NHS Lincolnshire

Prescribing and Clinical Effectiveness Bulletin

Volume 4; Number 12 **August 2010**

What's new this month:

- **After review, oxycodone/naloxone prolonged release tablets (Targinact) continue to be designated RED-RED (see page 2).**
- **Degarelix acetate injection (Firmagon), a new treatment for advanced hormone dependent prostate cancer, has been designated RED-RED (see page 3).**
- **Sitagliptin/metformin 50/1000 tablets (Janumet) have been approved for use. Designation: GREEN (see page 4).**
- **Prescribers are reminded that all glucosamine and glucosamine/chondroitin preparations are not recommended for prescribing. All patients currently receiving glucosamine on NHS prescription should be reviewed; where the patient is deriving real or perceived benefit they should be advised to purchase their own supplies in the future from their local health food shop, community pharmacy or supermarket (see page 6).**

CONTENTS

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.lpct.nhs.uk). Click on 'Commissioning' and follow the links to PACEF.

SUMMARY OF PACEF DECISIONS: JUNE 2010 UPDATE

Drug	Indication(s)	Traffic Light Status
Degarelix acetate injection (Firmagon)	Licensed for the treatment of advanced hormone dependent prostate cancer	RED-RED
Glucosamine hydrochloride tablets 750mg (Alateris)	Relief of symptoms in mild to moderate osteoarthritis of the knee	RED-RED N.B. Unlicensed food supplement formulations of glucosamine

		hydrochloride such as Cozachew Meltdown and Cozachew Combi Meltdown are also RED-RED
Glucosamine sulphate (all formulations including glucosamine/chondroitin combination products)	Not licensed Used for relief of symptoms in mild to moderate osteoarthritis of the knee	RED-RED Where indicated, the patient should be advised to buy their own supply from their preferred retailer.
Glucosamine sulphate powder 1500mg (Glusartel)	Licensed for mild to moderate osteoarthritis of the knee	RED-RED
Glucosamine sulphate tablets 1500mg (Dolenio)	Licensed for mild to moderate osteoarthritis of the knee	RED-RED
Oxycodone/naloxone prolonged release tablets 10mg/5mg and 20mg/10mg (Targinact)	Licensed for the treatment of severe pain.	RED-RED
Sitagliptin/Metformin 50mg/1000mg tablets (Janumet)	Licensed as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus inadequately controlled on their maximal dose of metformin alone or those already being treated with the combination of sitagliptin and metformin. Licensed for triple therapy in combination with either a sulphonylurea or thiazolidinedione (glitazone); also licensed for use with insulin.	GREEN

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 within licensed indications**. Specialist initiation and shared care guidelines are not considered necessary.

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.**

RAPID REVIEW: OXYCODONE/ NALOXONE PROLONGED RELEASE TABLETS (TARGINACT)

Targinact is a prolonged release (PR) tablet formulation of oxycodone in combination with naloxone; it is licensed for the treatment of severe pain. The theory behind this combination is that the opioid antagonist, naloxone, will counteract the opioid induced constipation associated with oxycodone. Targinact was originally assessed by PACEF in July 2009; our assessment was published in *PACE Bulletin* Vol 3 No 8 (August 2009). ULHT Drug and Therapeutics Committee have recently reviewed that assessment and have concluded that there is no new evidence necessitating a change to our existing position.

PACEF Recommendation:
In published trials, oxycodone/naloxone (Targinact) has been shown to marginally reduce laxative use in some patients without any impairment of analgesic effect or symptoms of opioid withdrawal. However, no comparative studies have yet been published comparing Targinact with separate

opioid/laxative combination therapy. In addition, the short-term nature of existing studies provides no assurance of long-term safety, nor is there published data on the use of the product in the treatment of cancer pain. The cost in comparison to other opioids and standard laxatives is excessive, particularly as many of the patients prescribed Targinact still require concurrent laxative treatment. Fixed dose combination analgesics can also create problems during incremental dose adjustment and titration as it is impossible to adjust the dose of one component without adjusting the dose of both. After consideration of all these factors oxycodone/naloxone PR tablets (Targinact) continue to be designated: RED-RED.

RAPID DRUG ASSESSMENT: DEGARELIX ACETATE INJECTION (FIRMAGON)

Degarelix (Firmagon) is the first Gonadotrophin-Releasing Hormone (GnRH) licensed in the UK. It is indicated for the treatment of advanced hormone dependent prostate cancer; it acts by binding to pituitary GnRH receptors thus reducing the secretion of testosterone by the testes. Because degarelix does not induce a testosterone surge or tumour flare, concurrent anti-androgen therapy is not required.

