 9).**
- **A European review of the latest evidence on the risk of venous thromboembolism (VTE) with combined hormonal contraceptives (CHCs) has confirmed that the level of risk of VTE with all low-dose CHCs (ethinylestradiol <50 micrograms) remains small and that the products with the lowest risk of VTE are those containing the progestogens, levonorgestrel, norethisterone and norgestimate (see page 10).**
- **A new edition of the *Policy Relating to the Prescribing, Supply, Storage and Disposal of Controlled Drugs in Primary Care* (March 2014) has been approved by PACEF and is**

now available through the PACEF section of the NHS in Lincolnshire website (see page 12).

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SUMMARY OF PACEF DECISIONS: *MARCH 2014 UPDATE*

Drug	Indication(s)	Traffic Light and Joint Formulary Status
Accu-Chek Active blood glucose testing meter and strips	Blood glucose monitoring	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary*.
Granisetron transdermal patch 3.1mg in 24 hours (*Sancuso*)	For the prevention of acute nausea and vomiting in adults receiving moderately or highly emetogenic chemotherapy for three to five consecutive days, who find swallowing difficult.	RED Approved for inclusion in the *Lincolnshire Joint Formulary*
Inactivated quadrivalent influenza vaccine (*Fluarix Tetra*)	Influenza immunisation	RED-RED for adult patients. Limited role in children.
Nalmefene tablets 18mg (*Selincro*)	For the reduction of alcohol consumption in adult patients with alcohol dependence who have a high drinking risk level without physical withdrawal symptoms and who do not need immediate detoxification.	RED Approved for restricted use within LPFT only. Approved for inclusion in the *Lincolnshire Joint Formulary*.

This bulletin has been created specifically to convey details of decisions taken at the Prescribing and Clinical Effectiveness Forum (PACEF) to all stakeholders across the Lincolnshire Healthcare Community in both primary and secondary care. Back issues of the *PACE Bulletin* and other PACEF publications are available through the NHS in Lincolnshire website (www.lincolnshire.nhs.uk); follow the commissioning link to PACEF. Electronic copies of both the *PACE Bulletin* and our sister publication *PACE Shorts* (a short summary of the *PACE Bulletin*) are circulated to a wide readership via email. If you are not currently on our distribution list and wish to receive regular copies of PACEF publications please contact Sandra France on sandra.france@gemcsu.nhs.uk.

The *Lincolnshire Joint Formulary* is available on line and is fully searchable; it can be accessed at www.lincolnshirejointformulary.nhs.uk

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INCREASED RISK OF TUBERCULOSIS WITH ANTI-TNF ALPHA TREATMENTS

The recent death in Lincolnshire of a young man from disseminated tuberculosis (TB) has highlighted the potentially fatal link between anti-Tumour Necrosis Factor (TNF) alpha drugs and infectious diseases like TB.

In this case, a patient with Crohn's disease receiving infliximab treatment through specialist gastroenterology services was investigated and treated over a period of time for suspected

chest infections. During this period, the patient was seen by their GP and various other primary care services including a walk in centre and the university medical centre. The coroner has asked us to remind all Lincolnshire healthcare professionals of the importance of pre-treatment screening and vigilance for tuberculosis required with all of the ant-TNF alpha drugs including adalimumab (*Humira*), certolizumab pegol (*Cimzia*), etanercept (*Enbrel*), golimumab (*Simponi*) and infliximab (*Remicade*). These medicines are authorized for a range of different indications as summarized below:

