NHS Lincolnshire

Prescribing and Clinical Effectiveness Bulletin

Volume 5; Number 11 **June 2011**

What's new this month:

- **Generic anastrozole 1mg tablets and risedronate 35mg tablets are now available, Both products should be prescribed generically. The saving across Lincolnshire is likely to be in excess of £900,000pa (see page 4).**
- **NICE have approved the three acetylcholinesterase (AChE) inhibitors, donepezil (Aricept), galantamine (Reminyl) and rivastigmine (Exelon), as options for the management of mild to moderate Alzheimer's disease (AD). Designation: AMBER subject to specialist initiation and shared care guideline (see page 4).**
- **NICE have also endorsed memantine (Ebixa) for severe AD; use in moderate AD is restricted to patients intolerant to AChE inhibitors or where their use is contraindicated on clinical grounds. Designation: AMBER subject to specialist initiation, shared care guideline and NICE restrictions (see page 4).**
- **New evidence has highlighted the increased fracture risk with higher doses of levothyroxine (see page 8).**
- **New guidance on drug interactions and hormonal contraception has been published by the Royal College of Obstetricians and Gynaecologists (see page 9).**
- **The *Drug and Therapeutics Bulletin* has re-emphasized the long term safety risks of Proton Pump Inhibitors (PPIs) (see page 9).**
- **Two new shared care guidelines have been approved: Hydroxychloroquine in Rheumatology; and Methylphenidate, atomoxetine and dexamfetamine in the management of Attention Deficit Hyperactivity Disorder (see page 12).**

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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 Lincolnshire website (www.lincolnshire.nhs.uk). Click on 'Commissioning' and follow the links to PACEF.

SUMMARY OF PACEF DECISIONS: MAY 2011 UPDATE

Drug	Indication(s)	Traffic Light Status
Donepezil tablets (Aricept)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required.
Donepezil orodispersible tablets (Aricept Evess)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required. Should be reserved solely for patients with swallowing difficulties.
Everolimus tablets (Afinitor)	Licensed for the treatment of advanced renal cell carcinoma when the disease has progressed despite treatment with vascular endothelial growth factor targeted therapy	RED-RED
Galantamine tablets (Reminyl)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required.
Galantamine modified release capsules (Reminyl XL)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required. Standard release twice daily formulation is preferred.
Galantamine oral solution (Reminyl)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required. Should be reserved solely for patients who cannot take solid dose formulations.
Golimumab injection (Simponi)	Licensed for the treatment of active and progressive psoriatic arthritis as monotherapy or in combination with methotrexate when response to DMARD therapy has been inadequate	RED Subject to NICE restrictions
Rivastigmine capsules (Exelon)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease or in Parkinson's disease	AMBER Specialist initiation; shared care guideline is required.
Rivastigmine oral solution (Exelon)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease or in Parkinson's disease	AMBER Specialist initiation; shared care guideline is required. Should be reserved solely for patients who cannot take solid dose formulations
Rivastigmine patches (Exelon)	Licensed for the treatment of mild to moderate dementia in Alzheimer's disease or in Parkinson's disease	AMBER Specialist initiation; shared care guideline is required. The use of the patch should be restricted to those for whom rivastigmine is considered an appropriate therapy and the patch an appropriate formulation.
Memantine tablets (Ebixa)	Licensed for moderate to severe dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required. Memantine should only be used in moderate AD in those who are intolerant of or have a contraindication to AChE inhibitors. NICE have approved memantine for use in both moderate to severe dementia in AD.

Memantine oral solution (Ebixa)	Licensed for moderate to severe dementia in Alzheimer's disease	AMBER Specialist initiation; shared care guideline is required. Memantine should only be used in moderate AD in those who are intolerant of or have a contraindication to AChE inhibitors. NICE have approved memantine for use in both moderate to severe dementia in AD. Should be reserved solely for patients who cannot take solid dose formulations.
Romiplostim injection (Nplate)	Licensed for the treatment of chronic idiopathic thrombocytopenic purpura in splenectomised patients refractory to other treatments, such as corticosteroids or immunoglobulins, or as a second-line treatment in non-splenectomised patients when surgery is contra-indicated.	RED
Trabectedin injection (Yondelis)	Licensed for the treatment of relapsed platinum-sensitive ovarian cancer in combination with pegylated liposomal doxorubicin Licensed for the treatment of advanced soft tissue sarcoma when treatment with anthracyclines and ifosfamide has failed, is inappropriate or is not tolerated	RED-RED RED