Supporting evidence for the use of this drug comes from one randomised open label parallel-group study. In this twelve month trial in 610 patients (median age 72) with adenocarcinoma of the prostate, the efficacy and safety of degarelix was evaluated in comparison to leuprorelin. The primary outcome was the achievement and maintenance of testosterone suppression. The results showed that degarelix was non-inferior to leuprorelin at maintaining low testosterone levels over a 12 month treatment period. Secondary outcomes showed that degarelix suppressed testosterone and Prostate Specific Antigen (PSA) significantly faster than leuprorelin.

A number of criticisms of this trial were considered:

- The dose of leuprorelin used in the trial was not reflective of licensed dosage and usual prescribed dosage in the UK.
- Only 20% of patients included within the study had metastatic disease; this is low compared to what would be expected in clinical practice.
- Few patients in the leuprorelin treatment arm used initial anti-androgen therapy against potential tumour flare. Post trial analysis of data suggested that PSA suppression in days 14 to 28 would have been considerably improved if anti-androgen therapy had been given.
- A high incidence of injection site reactions was also reported with degarelix.

A cost comparison of degarelix with alternative therapies reveals the following:

Drug	Dose range	Cost (£) pa
Degarelix (Firmagon)	**240mg initially, then 80mg every 28 days**	**£1,423.07**
Goserelin (Zoladex LA) **plus** Cyproterone start 3 days before goserelin and continue for 3 weeks	10.8mg every 12 weeks 300mg daily	£1,069.92 £77.50 Total - £1,147.42
Alternative gonadorelin analogues		
Goserelin (Zoladex)	3.6mg every 28 days	£845

Leuprorelin acetate (Prostap 3)	11.25mg every 3 months	£902.88
Leuprorelin acetate (Prostap SR)	3.75mg monthly	£978.12
Triptorelin (Decapetyl S.R)	11.25mg every 3 months	£828.00
Triptorelin (Decapeptyl S.R)	3mg every 28 days	£897
Triptorelin (Gonapeptyl)	3.75mg every 28 days	£1061.97
Alternative anti-androgens		
Flutamide commence 3 days prior to GA and continue for 3 weeks	250mg three times daily	£21.65 (28 days)
Bicalutamide commence 3 days prior to GA and continue for 3 weeks	50mg daily	£10.93

PACEF Recommendations

PACEF were concerned that the key trial supporting the use of this product compared degarelix against a dose of leuprorelin not currently used in the UK. As this trial is not reflective of current UK practice, it is of limited relevance. There are no further comparative studies against other gonaderelin analogues or orchidectomy. In addition, the cost comparison with alternative therapies reveals that degarelix is significantly more expensive than other options. In terms of frequency of dosage, monthly degarelix compares poorly to alternative gonaderelin analogue formulations that can be given every three months (e.g. Zoladex LA and Prostap 3). As a result of this, degarelix acetate injection (Firmagon) has been designated: RED-RED.

RAPID DRUG ASSESSMENT: SITAGLIPTIN/ METFORMIN 50/1000 TABLETS (JANUMET)

Sitagliptin is now available in a combination product with metformin marketed as Janumet; each tablet contains 50mg of sitagliptin and 1000mg of metformin. Janumet is licensed as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus inadequately controlled on their maximal dose of metformin alone or those already being treated with the combination of sitagliptin and metformin. It is also licensed for triple therapy in combination with either a sulphonylurea or thiazolidinedione (glitazone) and for use with insulin.

PACEF have already approved both constituent medicines for local use within the context of NICE Clinical Guideline 87: *the management of type 2 diabetes* (May 2009). A cost comparison reveals that Janumet is less expensive than the constituent medicines prescribed separately:

Drug	Daily dose range	Cost per pack	Cost (£) pa
Janumet 50/1000	1 tablet twice daily	£34.56(56)	£449.28
Sitagliptin 100mg	1 tablet daily	£33.26(28)	£432.38
Metformin 500mg	2000mg daily	£1.61(84)	£27.91
	Total	£35.41* (28 days supply)	£460.29pa
Alternative gliptins			

Vildagliptin 50mg	1 tablet twice daily	£31.76	£412.88
Vildagliptin 50mg + metformin 850mg	1 tablet twice daily	£31.76	£412.88
Vildagliptin 50mg + metformin 1000mg	1 tablet twice daily	£31.76	£412.88
Saxagliptin 5mg	1 tablet daily	£31.60	£410.80

PACEF Recommendation: Janumet

Janumet is approved for use where combination sitagliptin and metformin therapy is indicated subject to initiation criteria in NICE CG87. Designation: GREEN. Prescribers are reminded of existing PACEF advice on DPP-4 inhibitors (gliptins) as follows:

PACEF Recommendations: DPP-4 inhibitors

DPP-4 inhibitors are advocated by NICE at both steps 2 and 3 of the Clinical Guideline for type 2 diabetes. At step 2 they should be considered in combination with first line metformin in patients at significant risk of hypoglycaemia (where a sulfonylurea might be problematic), people living alone or in those for whom a sulfonylurea is contraindicated or not tolerated. Alternatively, they should be considered in combination with sulfonylurea monotherapy in patients unable to tolerate metformin or for whom metformin is contraindicated. At step 3 sitagliptin can be considered as part of triple therapy with metformin and a sulfonylurea when control of blood glucose remains or becomes inadequate and insulin is unacceptable or inappropriate.