Drug	**Authorised indications**
Adalimumab injection (*Humira*)	Moderate to severe chronic plaque psoriasis. Moderate to severe active rheumatoid arthritis. Severe, active and progressive RA. Active and progressive psoriatic arthritis Severe active ankylosing spondylitis Severe axial spondyloarthritis Active polyarticular juvenile idiopathic arthritis. Moderate to severe active Crohn's disease. Moderate to severe active ulcerative colitis. Severe active Crohn's disease in children.
Certolizumab pegol (*Cimzia*),	Moderate to severe active rheumatoid arthritis. Severe active ankylosing spondylitis Severe axial spondyloarthritis Active psoriatic arthritis.
Etanercept injection (*Enbrel*),	Moderate to severe plaque psoriasis in adults. Chronic severe plaque psoriasis in children and adolescents $\geq$ 6 years. Moderate to severe active rheumatoid arthritis. Severe, active and progressive RA in adults. Active and progressive psoriatic arthritis Severe active ankylosing spondylitis Juvenile idiopathic arthritis. Polyarthritis, extended oligoarthritis and psoriatic arthritis. Enthesitis related arthritis
Golimumab (*Simponi*)	Moderate to severe active RA. Severe, active and progressive RA. Active and progressive psoriatic arthritis Severe active ankylosing spondylitis. Moderate to severe active ulcerative colitis.
Infliximab infusion (*Remicade*).	Moderate to severe plaque psoriasis. Active RA. Active and progressive RA. Active and progressive psoriatic arthritis Severe active ankylosing spondylitis. Moderate to severe active Crohn's disease. Fistulising Crohn's disease. Moderate to severe active ulcerative colitis. Severe active Crohn's disease in children.

Standard advice in the *British National Formulary* for all of these medicines is as follows:

(1) Patients should be evaluated for both active and latent tuberculosis prior to initiation of treatment. In all patients, a detailed medical history should be taken and a number of screening tests performed including tuberculin skin test and chest X ray.
(2) Active tuberculosis should be treated with standard treatment for at least 2 months before starting any of these treatments.
(3) Patients who have previously been adequately treated for tuberculosis can be started on one of these treatments, but should be monitored every 3 months for possible recurrence.
(4) In patients without active tuberculosis who were previously not treated adequately, chemoprophylaxis should ideally be completed before starting one of these treatments.

(5) In patients at high risk of tuberculosis who cannot be assessed by tuberculin skin test, chemoprophylaxis can be given concurrently with one of these treatments.
(6) Patients should be advised to seek medical attention if symptoms suggestive of tuberculosis (e.g. persistent cough, weight loss and fever) develop. The atypical nature of presenting symptoms in patients taking anti-TNF alpha treatment can make the diagnosis of TB particularly difficult in these patients.

PACEF Recommendation:
All of the anti-TNF alpha medicines are designated RED for NICE approved indications and should only be prescribed and administered within specialist services in secondary and tertiary care. As a result of this, most of the pre-treatment screening for and decision making around tuberculosis falls under the responsibility of the specialist service prescribing and administering the treatment. Nonetheless, clear communication between the specialist service and the GP around treatments prescribed and administered remains crucial and primary care clinicians retain an important role in remaining vigilant and responsive to signs suggestive of tuberculosis if they appear in patients receiving anti-TNF alpha therapies. The atypical nature of presenting symptoms can make the diagnosis of TB particularly difficult in these patients.

Reference:
British National Formulary, 65, March – September 2013, pp 682-90.

NEW DRUG ASSESSMENT: *NALMEFENE TABLETS 18MG (SELINCRO)*

Nalmefene (*Selincro*) is a first in class opioid system modulator which works by controlling the urge to continue drinking in problem drinkers. It is thought to work by interrupting reward mechanisms in the brain. It is licensed for the reduction of alcohol consumption in adult patients with alcohol dependence who have a high drinking risk level without physical withdrawal symptoms and who do not need immediate detoxification.

