NHS Lincolnshire

Prescribing and Clinical Effectiveness Bulletin

Volume 6; Number 12 **August 2012**

What's new this month?

- **Several adverse incidents have occurred in Lincolnshire related to the prescribing, dispensing and administration of zuclopenthixol acetate injection (Clopixol Acuphase) to patients intended to receive zuclopenthixol decanoate injection (Clopixol Depot/Clopixol Conc). Zuclopenthixol acetate injection (Clopixol Acuphase) is designated RED and should only be prescribed through specialist mental health services and confined within secondary care. All requests to GPs to prescribe zuclopenthixol acetate or Clopixol Acuphase should be refused. All requests to prescribe an unspecified salt of zuclopenthixol should be clarified and confirmed as decanoate. All prescriptions for zuclopenthixol acetate or Clopixol Acuphase presented to community pharmacists or GP dispensary staff should be verified with the prescriber. Within this context, zuclopenthixol acetate (Clopixol Acuphase) is designated RED. Zuclopenthixol decanoate (Clopixol Depot/Clopixol Conc) remains appropriate for GP prescribing and is designated AMBER (see page 3).**
- **Following the patent expiry of Lipitor, low cost generic atorvastatin is now available. Updated information on cost in comparison to alternative agents is provided (see page 4).**
- **Ivabradine (Procoralan) is approved for use in the treatment of stable congestive heart failure. Designation: AMBER (without shared care) (see page 5).**
- **Exenatide (Byetta) has been approved for use in combination with insulin in the treatment of type 2 diabetes mellitus. Designation: AMBER (without shared care) (see page 6).**
- **The risk of serious ventricular arrhythmias or sudden cardiac death with domperidone *may* be higher in patients over 60 and in *any* patient on a dose higher than 30mg per day. MHRA advice is reviewed (see page 8).**
- **Prescribers are urged to review all patients on strontium ranelate with the intention to stop therapy in those who have a current or previous VTE (including deep vein thrombosis or pulmonary embolism) or are temporarily or permanently immobilized and/or aged 80 or over. The need for continued strontium treatment should be re-evaluated in those over 80 years of age who have been diagnosed at risk of VTE (see page 9).**
- **All oral tacrolimus products should be prescribed and dispensed by brand name in future to avoid the risk of medication errors (see page 9).**
- **Recent changes to the *Drug Tariff* are explained (see page 10).**

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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: *JUNE/JULY 2012 UPDATE*

Drug	Indication(s)	Traffic Light Status
Exenatide injection 5 microgram and 10 microgram (Byetta)	Licensed for use with insulin with or without metformin and/or pioglitazone for type 2 diabetes mellitus inadequately controlled by these agents.	AMBER (without shared care)
Ivabradine tablets 5mg and 7.5mg (Procoralan)	Licensed for the treatment of stable congestive heart failure (NYHA class II to IV) with systolic dysfunction in patients in sinus rhythm with heart rate ≥75 beats per minute (bpm) in combination with a beta-blocker (BB) or when BB therapy is contraindicated or not tolerated.	AMBER (without shared care)
Zuclopenthixol acetate injection 50mg/1ml (1ml and 2ml) (Clopixol Acuphase)	Licensed for the *initial* treatment of acute psychoses including mania and exacerbation of chronic psychoses, particularly where a *rapid onset of action* and a duration of effect of two to three days is desirable.	RED
Zuclopenthixol decanoate injection 200mg/1ml (Clopixol Depot) and 500mg/ 1ml Clopixol Conc)	Licensed for the *maintenance* treatment of schizophrenia and paranoid psychoses.	AMBER (without shared care)

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.**

RISK TO PATIENTS OF INAPPROPRIATE USE OF ZUCLOPENTHIXOL ACETATE INJECTION (*CLOPIXOL ACUPHASE*) WHERE ZUCLOPENTHIXOL DECANOATE INJECTION (*CLOPIXOL*) WAS INTENDED

A number of patient-related incidents have occurred in Lincolnshire as a result of zuclopenthixol acetate injection (*Clopixol Acuphase*) being prescribed, dispensed and administered where zuclopenthixol decanoate injection (*Clopixol*) was intended.

Zuclopenthixol acetate (*Clopixol Acuphase*) is licensed for:

- the *initial* treatment of acute psychoses including mania and exacerbation of chronic psychoses, particularly where a *rapid onset of action* and a duration of effect of two to three days is desirable.