RED-RED: This signifies that a product is **not recommended** for prescribing in **either** primary or secondary care. All new products are classified as RED-RED pending assessment by PACEF.
RED: This signifies that a product has been approved for use within secondary care, tertiary care or a primary care hosted specialist service only and **should not be routinely prescribed in primary care**. RED drugs may be used within ULHT or LPFT subject to approval for use within each Trust. ULHT and LPFT reserve the right to determine whether or not RED drugs will be used within their Trusts. RED classification does not automatically signify that a drug will be available within secondary/tertiary care.
AMBER: This signifies that a drug has been approved for use in primary care **subject to specialist initiation; a shared care guideline (SCG) may also be required**. The main purpose of the SCG will be to clearly define both specialist and GP responsibilities. Not all AMBER drugs that require SCGs are currently covered by formal documents; PACEF are working to rectify this.
GREEN: This signifies a product that is **approved for initiation in either primary or secondary care.**

REPORTING INCIDENTS TO THE NATIONAL PATIENT SAFETY AGENCY (NPSA)
The NPSA are keen to encourage the anonymous reporting of patient safety errors and systems failures both from healthcare professionals and patients. The National Reporting and Learning System (NRLS) has been set up to facilitate this process. Healthcare professionals can either report patient safety incidents through their local risk management scheme or directly into the NRLS using the eForm on the NPSA website. Please access www.npsa.nhs.uk for more information. **All healthcare professionals are encouraged to report incidents, errors and systems failures; the aim is to help the NHS to learn from things that go wrong.**

NEW PATENT EXPIRIES: ANASTROZOLE AND RISEDRONATE

Following the patent expiry of anastrozole (Arimidex) and risedronate (Actonel) both drugs are due to move into Category M of the *Drug Tariff* in July 2011 (see July edition). The scale of the price reductions are as follows:

	Dose	Cost (28 days) (July 2011)
Anastrozole 1mg tablets (generic)	1mg daily	£7.86
Anastrozole 1mg tablets (Arimidex)	1mg daily	£68.56
Risedronate 35mg tablets (generic)	35mg once weekly	£2.20
Risedronate 35mg tablets (Actonel Once a Week)	35mg once weekly	£19.12

Subject to 100% generic prescribing, estimated savings across the whole of the Lincolnshire Healthcare Community will be £306,500pa for risedronate and £633,000pa for anastrozole. At present 91.5% of prescriptions for risedronate 35mg are generic; in contrast only 79.5% of anastrozole 1mg prescriptions are generic.

PACEF Recommendation:
Practices should ensure that all prescribing of anastrozole 1mg tablets and risedronate 35mg tablets is generic. There is no reason why both of these products cannot be prescribed generically. Local oncologists have confirmed their support for such an initiative around anastrozole. Full implementation will generate full year savings of over £900,000pa across the county.

NICE UPDATE

NICE TECHNOLOGY APPRAISAL 217: *DONEPEZIL, GALANTAMINE, RIVASTIGMINE AND MEMANTINE FOR THE TREATMENT OF ALZHEIMER'S DISEASE* (MARCH 2011)

The NICE recommendations are as follows:

- The three acetylcholinesterase (AChE) inhibitors donepezil (Aricept), galantamine (Reminyl) and rivastigmine (Exelon) are recommended as options for managing mild to moderate Alzheimer's disease (AD).

PACEF Comment:
NICE guidance now covers the full licensed indications for all three AChE inhibitors (i.e. the treatment of mild to moderate Alzheimer's disease). New evidence reviewed by NICE from placebo controlled randomised trials published since 2004 has shown that each of the AChE inhibitors offer benefits in terms of best supportive care for cognitive and global outcomes and may offer some benefit in terms of behavioural outcomes, although the nature and extent of these are uncertain. The majority of trials were of 6 months duration, although some open label studies have shown benefits that persist for 2 to 3 years.

- Memantine (Ebixa) is recommended as an option for managing AD for people with moderate AD who are intolerant of or have a contraindication to AChE inhibitors or in those with severe disease.