The World Health Organisation defines Drinking Risk Level (DRL) as follows:

DRL	Total consumption in men (g/day)	Total consumption in men (units/day)	Total consumption in women (g/day)	Total consumption in women (units/day)
Very high risk	>100	>12.5	>60	>7.5
High risk	>60-100	>7.5 – 12.5	>40-60	>5-7.5
Medium risk	>40-60	>5 – 7.5	>20-40	>2.5-5
Low risk	1-40	0.13 - 5	1-20	0.13-2.5
Abstinent	0	0	0	0

Trial evidence shows that nalmefene plus psychosocial intervention performs better than placebo plus psychosocial intervention in reducing drinking in high risk/mildly alcohol dependent patients. From this, PACEF concluded that nalmefene taken as needed 1 to 2 hours prior to anticipated time of drinking can help to significantly reduce the patient's drinking risk level. There are no comparative data against alternative agents such as disulfiram, naltrexone and acamprosate, although indirect comparison suggests that alternatives are of similar or lower efficacy.

In terms of side effects, nalmefene is well tolerated with the most common side effects documented as dizziness, nausea, headache and insomnia, all of which are documented with alcohol itself. Long-term safety data is currently available for up to a year.

The Summary of Product Characteristics for *Selincro* specifies that it **should only be prescribed in conjunction with continuous psychosocial support focused on**

treatment adherence and reducing alcohol consumption. At the initial patient contact, clinical status, alcohol dependence and level of alcohol consumption (based on patient reporting) should be evaluated. The patient should then be asked to record his/her alcohol consumption for 2 weeks. On evaluation of the alcohol diary, patients identified as having a high DRL but not considered to require assisted withdrawal or detoxification could be initiated on nalmefene subject to their commitment to therapy and provision of psychosocial support.

Nalmefene is the first licensed therapy designed to support the reduction in alcohol consumption in adults. As such, it is not directly comparable with treatments designed to support abstinence after withdrawal. The table below reveals that nalmefene is potentially higher in cost than acamprosate, disulfiram or naltrexone:

Drug	Licensed indication	Dose	Cost (28 days)
Treatments to reduce alcohol consumption			
Nalmefene 18mg tablets (*Selincro*)	For use with psychosocial support to reduce alcohol consumption in adults with alcohol dependence who have a high drinking risk (at initial assessment and 2 weeks later) without physical withdrawal symptoms and who do not require immediate detoxification.	1 tablet daily when the patient perceives a risk of drinking alcohol, preferably 1-2 hours before anticipated drinking.	£84.84 (assuming daily usage) £42.42 (assuming alternate day use)
Treatments to support abstinence after alcohol withdrawal			
Acamprosate 333mg tablets (*Campral EC*)	For the maintenance of abstinence in alcohol dependent patients, in conjunction with counselling	2 tablets three times a day (for adults over 60kg); commence immediately after alcohol withdrawal and continue for 1 year.	£28.80
Disulfiram tablets 200mg (*Antabuse*)	For use as an adjunct in alcoholism	Half to one tablet daily for as long as advised; no longer than 6 months without review.	£8.68-17.36
Naltrexone 50mg tablets (*Adepend*)	For the maintenance of abstinence in alcohol dependence	1 tablet daily for at least 3 months	£47.43

PACEF Recommendation

Trial evidence suggests that the potential benefits of nalmefene in patients with a high drinking risk level are dependent upon initial evaluation using a two week alcohol consumption diary to identify appropriate patients followed by continuous psychosocial support focused on treatment adherence and reduction of alcohol consumption for those that end up on prescribed therapy. As this level of support is only available through specialist alcohol services, nalmefene tablets 18mg (*Selincro*) are only approved for restricted use within the *Lincolnshire Joint Formulary* and are designated RED. There is no requirement for GPs to prescribe this treatment and any requests received from specialist services should be refused. Primary care clinicians are encouraged to undertake opportunistic screening for alcohol use disorders using the Alcohol Use Disorders Identification Test (AUDIT); referral to specialist services is recommended for all patients scoring 20-40 (see below).