It is not intended for long-term use and duration of treatment should not be for more than two weeks. The maximum accumulated dosage in a course should not exceed 400mg and the number of injections should not exceed four. **Zuclopenthixol acetate (*Clopixol Acuphase*) is shorter acting and more sedating than zuclopenthixol decanoate (*Clopixol*) and should only be prescribed through specialist mental health services and confined within secondary care. It is designated RED and is not considered appropriate for GP prescribing or shared care.**

Where long-term treatment with zuclopenthixol is required, either zuclopenthixol dihydrochloride tablets (*Clopixol*) or zuclopenthixol decanoate injection (*Clopixol Depot/Clopixol Conc*) should be prescribed. **Zuclopenthixol decanoate injection (*Clopixol Depot/Clopixol Conc*) is designed for *long-term maintenance* therapy. It is licensed for the *maintenance* treatment of schizophrenia and paranoid psychoses. Zuclopenthixol decanoate injection (*Clopixol Depot/Clopixol Conc*) is considered appropriate for prescribing by GPs subject to specialist initiation and regular review; no shared care guideline is in place at this time.**

Summary

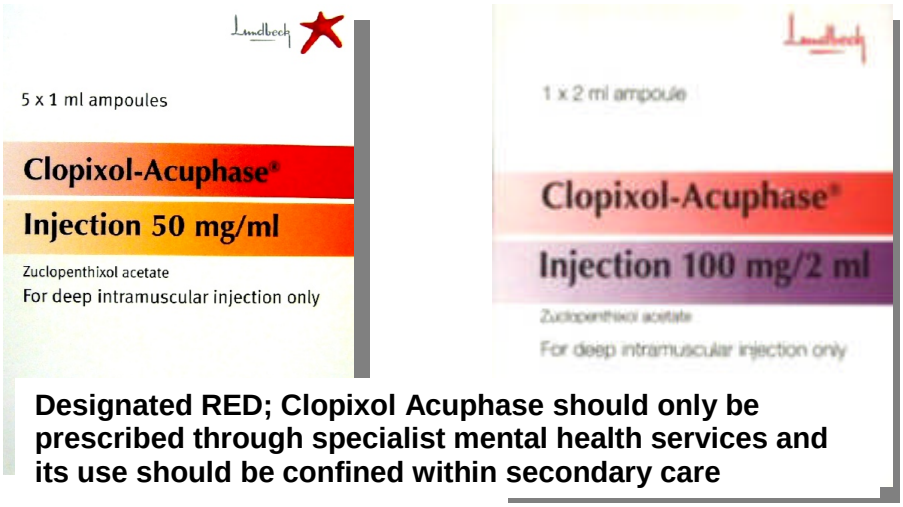
	Zuclopenthixol acetate (*Clopixol Acuphase*)	Zuclopenthixol decanoate (Clopixol)
Duration of action	2 to 3 **days**	2 to 4 **weeks**
Peak	24 to 40 hours	4 to 9 days
Half-life	32 hours +/- 7 hours	17 – 21 days

Know Your Zuclopenthixol (Clopixol)

Zuclopenthixol Acetate (Clopixol Acuphase)

For the *initial* treatment of acute psychoses including mania and exacerbation of chronic psychoses, particularly where a rapid onset of action, and a duration of effect of 2-3 days is desirable.

Short-term



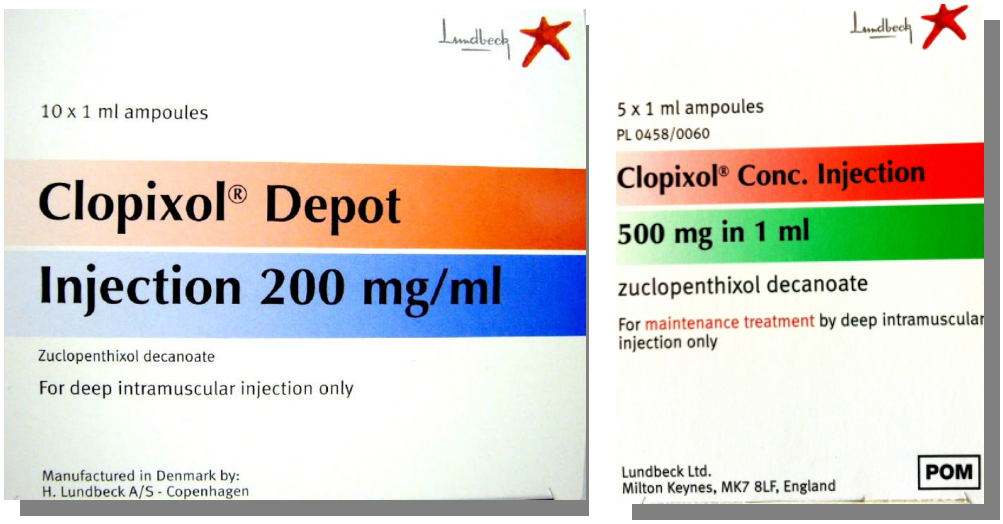
Designated RED; Clopixol Acuphase should only be prescribed through specialist mental health services and its use should be confined within secondary care