PACEF Comment:
Memantine (Ebixa) has a UK product license covering its use in the treatment of moderate to severe dementia in AD. The NICE TA endorses its role in severe disease but only approves a role in moderate AD in patients intolerant to AChE inhibitors or where their use is contraindicated on clinical grounds. Memantine has a different mode of action to the AChE inhibitors and is used later in the care pathway in people with more severe disease, particularly those exhibiting more behavioural symptoms (e.g. agitation, aggression and/or psychotic symptoms).

- Treatment should only be initiated by specialists in the care of patients with dementia (i.e. psychiatrists including those specialising in learning disabilities, neurologists and physicians specialising in the care of the older people). The carer's view on the patient's condition at baseline should be sought.
- Treatment should only be continued if it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms.
- Patients who continue on treatment should be reviewed regularly using cognitive, global, functional or behavioural assessment. Treatment should be reviewed by a specialist team unless there are locally agreed protocols for shared care. Carers view on the patient's condition at follow-up should be sought.

PACEF Comment:
The requirement for specialist initiation means that all four of these drugs are designated AMBER within licensed indications (subject to NICE constraints). The need for regular and complex monitoring has necessitated a review of local shared care arrangements. An updated shared care guideline is in preparation and will be available shortly.

- When prescribing an AChE inhibitor, treatment should be started with the drug of lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started. However an alternative AChE inhibitor could be prescribed if considered appropriate when taking into account adverse event profile, expectations about adherence, medical co morbidity, possibility of drug interactions and dosing profiles.

A cost comparison of the available AChE inhibitors reveals the following:

	Daily maintenance dose	Cost / 28 days
Donepezil	10-mg	£83.89
Donepezil orodispersible	10mg	£83.89
Galantamine	8-12mg twice daily	£68.32 -£84.00
Galantamine modified release	16-24mg daily	£64.90 -£79.80
Rivastigmine	3-6mg twice daily	£66.50
Rivastigmine patches	4.6mg-9.5mg once every 24 hours	£72.77
Memantine	10-20mg	£34.50 – £69.01

PACEF Comment:
There is insufficient evidence to differentiate in terms of clinical efficacy and cost-effectiveness between the various AChE inhibitors. Galantamine and rivastigmine are currently the lowest cost AChE inhibitors depending on the dose used. However, the patents on all three AChE inhibitors are due to expire in 2012: galantamine (January 2012), donepezil (February 2012) and rivastigmine tablets (July 2012). The memantine patent does not expire until April 2014. Memantine is not cost effective compared to AChE inhibitors in moderate disease and should not be used preferentially to AChE inhibitors for this indication. Memantine is cost effective in people with severe AD, although the average incremental cost-effectiveness ratio (ICER) is relatively high (£26,500 per QALY gained).

PACEF Recommendations:
All three of the available AChE inhibitors are approved for use for the treatment of mild to moderate dementia in Alzheimer's disease. Standard release oral formulations are recommended first line. Memantine has a second line role in moderate AD in patients intolerant to AChE inhibitors or where their use is contraindicated on clinical grounds. Memantine is also the only licensed treatment for severe AD and is particularly useful for those exhibiting behavioural symptoms (e.g. agitation, aggression and/or psychotic symptoms). Standard release memantine tablets are the preferred formulation. All of these drugs are designated AMBER and should only be initiated by a specialist within licensed indications and NICE restrictions. The existing shared care guideline is in the process of being updated to reflect these changes. All of the AChE inhibitors are due for patent expiry in 2012, with lower cost generic formulations to follow.

NICE TECHNOLOGY APPRAISAL 219: *EVEROLIMUS FOR THE SECOND-LINE TREATMENT OF ADVANCED RENAL CELL CARCINOMA* (APRIL 2011)

The NICE recommendations are as follows:

- Everolimus is not recommended for the second-line treatment of advanced renal cell carcinoma.

PACEF Recommendation:
Everolimus tablets (Afinitor) are designated RED-RED for the treatment of advanced renal cell carcinoma.

NICE TECHNOLOGY APPRAISAL 220: *GOLIMUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS (*APRIL 2011)

The NICE recommendations are as follows:

Golimumab is recommended as an option for the treatment of active and progressive psoriatic arthritis in adults only if:

- it is used as described for other tumour necrosis factor (TNF) inhibitor treatments in 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis' (NICE TA199).

The implications of this are as follows:

1. Etanercept, infliximab, golimumab and adalimumab are all recommended by NICE for the treatment of adults with active and progressive psoriatic arthritis when the following criteria are met
    - The person has peripheral arthritis with three or more tender joints and three or more swollen joints, and
    - The psoriatic arthritis has not responded to adequate trials of at least two standard disease-modifying antirheumatic drugs (DMARDs), administered either individually or in combination.