Alcohol Use Disorders Identification Test (AUDIT): Interview Questions

Question	
1. How often do you have a drink containing alcohol?	(0) Never [Skip to Qs 9-10] (1) Monthly or less (2) 2 to 4 times a month (3) 2 to 3 times a week (4) 4 or more times a week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	(0) 1 or 2 (1) 3 or 4 (2) 5 or 6 (3) 7, 8, or 9 (4) 10 or more.
3. How often do you have six or more drinks on one occasion?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily.
Skip to Questions 9 and 10 if Total Score for Questions 2 and 3 = 0	
4. How often during the last year have you found that you were not able to stop drinking once you had started?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily.
5. How often during the last year have you failed to do what was normally expected from you because of drinking?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily.
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily.
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?	(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily.
9. Have you or someone else been injured as a result of your drinking?	(0) No (2) Yes, but not in the last year (4) Yes, during the last year
10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?	(0) No (2) Yes, but not in the last year (4) Yes, during the last year

Risk Level	**Intervention**	**AUDIT score**
1	Alcohol Education	0-7
2	Simple Advice	8-15
3	Simple Advice plus Brief Counselling and Continued Monitoring	16-19

4	Referral to Specialist for Diagnostic Evaluation and Treatment	20-40

RAPID DRUG ASSESSMENT: *INACTIVATED QUADRIVALENT INFLUENZA VACCINE (FLUARIX TETRA)*

Inactivated quadrivalent influenza vaccine (*Fluarix Tetra*) has an extremely limited role in the vaccination of children against influenza; it should not be prescribed or administered to adults at all as part of the forthcoming 2014/15 influenza season.

Fluarix Tetra is a new quadrivalent influenza vaccine that was launched last year by GlaxoSmithKline and contains four strains of inactivated influenza virus. All other alternative products are trivalent and contain three strains. The current edition of *Immunisation Against Infectious Disease*, the so-called 'Green Book', provides guidance on the use of quadrivalent influenza vaccine in Chapter 19 (September 2013). The algorithm (see page 203) makes clear that the role of quadrivalent influenza vaccine is in children who for whatever reason cannot receive the intranasal vaccine *Fluenz*. It is stressed that quadrivalent influenza vaccine should **only** be available for children aged 3 years and older (i.e. age 3 to 18). All other at risk groups should be vaccinated with the trivalent vaccine as in previous years. As *Fluarix Tetra* is not recommended for children under 3 years, inactivated trivalent vaccine should be used where a child less than 3 years needs to be vaccinated; it should also be preferred where adults aged 18 years require vaccination. **As a result of this, it can be concluded that, while *Fluarix Tetra* has a confirmed role in the national vaccination programme against influenza, this role is confined to children between the ages of 3 and 18 for whom *Fluenz* is inappropriate, for example due to contra-indication or precaution.**

It has also been confirmed that plans are well developed for supply of influenza vaccine for children to be administered centrally for the 2014 Flu vaccination programme. This means that it is highly likely that all vaccine for children up to the age of 18 will be supplied free of charge to practices through the established supply route for other childhood vaccinations. Practices are due to be notified of this shortly. As a result of this, it is strongly recommended that practices do not purchase *Fluarix Tetra* as their preferred or one of their preferred influenza vaccines for the 2014/15 influenza season. Whilst there is a limited role in children aged 3 to 18, this will be entirely covered through the national supply arrangements.

A cost comparison of the available vaccines also reveals that the NHS reimbursement price of *Fluarix Tetra* is almost twice that of many trivalent competitors:

Name of Product	Vaccine type	Age indications	NHS reimbursement price
Agrippal	Trivalent inactivated	From 6 months	£5.85 (single dose) £58.50 (10 dose)
Enzira	Trivalent inactivated	From 5 years (may be associated with a higher than expected rate of fever in children aged 5 to 9, consider alternatives in this group)	£5.25 (single dose) £52.50 (10 dose)
Fluarix	Trivalent inactivated	From 6 months	£5.39(single dose) £53.89 (10 dose)
Fluarix Tetra	**Quadrivalent inactivated**	**From 3 years**	**£99.40 (10 dose)**
Fluenz Nasal Spray	Trivalent live attenuated	From 24 months to less than 18 years	£140.00 (10 dose)
Fluvirin	Trivalent inactivated	From 4 years	£5.55(single dose) £55.50 (10 dose)
Imuvac	Trivalent inactivated	From 6 months	£6.59 (single dose) £65.90 (10 dose)