Clopixol Acuphase preparations are for short-term use only

Zuclopenthixol Decanoate (Clopixol)

For the *maintenance* treatment of schizophrenia and paranoid psychoses.

Long-term



Clopixol Depot and Clopixol Conc are for long-term maintenance therapy

PACEF Recommendation:

Zuclopenthixol acetate (*Clopixol Acuphase*) is designed for the *initial* treatment of acute psychoses including mania and exacerbation of chronic psychoses, particularly where a *rapid onset of action* and a duration of effect of two to three days is desirable; it has no role in primary care prescribing and is not supported by shared care guidance. The risk of confusion between zuclopenthixol acetate injection (*Clopixol Acuphase*) and zuclopenthixol decanoate injection (*Clopixol Depot* or *Clopixol Conc*) is extremely high with significant risk of harm to the patient if a mistake occurs. As a result of this, zuclopenthixol acetate injection (*Clopixol Acuphase*) has been designated RED; it should only be prescribed through specialist mental health services and its use should be confined within secondary care. All requests to GPs to prescribe zuclopenthixol acetate injection (*Clopixol Acuphase*) should be challenged and referred back to specialist mental health services. All community pharmacists and GP dispensary staff are urged to verify all prescriptions for zuclopenthixol acetate injection (*Clopixol Acuphase*) with the prescriber on the basis that they are likely to have been issued in error. Care should be taken to ensure that all future prescriptions clearly specify the full approved name of the drug including salt (i.e. zuclopenthixol decanoate injection). Long-term maintenance depot antipsychotic therapy remains appropriate for GP prescribing and zuclopenthixol decanoate injection (*Clopixol Depot* or *Clopixol Conc*), the licensed product, is designated AMBER (without shared care) for this purpose. Prescribers are reminded that any patient currently prescribed depot antipsychotic therapy should be reviewed annually by their supervising psychiatrist. Any patient currently prescribed an antipsychotic depot injection who has not been reviewed at least annually should be urgently identified by their GP and referred back to specialist mental health services for the appropriate review.

Prescribers are particularly cautioned around the risks of antipsychotic drugs in the treatment of patients with behavioural and psychological symptoms of dementia (BPSD). In *PACE Bulletin* Vol 6 No 10 (July 2012), we discussed the evidence that antipsychotic drugs are of limited benefit in these patients and their association with increased risk of stroke and death. Review of antipsychotic use for BPSD is a national priority. Prescribers are encouraged to review their use in accordance with NICE-SCIE guidance and the NICE Quality Standard on dementia.

GENERIC ATORVASTATIN PRICE REDUCTIONS

Since the patent expiry of atorvastatin (Lipitor) in May 2012, the NHS reimbursement prices of the various strengths of atorvastatin tablets have fallen as follows:

	May 2012 *Tariff*	June 2012 *Tariff*	August 2012 *Tariff*
Atorvastatin 10mg	£13.00 (28)	£3.25 (28)	£1.92 (28)
Atorvastatin 20mg	£24.64 (28)	£6.16 (28)	£2.66 (28)
Atorvastatin 40mg	£24.64 (28)	£6.16 (28)	£2.79 (28)
Atorvastatin 80mg	£28.21 (28)	£10.00 (28)	£4.17 (28)
Simvastatin 40mg	£1.19 (28)	£1.19 (28)	£1.20 (28)

The standard summary table of comparative 28 day cost, reduction in LDL cholesterol and total cholesterol and incidence of myopathy updates as follows:

Cost Comparison and Percentage Reductions in LDL Cholesterol and Total Cholesterol (August 2012)