2. Treatment as described in (1) should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose). This may need to be varied for individual patients because of differences in the method of administration and treatment schedules.
3. Etanercept, adalimumab, golimumab or infliximab treatment should be discontinued in people whose psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 12 weeks. An adequate response is defined as an improvement in at least two of the four PsARC criteria, (one of which has to be joint tenderness or swelling score) with no worsening in any of the four criteria. People whose disease has a Psoriasis Area and Severity Index (PASI) 75 response at 12 weeks but whose PsARC response does not justify continuation of treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see 'Etanercept and efalizumab for the treatment of adults with psoriasis' [NICE TA 103], 'Infliximab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 134] and 'Adalimumab for the treatment of adults with psoriasis' [NICE technology appraisal guidance 146] for guidance on the use of tumour necrosis factor [TNF] inhibitors in psoriasis).

PACEF Recommendation:
Golimumab injection (Simponi) is designated RED for the treatment of active and progressive psoriatic arthritis. Decision making in relation to the least expensive drug within this context is dependent upon secondary care acquisition and administration costs and choice will be determined in conjunction with ULHT Drug and Therapeutics Committee.

NICE TECHNOLOGY APPRAISAL 221: *ROMIPLOSTIM FOR THE TREATMENT OF CHRONIC IMMUNE (IDIOPATHIC)THROMBOCYTOPENIC PURPURA* (APRIL 2011)

The NICE recommendations are as follows:

Romiplostim is recommended for the treatment of adults with chronic immune (idiopathic) thrombocytopenia purpura:

- whose condition is refractory to standard active treatments and rescue therapies **or**
- who have severe disease and a high risk of bleeding that needs frequent courses of rescue therapies
- **and** if the manufacturer makes romiplostim available with the discount agreed as part of the patient access scheme.

Only a haematologist should start and supervise treatment with romiplostim.

PACEF Recommendation:
Romiplostim injection (Nplate) is designated RED for the treatment of chronic immune (idiopathic) thrombocytopenia purpura within NICE restrictions.

NICE TECHNOLOGY APPRAISAL 222: *TRABECTEDIN FOR THE TREATMENT OF RELAPSED OVARIAN CANCER* (APRIL 2011)

The NICE recommendation is as follows:

Trabectedin in combination with pegylated liposomal doxorubicin hydrochloride (PLDH) is not recommended for the treatment of women with relapsed platinum-sensitive ovarian cancer.

PACEF Recommendation:
Trabectedin injection (Yondelis) is designated RED-RED for the treatment of relapsed platinum-sensitive ovarian cancer in combination with pegylated liposomal doxorubicin. It has been previously approved by NICE for the treatment of advanced soft tissue sarcoma and is designated RED for this indication.

NEW TRIALS IN BRIEF

HIGHER DOSES OF LEVOTHYROXINE AND FRACTURE RISK

A cohort of 213,511older adults (aged 70 to 105) taking levothyroxine between 2002 and 2007 was identified from a Canadian healthcare database. Fracture cases were matched with up to 5 controls by age, sex and duration in the cohort. The study found that higher doses of levothyroxine (mean > 93mcg) were associated with a two–threefold increase in fractures compared with lower doses. Thyroid function was not assessed as part of the study.

PACEF Comment:
This observational study suggests an increased risk of fractures associated with levothyroxine treatment in older people, with a clear dose-response relationship. This seems biologically plausible given that hyperthyroidism is a known risk factor for osteoporosis and fractures. More research is needed, but prescribers should be mindful that doses of levothyroxine may need reducing as patients age. Review of elderly patients on levothyroxine 100microgram daily or more might be worthwhile, particularly of those with suppressed TSH concentrations.

Reference:
Turner M et al. Levothyroxine dose and risk of fractures in older adults: nested case-control study. *BMJ* 2011; 342:d2238 doi:10.1136/bmj.d2238

ANGIOTENSIN RECEPTOR BLOCKERS AND CARDIOVASCULAR RISK

This systematic review and meta-analysis of 37 Angiotensin Receptor Blocker (ARB) randomised controlled trials included 147,000 people and assessed cardiovascular risk associated with ARBs, in particular the possible association between ARBs and increased risk of myocardial infarction (MI). No association between ARBs and increased risk of MI was found when compared with controls. Similar results were reported for the individual outcomes of death, CV death and angina. ARBs were associated with reductions in risk of stroke, heart failure, and new onset diabetes compared with controls. This analysis did not include the recent studies of olmesartan to reduce microalbuminuria which identified an increased risk of CV death with olmesartan (see *PACE Bulletin*, Vol 5, No 9 (May 2011).