Inactivated influenza vaccine (split virion) (MASTA)	Trivalent inactivated	From 6 months	£6.59 (single dose)
Inactivated influenza vaccine (Pfizer)	Trivalent inactivated	From 5 years (may be associated with a higher than expected rate of fever in children aged 5 to 9, consider alternatives in this group)	£6.59 (single dose)
Inactivated influenza vaccine (split virion) (Sanofi Pasteur MSD)	Trivalent inactivated	From 6 months	£6.59 (single dose)
Influvac Desu	Trivalent inactivated	From 6 months	£5.22 (single dose) £52.20 (10 dose)
Intanza 9 microgram	Trivalent inactivated	From 18 to 59 years	£9.05 (single dose) £90.50 (10 dose)
Intanza 15 microgram	Trivalent inactivated	From 60 years	£9.05 (single dose) £90.50 (10 dose)
Optaflu	Trivalent inactivated	From 18 years	£6.59 (single dose) £65.90 (10 dose)
Viroflu	Trivalent inactivated	From 6 months (may be associated with a higher than expected rate of fever in children aged under 5, consider alternatives in this group)	£65.90 (10 dose)

PACEF Recommendation:
Inactivated quadrivalent influenza vaccine (*Fluarix Tetra*) should only be used in children aged 3 to 18 as defined in the influenza chapter of *Immunisation Against Infectious Disease* (chapter 19). There is no role for the product in older age groups and it should not be prescribed or administered to this group as part of the influenza vaccination programme for 2014/15. The product is designated RED-RED for this indication.

Reference:
Immunisation Against Infectious Disease, Chapter 19, Influenza (September 2013)

RAPID ASSESSMENT: *ACCU-CHEK ACTIVE BLOOD GLUCOSE METER AND TEST STRIPS*

In *PACE Bulletin* Volume 8 Number 2 (February 2014), we reviewed a wide range of lower cost blood glucose testing strips (BGTS) and meters against a number of key criteria. Accu-Chek *Active* has now been evaluated against the same criteria and has been found to be fully compliant as follows:

Blood Glucose Testing Meter and Strip	Compliant with ISO 15197: 2013?	Is the memory capacity more than 450 tests?	Is the memory easily deletable?	Can results be down loaded?	Is calibration required?	Are results displayed in mmol/l?	Does the device turn on automatically?
Accu-Chek Active	**Fully compliant**	**Yes**	**No**	**Yes**	**No**	**Yes**	**Yes**
Element	Fully compliant	Yes	No	Yes	No	Yes	Yes
GlucoLab	Fully compliant	Yes	No	Yes	No	Yes	Yes
GlucoMen GM	Fully compliant	No	No	Yes	No	Yes	Yes
GlucoRx Nexus	Fully compliant	Yes	No	Yes	No	Yes	Yes
GlucoRx Nexus Mini	Fully compliant	Yes	No	Yes	No	Yes	Yes
GlucoRx	Fully	Yes	No	Yes	No	Yes	Yes

Nexus Voice	compliant						
iCare Advanced	Fully compliant	Yes	No	Yes	No	Yes	Yes
Microdot +	Fully compliant	Yes	No	Yes	No	Yes	Yes
MyLife Pura	Fully compliant	Yes	No	Yes	No	Yes	Yes
Omnitest 3	Fully compliant	No	Yes	Yes	No	Yes	Yes
TRUEyou	Fully compliant	Yes	No	Yes	No	Yes	Yes
WaveSense JAZZ	Fully compliant	Yes	No	Yes	No	Yes	Yes

PACEF Recommendation:
As a result of this, *Accu-Chek Active* is confirmed as fully compliant with PACEF criteria and is designated GREEN; it is also approved for inclusion in the *Lincolnshire Joint Formulary.* The online version of the *PACE Bulletin* evaluating lower cost BGTS (Vol 8 No 2 (February 2014)) has been updated to include this product.