Statin	28 day cost	Percentage reduction in LDL-C	Percentage reduction in total cholesterol	Incidence of myopathy
Atorvastatin 10mg	£1.92	37%	32%	0.4%
Atorvastatin 20mg	£2.66	43%	36%	0.4%
Atorvastatin 40mg	£2.79	49%	42%	0.4%
Atorvastatin 80mg	£4.17	55%	47%	0.5%
Pravastatin 40mg	£2.46	29%	29%	
Rosuvastatin 5mg	£18.03	38%	33%	0.2%
Rosuvastatin 10mg	£18.03	43%	37%	0.1%
Rosuvastatin 20mg	£26.02	48%	40%	0.1%
Simvastatin 40mg	£1.20	37%	31%	0.4%
Simvastatin 80mg	£2.05	42%	35%	0.9%

(Prices quoted are from the *Drug Tariff*, August 2012)

PACEF Comment:
PACEF plan to review local lipid modification guidance in the Autumn to reflect changing prices and the outcome of our recent review of ezetimibe. In the meantime, prescribers are reminded that generic simvastatin 40mg remains the preferred first line statin. For patients intolerant of simvastatin 40mg, pravastatin 40mg should be considered. Atorvastatin is the preferred high-potency statin and should be used in preference to rosuvastatin. Many practices are now in the process of switching existing rosuvastatin patients to equivalent dose atorvastatin where possible. It is acknowledged that some patients will need to remain on rosuvastatin due to tolerability problems with alternatives. The cost comparison above illustrates the significant difference in price between lower cost generically available statins and rosuvastatin; it also illustrates the lower incidence of myopathy with rosuvastatin that provides an evidence base for the residual role in those genuinely intolerant to alternative agents.

NEW INDICATION ASSESSMENTS

NEW INDICATION ASSESSMENT: *IVABRADINE (PROCORALAN) FOR THE TREATMENT OF CHRONIC HEART FAILURE*

In addition to an existing marketing authorisation for the treatment of angina, ivabradine (Procoralan) has now been licensed for the treatment of chronic heart failure (CHF). Specifically, the licensed indication is for stable CHF (NYHA class II to IV) with systolic dysfunction in patients in sinus rhythm with heart rate ≥75 beats per minute (bpm) in combination with a beta-blocker (BB) or when BB therapy is contraindicated or not tolerated.

PACEF reviewed the results of the Systolic Heart Failure treatment with I_f Inhibitor Ivabradine Trial (SHIFT), a randomised controlled trial involving 6,558 patients on optimum background standard treatment for heart failure who were randomised to receive either ivabradine or placebo twice daily. Ivabradine was started at 5mg daily for 14 days and titrated to 2.5mg to 7.5mg twice daily. Patient selection criteria ensured the trial population were adult patients with stable, symptomatic, moderate to severe chronic heart failure classed as NYHA class II-IV with a reduced left-ventricular fraction (LVEF) ≤35% and a heart rate of ≥70bpm. Patients were already receiving optimal background standard treatment for heart failure with 89% on BBs, 79% on ACE inhibitors and 14% on Angiotensin Receptor Blockers (ARBs) at baseline. The primary outcome was a composite of cardiovascular mortality or hospitalisation due to heart failure. Results showed a significant reduction in the number of hospital admissions for worsening of heart failure in those in the ivabradine group compared to placebo. However, unlike BBs, ivabradine was not shown to *significantly* affect cardiovascular mortality (ivabradine did reduce the incidence of CV death, but results were not statistically significant). Symptomatic bradycardia was a more significant problem in the ivabradine group than in the placebo group with a number needed to harm of 212 over 22.9 months,

Ivabradine is significantly more costly than almost any other standard therapy in use in the treatment of CHF:

Drug	**Daily dose range**	**Cost (£) pa**
Ivabradine	7.5mg twice daily	£507
Beta-blockers		
Bisoprolol	10mg daily	£15.08
Carvedilol	25mg twice daily	£20.80
Nebivolol	10mg once daily	£54.34
ACE inhibitors		
Captopril	150mg daily	£31.00
Cilazapril	5mg daily	£256.23
Enalapril	20mg twice daily	£29.12
Fosinopril	40mg once daily	£90.74
Lisinopril	35mg daily	£39.39
Perindopril	5mg daily	£107.50
Quinapril	40mg daily	£35.10
Ramipril	5mg twice daily	£31.72
Angiotensin Receptor Blockers		
Candesartan	32mg daily	£209.69
Losartan	300mg daily	£56.16
Valsartan	320mg daily	£137.02

However, the estimated number of patients potentially requiring the treatment in Lincolnshire is relatively low (25 to 50 in the first year rising to 180 in future years). In the economic model, the increased drug costs are offset by reduced hospital admission costs: the cost of an admission for heart failure is approximately £1,500 per bed day per patient.