PACEF Comment:
A trial comparing valsartan and amlodipine published in 2004 suggested that ARB treatment increased the risk of MI compared to control therapy. This more recent meta-analysis did not confirm an increased risk of MI with ARB treatment compared to an active comparator or placebo. However, this study does not negate recent concerns over olmesartan and CV risk as the relevant olmesartan studies were not included in this analysis.

Reference:
Bangalore S et al. Angiotensin receptor blockers and risk of myocardial infarction: meta-analyses and trial sequential analyses of 147 020 patients from randomised trials. *BMJ* 2011; 342:d2234 doi:10,1136/bmj.d2234

NEWS IN BRIEF

NEW ADVICE ON DRUG INTERACTIONS AND HORMONAL CONTRACEPTION

- New guidance on drug interactions and hormonal contraception has been published by the Faculty of Sexual and Reproductive Healthcare (a division of the Royal College of Obstetricians and Gynaecologists).
- Serum concentrations of contraceptive hormones may be increased or decreased by concurrent drug use; hormonal contraceptives may themselves affect serum concentrations of concomitant drugs.

New advice is as follows:

- **Additional contraceptive precautions are not required during or after courses of antibacterials that do not induce enzymes. Rifampicin- like drugs (e.g. rifampicin, rifabutin) are the only antibacterials that are enzyme inducers and that have consistently been shown to reduce serum concentrations of ethinyloestradiol. There is no evidence to support the theory that broad spectrum antibacterials can precipitate contraceptive failure.**
- There is no consistent evidence supporting an interaction between hormonal contraception and coumarin anticoagulants (e.g. warfarin).
- All women starting enzyme inducing drugs should be advised to use a reliable contraceptive method unaffected by enzyme inducers.
- Griseofulvin is no longer considered to be a clinically important enzyme inducer.
- Combined hormonal contraception is not recommended in women on lamotrigine monotherapy due to the risk of reduced seizure control and the potential for lamotrigine toxicity during the seizure free week.
- Lansoprazole is no longer listed as an enzyme inducing drug.
- Ulipristal acetate (ellaOne) has the potential to reduce the efficacy of other hormonal contraception.

Reference:
Drug and Therapeutic Bulletin Select 3, April 2011

PROTON PUMP INHIBITORS: TOO MUCH OF A GOOD THING?

- Nationally, PPI prescribing continues to escalate: during the first quarter of 2010, 9 million prescriptions were issued nationally, an increase of 79% on 2005.
- There is accumulating published evidence suggesting harms associated with long-term use.

- An observational study involving 130,487 postmenopausal women followed up for almost 8 years found that PPIs were associated with a modest increase in the rate of spine, lower arm and total fractures.
- A pharmaco-epidemiological study of over 100,000 hospital discharges suggested that more intensive acid suppression increased the likelihood that hospital inpatients would develop nosocomial *Clostridium difficile* (by 70% in PPI users compared with non-users). A further retrospective cohort study of 1,166 patients treated with antibiotics for *C.difficile* suggested that concurrent PPI use increased the likelihood of recurrence of infection by around 40%.
- A systematic review has linked the use of acid suppressant drugs with increased risk of pneumonia.

PACEF Comment:
PPIs should not be prescribed long-term or in high doses without regular review and discussion of risks and benefits with the patient.

Reference:
DTB, Vol 49, No 5, May 2011

GABAPENTIN FOR NEUROPATHIC PAIN

- An updated Cochrane systematic review has reassessed the use of gabapentin in neuropathic pain. The review included data from 29 randomised placebo controlled trials involving 3,751 patients with a chronic pain condition (such as postherpetic neuralgia, diabetic neuropathy, fibromyalgia).
- The review found that more patients on gabapentin (in doses of at least 900mg daily) experienced substantial improvement or at least moderate improvement compared to placebo.
- More patients on gabapentin 1200mg or more daily withdrew due to an adverse event (number needed to harm 32) with somnolence, dizziness, peripheral oedema and ataxia or gait disturbance occurring more often with gabapentin than placebo.
- Gabapentin emerges as a reasonably effective treatment for a variety of neuropathic pain conditions, although over 50% of those treated will not have worthwhile pain relief.