RAPID DRUG ASSESSMENT: *GRANISETRON 3.1MG IN 24 HOURS TRANSDERMAL PATCH (SANCUSO)*

Granisetron transdermal patch (*Sancuso*) is the first 5-HT_3 receptor antagonist transdermal patch; it is licensed for the prevention of acute nausea and vomiting in adults receiving moderately or highly emetogenic chemotherapy for three to five consecutive days, who find swallowing difficult. *Sancuso* matrix patch contains 34.3mg of granisetron which is released at a rate of 3.1mg every 24 hours; it is worn on the upper arm or abdomen for up to 7 days.

PACEF reviewed evidence from a single double-blind, phase III study. 641 patients were randomised to receive either:

- *Sancuso* applied 24 to 48 hours before first chemotherapy dose and worn for seven days plus oral placebo once daily or:
- Oral granisetron 2mg once daily taken one hour before each dose of chemotherapy plus placebo patch.

60% of patients receiving *Sancuso* and 65% receiving oral granisetron achieved complete control of chemotherapy induced nausea and vomiting (CINV). PACEF accepted this as evidence that *Sancuso* was non-inferior to oral granisetron in this patient group, but were disappointed by the paucity of supporting evidence and the lack of comparative data against other alternatives.

The most common adverse reactions of 5-HT_3 antagonists are constipation and headache. In the trial, adverse events with *Sancuso* transdermal patches were similar to those with oral granisetron except that more patients reported constipation (6.6% vs. 3.1%) and fewer reported headache (0.3% vs. 2.5%). Application site reactions were generally mild and did not lead to discontinuation.

A cost comparison of secondary care prices revealed that oral ondansetron 8mg tablets, granisetron 1mg and 2mg tablets and ondansetron 4mg in 5ml syrup were all lower cost options than *Sancuso* transdermal patches.

PACEF Recommendation:
Granisetron transdermal patch 3.1mg in 24 hours (*Sancuso*) is approved for use as a third line alternative to oral ondansetron and granisetron in secondary care. It is designated RED and is approved for inclusion in the *Lincolnshire Joint Formulary*.

MONITORING OF PATIENTS PRESCRIBED LITHIUM

A recent audit of patients prescribed lithium therapy that was undertaken within LPFT has identified a number of recurrent problems both with the monitoring of the drug itself and the monitoring of the patients' health and wellbeing. Learning points from the audit include:

(1) Patients prescribed lithium should have their renal and thyroid function checked before treatment is started and every six months thereafter.
(2) Lithium plasma levels should be checked one week after initiation (and after every dose change) and every three months thereafter. The therapeutic range is 0.6 to 0.8mmol/L.
(3) All patients taking lithium should be aware of potential side effects and the signs, symptoms and risk factors for lithium toxicity.

MEDICINES AND HEALTHCARE REGULATORY AGENCY: *DRUG SAFETY UPDATE* (FEBRUARY 2014)

COMBINED HORMONAL CONTRACEPTIVES AND VENOUS THROMBOEMBOLISM: REVIEW CONFIRMS RISK IS SMALL – CONSIDER RISK FACTORS AND REMAIN VIGILANT FOR SIGNS AND SYMPTOMS

In January, all prescribers received a letter through the Central Alerting System (CAS) informing them of the outcome of a European review of the latest evidence on the risk of venous thromboembolism (VTE) with combined hormonal contraceptives (CHCs). The review confirmed that the level of risk of VTE with all low-dose CHCs (ethinylestradiol <50 micrograms) remains small and that the products with the lowest risk of VTE are those containing the progestogens, levonorgestrel, norethisterone and norgestimate. The table below details progestogen-specific estimates of VTE incidence. This is adapted from a version that originally appeared in the MHRA *Drug Safety Update* in February 2014 and contains additional information signifying which brands contain each progestogen.