PACEF Recommendation:

Ivabradine tablets 5mg and 7.5mg (Procoralan) may be an appropriate adjunct to optimal BB /ACEI therapy in patients unable to achieve sufficient heart rate reduction on standard therapy or for those in whom BBs are not tolerated or contraindicated and who still have a high pulse rate. As a result of this, ivabradine is approved for the treatment of CHF within the terms of its marketing authorisation (i.e. for stable CHF (NYHA class II to IV) with systolic

dysfunction in patients in sinus rhythm with heart rate ≥75 beats per minute (bpm) in combination with a beta-blocker (BB) or when BB therapy is contraindicated or not tolerated). Treatment should only be initiated by a physician who is experienced in the management of heart failure. Designation: AMBER (without shared care).

NEW INDICATION ASSESSMENT: *EXENATIDE (BYETTA) INJECTION IN COMBINATION WITH INSULIN IN TYPE 2 DIABETES MELLITUS*

Exenatide injection (Byetta) has been granted a license extension covering its use as an adjunct to basal insulin (either human or analogue) with or without metformin and/or pioglitazone in adults with type 2 diabetes mellitus who have not achieved adequate glycaemic control with these agents. The extension to the license was granted on the basis of a single short-term placebo controlled trial (duration 30 weeks) where 261 patients were randomised to receive either exenatide (138 patients) 5 microgram twice daily for 4 weeks and then 10 microgram twice daily thereafter or placebo injections (123 patients) within 60 minutes before morning and evening meals. Patients were aged over 18 years of age with type 2 DM and had been receiving insulin glargine at a minimum dose of 20 units per day alone or in combination with metformin or pioglitazone and had a HbA1c level of 7.1% to 10.5%, BMI 45 or less and a stable body weight (less than 5% change over 3 months). Investigators concluded that adding twice daily exenatide to an already established insulin regime improved glycaemic control without increased hypoglycaemia or weight gain. Adverse effects were more frequent in the exenatide group; the most common adverse effects in the exenatide group were nausea, vomiting, diarrhoea, headache or constipation.

Exenatide is the first Glucagon Like Peptide-1 (GLP-1) analogue to be licensed for use as an adjunct therapy with basal insulin. In the Summary of Product Characteristics (SPC) for liraglutide (Victoza) it states that the addition of liraglutide to the therapy of patients already treated with insulin has not been evaluated and is not recommended. Nonetheless, insulin determir (Levimer) is licensed to be used as an add-on therapy (as a single daily dose) to pre-existing liraglutide treatment.

PACEF Recommendation:
PACEF were concerned by the short duration of the trial and the wider paucity of published evidence to support the use of combination exenatide and insulin therapy in type 2 diabetes mellitus. Nonetheless, it was recognised that unlicensed combination therapy was already being prescribed in county by GPs at the request of diabetes specialists and that the availability of a licensed product would help to resolve existing and future medico-legal concerns around this increasing group of patients. As a result of this: exenatide injection (Byetta) was designated AMBER (without shared care) for this indication. Where combination GLP-1 analogue and insulin therapy is indicated, current licensed indications support the use of exenatide in preference to liraglutide (see above). PACEF intend to keep this therapy area under regular review as the range of licensed indications for existing products continues to expand and new products continue to appear.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY: DRUG SAFETY UPDATE (MAY 2012)

Fingolimod (Gilenya) and the risk of cardiovascular adverse reactions – new advice

Fingolimod 500 microgram tablets (Gilenya) are licensed for the treatment of relapsing remitting multiple sclerosis in patients whose disease has failed to respond to beta-interferons or is severe and getting worse rapidly. NICE have recently approved fingolimod for use within the NHS within licensed indications.

Safety concerns relating to fingolimod were first raised by the MHRA in February 2012. It is known that fingolimod causes transient bradycardia and heart block after the first dose. A world wide review of data found 15 cases of sudden or unexplained death associated with fingolimod. Most of the deaths occurred in patients with a history of cardiovascular disease or in those taking other medicines. However, review of the data has not conclusively confirmed that fingolimod was the direct cause of the deaths.