PACEF Comment:
This review tends to support the role for gabapentin recently advocated in the PACEF Neuropathic Pain guidance.

Reference:
DTB Select, 4, May 2011

DOPAMINE AGONISTS FOR RESTLESS LEGS SYNDROME

- Restless legs syndrome (RLS) is a sensorimotor disorder, usually chronic, which is characterised by an urge to move the limbs, associated with unpleasant sensations (e.g. feelings of burning, tickling or crawling, pain, cramping, numbness or weakness). Symptoms are worse at rest and at night and improve with movement.
- A Cochrane systematic review has been undertaken including data from 35 placebo controlled and 3 active controlled randomised trials, involving a total of 7,365 patients with moderate to very severe RLS.
- It found that dopamine agonists reduced the duration and severity of symptoms to a clinically relevant extent and improved sleep quality and quality of life with

small to moderate effect sizes. The drugs included in the review were pramipexole, ropinirole and rotigotine (all licensed in the UK for RLS), cabergoline and pergolide (licensed in the UK for Parkinson's disease, but not RLS) and lisuride. The most effective drugs were cabergoline and pergolide.

- The *DTB* conclude that dopamine agonists are worth a try in patients with severe symptoms of RLS. However, augmentation of symptoms has been reported in 20-30% of patients taking pramipexole or pergolide. Ergot derived dopamine agonists (cabergoline, lisuride and pergolide) have been associated with pulmonary, retroperitoneal and pericardial fibrosis; patients taking these drugs should be monitored for breathlessness, persistent cough, chest pain, cardiac failure and abdominal pain or tenderness.

PACEF Comment:
In response to this, PACEF intend to review the Traffic Light classification and existing arrangements for the prescribing of RLS treatments in Lincolnshire.

Reference:
DTB Select, 4, May 2011

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY: *DRUG SAFETY UPDATE* (MAY 2011)

PRASUGREL: RARE BUT SERIOUS HYPERSENSITIVITY REACTIONS

Prasugrel is indicated for the prevention of atherothrombotic events in patients with acute coronary syndrome.

- Prasugrel (Efient) has been rarely associated with reports of serious hypersensitivity reactions including, very rarely, angioedema, some of which occurred in patients with a history of hypersensitivity to clopidogrel.
- As of April 2011, nine cases have been reported worldwide in association with use in approximately 727 000 patients.
- At present the mechanism for these allergic reactions are unclear. The time to onset of symptoms ranged from immediately after treatment to up to 5-10 days later.

The MHRA have issued the following advice to healthcare professionals:

- Prescribers should be aware of the potential risk of rare but serious hypersensitivity reactions with prasugrel and should monitor for signs in all patients, including those with a previous known history of hypersensitivity reactions to thienopyridines.
- When prescribing prasugrel, inform patients of the potential risk of hypersensitivity reactions, including angioedema.
- All healthcare professionals are reminded to report all suspected adverse reactions with prasugrel through the Yellow Card Scheme.

Advice for patients:

- Patients should inform their doctor immediately if they experience symptoms suggesting hypersensitivity or allergic reaction (e.g. swelling of the face, neck, tongue, lips or throat, rash, itching or shortness of breath).

PACEF Comment:
NICE TA 182 (October 2009) recommends prasugrel in combination with aspirin as an option for preventing atherothrombotic events in people with acute coronary syndromes having percutaneous coronary intervention only when:

- **immediate primary percutaneous coronary intervention for ST-segment-elevation myocardial infarction is necessary or**
- **stent thrombosis has occurred during clopidogrel treatment or**
- **the patient has diabetes mellitus.**

Prasugrel is classified as a RED drug approved for use within secondary care, tertiary care or a primary care hosted specialist service only and should not be routinely prescribed in primary care.

SHARED CARE GUIDELINES

PACEF have approved two new shared care guidelines:

Hydroxychloroquine in Rheumatology
Methylphenidate, atomoxetine and dexamfetamine in the management of Attention Deficit Hyperactivity Disorder

Copies are available through the NHS Lincolnshire website (www.lincolnshire.nhs.uk) or from Cathy Johnson, Interface Lead Pharmacist on cathy.johnson@lpct.nhs.uk

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