Progestogen in CHC (combined with ethinylestradiol, unless stated)	**Brand**	**Relative risk vs levonorgestrel**	**Estimated VTE incidence (Cases per 10,000 women per year of use)**
Non-pregnant, non-user of CHC		-	2
Levonorgestrel	*Elevin, Levest, Microgynon 30* (also *ED*), *Ovranette, Rigevidon, Logynon* (also *ED*).	ref	5-7
Norgestimate Norethisterone	*Cilest, Lizinna* *Brevinor, Loestrin 20, Loestrin 30, Norimin, Ovysmen BiNovum Synphase TriNovum*	1.0	5-7
Gestodene	*Femodene* (also	1.5-2.0	9-12

Desogestrel Drospirenone	ED), *Femodette, Katya, Millinette 20/75, Millinette 30/75, Sunya, Triadene.* *Cimizt, Gedarel 20/150, Gedarel 30/150, Lestramyl, Marvelon, Mercilon.* *Yasmin*		
Etonogestrel Norelgestromin	*NuvaRing* *Evra* patches	1.0-2.0	6-12
Dienogest with estradiol Nomegestrel acetate with estradiol	*Qlaira* *Zoely*	Further studies ongoing or planned to collect sufficient data to estimate risk for these products.	

The recent letter also included a prescribing checklist and a user card and information sheet for women designed to aid informed decision making by both the prescriber and the patient. The checklist specifies the conditions that contraindicate the use of a CHC and lists the factors that increase a woman's risk (such as older age, obesity, prolonged immobilisation, surgery, personal history of thromboembolism, smoking etc.). It also reminds prescribers that the presence of more than one risk factor may constitute a contraindication.

The user card describes the signs and symptoms of deep vein thrombosis, pulmonary embolism, stroke, and heart attack and states when the risk of a thromboembolism may be particularly high. The information sheet provides more detailed information on the risk of thromboembolism with CHCs in the form of questions and answers.

The MHRA have issued the following advice to healthcare professionals:

- There is no need for any woman to change her CHC on the basis of this review and the updated information.
- Consider using the prescribing checklist to help CHC consultations.
- As part of the prescribing decision, carefully consider any contraindications for use, the difference in risk of VTE between products and the woman's current risk factors.
- Risk factors should be re-assessed regularly as part of routine appointments.
- Discuss the risk of VTE with each woman, and raise awareness of the signs and symptoms of thromboembolism when prescribing a CHC; consider providing her with the further information mentioned above
- Always consider the possibility of a CHC-associated thromboembolism when presented with a woman who has relevant symptoms
- Ask all women with signs and symptoms of thromboembolism if they are "taking any medicines *or if they are using a combined hormonal contraceptive*"

POLICY RELATING TO THE PRESCRIBING, SUPPLY, STORAGE AND DISPOSAL OF CONTROLLED DRUGS IN PRIMARY CARE (MARCH 2014)

A new edition of the *Policy Relating to the Prescribing, Supply, Storage and Disposal of Controlled Drugs in Primary Care* (March 2014) has been approved by PACEF and is now available through the PACEF section of the NHS in Lincolnshire website.

Acknowledgements

Many thanks to Cathy Johnson, Interface Lead Pharmacist, GEM CSU; Sharon Hayler, Prescribing Adviser, GEMCSU; Robyn Thompson, Senior Pharmacist, ULH; and Shiraz Haider, Chief Pharmacist, LPFT for their help in the compilation of this *Bulletin*. Also thanks to Dr Tim Davies, Consultant Lead for Screening and Immunisation for NHS England Area Team (Leicestershire/Lincolnshire) and Public Health England for his help with the compilation of the article on *Fluarix Tetra.*

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April 2014

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