Updated advice for healthcare professionals is as follows:

Fingolimod is not recommended in the following patients:

- Those with second degree Mobitz type II or higher atrioventricular block, sick sinus syndrome or sino-atrial block.
- Those with significant QT prolongation (QTC >470ms in women and >450ms in men).
- Those with a history of symptomatic bradycardia or recurrent syncope, known ischaemic heart disease, cerebrovascular disease, history of myocardial infarction, congestive heart failure, history of cardiac arrest, uncontrolled hypertension or severe sleep apnoea.
- Those receiving treatment with anti-arrhythmic or heart rate lowering drugs

The MHRA have also updated the monitoring guidance following administration of the first dose.

- The maximum effect of fingolimod on decreasing heart rate occurs within six hours of the first dose. All patients should be monitored before, during and after the first 6 hours of treatment.
- If the patient's heart rate decreases to its lowest point at the end of the 6 hour treatment period, then monitoring should be extended until the heart rate increases.
- Monitoring may also need to be extended, at least overnight, if significant atrioventricular block, bradycardia or QTc prolongation occurs.

PACEF Comment:
PACEF in conjunction with United Lincolnshire Hospitals Trust are in the process of reviewing NICE TA 254 *Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis* (April 2012). At present, fingolimod remains RED-RED for this indication, although specialist prescribing within NICE proscribed criteria is likely to be approved later in the summer.

Domperidone –small risk of serious ventricular arrhythmia and sudden cardiac death.

Domperidone is a dopamine antagonist with antiemetic properties. It is normally prescribed for the treatment of nausea, vomiting, epigastric fullness, upper abdominal discomfort and regurgitation of gastric contents in adults. Lower dose products are

also sold over the counter from community pharmacies for the relief of minor gastrointestinal symptoms.

QT prolongation and ventricular arrhythmia are known cardiac risks for all domperidone products. A recent Europe wide study found the domperidone may be associated with a small increased risk of sudden cardiac death or ventricular arrhythmias; these risks may be higher in patients older than 60 years of age and in patients receiving daily doses of more than 30mg.

The MHRA have issued the following advice to health care professionals:

- Domperidone should be used at the lowest effective dose.
- Over-the-counter domperidone, sold under the supervision of a pharmacist, should not be supplied to people with underlying cardiac disease.
- Prescribers should exercise caution if prescribing for: (1) patients who have existing prolongation of cardiac conduction intervals (particularly QTc); (2) those with significant electrolyte disturbances; (3) those with underlying cardiac disease such as congestive heart failure. Particular caution is urged in those over the age of 60 years and those on daily doses in excess of 30mg.
- Domperidone use should be avoided in patients taking concomitant medication that prolongs the QT interval such as ketoconazole or erythromycin.
- Patients should be advised to seek prompt medical attention if symptoms such as syncope or tachyarrhythmias appear during treatment.

PACEF Recommendation:
The risk of serious ventricular arrhythmias or sudden cardiac death with domperidone *may* be higher in patients over 60 and in *any* patient on a dose higher than 30mg per day. Particular care should be taken where patients are taking domperidone in combination with concomitant medication known to cause QT prolongation or where the person has pre-existing cardiac disease or known electrolyte disturbances. In many patients, the benefits of domperidone therapy will continue to outweigh the risks as long as the risks have been minimised through dosage reduction and the elimination of potentially interacting concurrent medication. Community pharmacies should no longer sell OTC domperidone to any patient with underlying cardiac disease and questions related to this must be incorporated into the discussion with the patient/carer at the time of OTC sale.

Strontium ranelate - risk of venous thromboembolism

Strontium ranelate (Protelos) is licensed for the treatment of osteoporosis in postmenopausal women to reduce the risk of vertebral and hip fractures.
It is known to increase the risk of venous thromboembolic events (VTEs) and is also associated with serious skin reactions. The benefits of strontium ranelate have been reviewed in a study published in France. This reported that cardiovascular events (mainly VTE's) account for 52% of all post marketing reports of adverse events associated with strontium ranelate treatment and skin reactions for 26%. The risk of VTEs appears to be greater in patients who are permanently or temporarily immobilised and also appears to be greater in those aged over 80 years of age. In terms of serious skin reactions, the risk of serious hypersensitivity reactions such as DRESS (Drug Rash with Eosinophillia and Systemic Symptoms), Steven-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) is low.

Considering the potential severity of these adverse events the MHRA have issued the following advice to healthcare professionals:

- Strontium should not be used in patients with a current or previous VTE including deep vein thrombosis or pulmonary embolism and or patients with temporary or permanent immobility (e.g. post surgery recovery or prolonged bed rest).
- The need for strontium treatment should be re-evaluated in those over 80 years of age who have been diagnosed at risk of VTE.
- Patients should be advised of the likely time to onset of serious skin reactions. The highest risk for SJS or TEN is within the first few weeks of treatment and for DRESS 3-6 weeks.
- Patients should be aware of the symptoms and signs of these severe skin reactions and be advised to stop treatment and seek immediate medical advice if they occur.

PACEF Recommendation:
Prescribers are urged to review all patients on strontium ranelate with theintention to stop therapy in those who have a current or previous VTE (including deep vein thrombosis or pulmonary embolism) or are temporarily or permanently immobilized and/or aged 80 or over. The need for continued strontium treatment should be re-evaluated in those over 80 years of age who have been diagnosed at risk of VTE.

COMMISSION ON HUMAN MEDICINES: *ORAL TACROLIMUS PRODUCTS SHOULD BE PRESCRIBED AND DISPENSED BY BRAND NAME TO AVOID THE RISK OF MEDICATION ERRORS* (MAY 2012)

The Commission on Human Medicines have written to all healthcare professional with the following advice:

- Prescribers should prescribe oral tacrolimus products by brand name only. When prescriptions have previously been written using the generic name, the brand on which the patient is stabilised should be established to ensure that the patient is supplied with the same product.
- If a prescriber intends to switch between any tacrolimus brands, careful medical supervision and therapeutic monitoring are required.
- Pharmacists should always dispense the exact brand prescribed. They should contact the prescriber if the prescription is not clear to ensure the appropriate medicine is dispensed.
- Patients should be advised to take careful note of the name of their usual tacrolimus brand and should check with their doctor or pharmacist if they receive a different brand or if they have any other questions about the prescription (e.g. about the dose).

PACEF Comment:
At present, 38% of all prescribing of tacrolimus products in Lincolnshire is generic. Prescribers are urged to ensure that all remaining generic prescriptions for tacrolimus are reviewed with a view to establishing the brand regularly supplied and specifically designating that brand name on all future prescriptions for that patient.

UPDATED SHARED CARE GUIDELINES

The following shared care guidelines have been reviewed, updated and approved by PACEF. All requests from specialists at ULH to enter into shared care should be accompanied by a copy of the relevant local shared care guideline. Copies are also

available to download from the NHS Lincolnshire website (www.lincolnshire.nhs.uk). Click on Commissioning and follow the links to PACEF.

- Shared Care Guideline (SCG): *Sirolimus for Maintenance of Immunosuppression after Kidney Transplantation in Adults*
- SCG: *Tacrolimus for Maintenance of Immunosuppression after Kidney Transplantation in Adults*
- SCG: *Cinacalcet in the management of secondary hyperparathyroidism in adult patients with end-stage renal disease on dialysis*
- SCG: *Lanthanum in the management of hyperphosphataemia in adult patients receiving haemodialysis or periotoneal dialysis who did not respond to or were unable to tolerate treatment with sevelamer and for controlling hyperphosphataemia associated with chronic kidney disease (CDKD)*
- SCG: *Mycophenolate mofetil or mycophenolic acid for maintenance of immunosuppression after kidney transplantation in adults*
- SCG: *Sevelamer in the management of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis and for controlling hyperphosphataemia associated with chronic kidney disease (CKD)*

CHANGES TO THE *DRUG TARIFF*: APRIL AND JULY 2012

A number of changes to the *Drug Tariff* have been introduced in both April and July 2012; these changes have been made to simplify reimbursement arrangements, reduce endorsement requirements needed to claim payment and to help improve pricing accuracy. It is the purpose of this *PACE Bulletin* feature to detail key changes that may affect Lincolnshire prescribers and community pharmacies.

Changes to Community Pharmacists' Terms of Service

From the 1st of July if there is a patient pack available to fit the exact specification on the prescription, the contractor is required to supply it, if reasonable to do so. For example, if a prescription specifies 100 paracetamol tablets 500mg, the contractor could reasonably be expected to supply the 100 tablet pack rather than 3 x 32 pack plus 4 tablets snipped from a blister pack. These changes to the Terms of Service are further supported by the recent simplification of the *Tariff.*

Simplification of the *Drug Tariff*, April 2012

The following changes were introduced in the April 2012 *Tariff*:

- Purified water is no longer reimbursable unless specifically listed on a prescription.
- There is no longer a separate payment for dropper bottles, separate droppers or vaginal applicators. The consumable allowance (formerly known as the container allowance) now covers dropper bottles, separate droppers or vaginal applicators.
- Diluents will no longer be reimbursed unless specifically prescribed. For example, diamorphine powder for injection will be supplied without diluent unless the prescription includes it. Where a diluent is required but not prescribed, the pharmacist will need to contact the prescriber to request another prescription for the diluent (e.g. water for injection 2ml).
- When the quantity reconstituted from an original pack or packs is unavoidably greater than the quantity ordered and the contractor is unable to use the remainder to fill another prescription, payment will be based on the nearest pack or number of packs. For example, a prescription for 140ml amoxicillin125mg in

5ml oral suspension will result in the contractor being reimbursed for 2 x 100ml amoxicillin125mg in 5ml oral suspension (unless the contractor can use the remainder to fill another prescription).

PACEF Comment
Prescribers need to be mindful of the need to prescribe the diluent concurrently with the product to be diluted if they wish to avoid the inconvenience of having to issue a subsequent prescription for diluent or having to intervene where a product without the apporopriate diluent has been supplied.

Simplification of the *Drug Tariff,* July 2012

The following changes were introduced in the July 2012 *Tariff*:

- The consumable allowance (formerly known as the container allowance) has fallen from 3.24p to 1.24p. The consumable allowance is intended to cover, where necessary, the provision of a suitable container, a 5ml plastic spoon, a plastic oral syringe, a dropper bottle, a dropper or vaginal applicator (see above) and, in very exceptional circumstances, or where requested by the prescriber, dilution. Payment for consumables and containers is payable to pharmacy contractors only.
- Payment for containers will be at a rate of 10p for every prescription (except special containers) where the quantity ordered is outside the pack size. This has been termed the 'splitting fee'. An example would be a prescription for 30 clopidogrel 75mg tablets; the pack size in the Tariff is 28 and in order to give 30 the contractor will need to split another pack by providing an additional 2 tablets snipped from a blister strip from another pack. As stated above, revised terms of service now require the contractor to supply the exact quantity specified on the prescription.
- Anomalies around reimbursement prices for different pack sizes of the same medicine have been removed. The worked examples below illustrate this for four key products

Worked Examples (July 2012)

Drug	*Pack Size*	*Basic Price*	*Cost*
Aqueous cream	100g	£1.08	1.08p per gram
Aqueous cream	500g	£5.41	1.08p per gram
Co-codamol 8mg/500mg tablets	30	£1.10	3.66p per tablet
Co-codamol 8mg/500mg tablets	100	£3.66	3.66p per tablet
Paracetamol 500mg tablets	32	£0.90	2.8p per tablet
Paracetamol 500mg tablets	100	£2.81	2.8p per tablet

- This has removed some of the anomalies that made it more profitable for contractors to supply 5 x 100g tubes of Aqueous Cream rather than 1 x 500g tub or 3 x 32 (plus 4) paracetamol 500mg tablets rather than 1 x 100. In supplying the exact quantity on the prescription the patient should now receive most commonly the patient pack equating exactly to that quantity. This will not the preclude the

patient from requesting an alternative pack size (e.g. 5 x 100g tubes of aqueous cream) where they find this more convenient.

PACEF Comment:
Historically prescribers have been frustrated by the multiple packs being supplied in response to scripts for standard patient packs available on the *Tariff*. Recent changes should resolve most of these issues and should result in a patient pack being supplied wherever practical.

- From April 1st changes to payments for methadone oral liquid mean that the pharmacist will be paid per interaction with the client (i.e. if the patient collects twice a week, the contractor will receive two methadone fees (£4.05 for each methadone script). Each instalment dispensed will also attract a dispensing fee and a Controlled Drug fee.
- Out of Pocket expenses will only be paid in excess of 50p.
- Broken bulk can still be claimed for anything in Category C. In categories A and M, broken bulk can only be claimed if the cost of the smallest pack size is less than £50.

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