There are currently three DPP-4 inhibitors available in the UK, sitagliptin (Januvia), vildagliptin (Galvus) and saxagliptin (Onglyza); both sitagliptin and vildagliptin are now available in combination with metformin (Janumet and Eucreas respectively). PACEF have assessed all three of these drugs and have considered NICE CG87. NICE reviewed all clinically relevant trials involving sitagliptin and vildagliptin and concluded that DPP-4 inhibitors were non-inferior to sulfonylureas (specifically glipizide) and glitazones (pioglitazone and rosiglitazone) in terms of reduction in HbA1c. PACEF considered a head-to-head study comparing sitagliptin and saxagliptin and accepted broad equivalence in terms of both HbA1c reduction and side effect profile.

No cases of *severe* hypoglycaemia have been reported in any of the trials for the gliptins; this is the basis for the recommendation that DPP-4 inhibitors should be considered in people at risk of hypoglycaemia. DPP-4 inhibitors have also been found not to cause weight gain in most cases, although the lack of long-term safety and outcomes data remains a concern.

In a recent Cochrane review an increase in all-cause infections was reported with DPP-4 inhibitors and it was recommended that their use should be avoided in patients with a history of recurrent urinary tract infections. This is equally relevant to saxagliptin. DPP-4 inhibitors also contribute to T-cell activation which can compromise immune function.

NICE have supported a role for DPP-4 inhibitors in both dual and triple therapy. At present, sitagliptin is the only DPP-4 inhibitor licensed for *both* of these indications. In addition, vildagliptin is contra-indicated in congestive heart failure (NYHA class III-IV) and should only be prescribed with caution in CHF NYHA class I-II. This renders the use of vildagliptin as a possible alternative to

the glitazones potentially problematic. There have also been rare reports of liver dysfunction with vildagliptin; Liver Function Tests (LFTs) should be monitored before initiating treatment and three monthly for the first year; LFTs should be checked periodically therafter.

Saxagliptin offers no advantage to sitagliptin other than a marginally lower price. In common with vildagliptin it does not currently hold a license for triple therapy. As a result of this, PACEF confirm that sitagliptin (Januvia) and sitagliptin/metformin (Janumet) are GREEN subject to NICE initiation criteria; sitagliptin remains the DPP-4 inhibitor of choice; vildagliptin (Galvus), vildagliptin/metformin (Eucreas) and saxagliptin (Onglyza) are all designated RED-RED at present, but will be subject to regular review as licensing changes.

REVIEW OF GLUCOSAMINE PRESCRIBING

PACEF originally reviewed the published evidence for the use of glucosamine and glucosamine/chondroitin preparations in November 2007 (published in *PACE Bulletin*, Vol1 No 8 (December 2007)). It is the purpose of this feature, to revise and update the original review and to re-emphasize current PACEF guidance and the practical implications for the healthcare community. **In Lincolnshire alone, the annual cost of prescribing glucosamine and glucosamine/chondroitin preparations is in excess of £760,000pa.** PACEF were concerned to establish whether such a high level of investment could be justified on the basis of best evidence and represented a good use of taxpayers' money.

The Evidence

Glucosamine is a normal constituent of the polysaccharide chains of cartilage and synovial fluid and has a role in maintaining the elasticity, strength and resilience of cartilage. In recent years, the medicinal use of glucosamine, obtained either on prescription or purchased from health food stores, supermarkets and pharmacies, has been on the increase. Since PACEF issued guidance recommending that glucosamine preparations should not be prescribed, prescribing volume has been in gradual decline.

The evidence base for and against the use of glucosamine is as follows:

(1) The Glucosamine/chondroitin Arthritis Intervention (GAIT) study compared glucosamine sulphate, chondroitin, glucosamine/chondroitin, celecoxib and placebo in 1,583 patients with osteoarthritis of the knee. The dose of glucosamine sulphate used was1500mg daily and the primary outcome was a 20% decrease in knee pain from baseline to week 24 with glucosamine. The placebo effect was very large and the glucosamine/ chondroitin combination emerged as no better than placebo.

(2) The Cochrane Collaboration has twice reviewed glucosamine (in 1999 and 2005) and has reached different conclusions on each occasion. In 1999, they concluded from 12 studies that glucosamine sulphate 500mg three times daily was safe and effective in the treatment of OA of the knee, but remained concerned over long-term safety and effectiveness. In 2005, they reviewed 20 studies of glucosamine in OA hip and knee and were more sceptical, concluding that glucosamine showed no appreciable benefit over placebo.

(3) More recently, a Bandolier meta-analysis concluded that glucosamine sulphate 1500mg daily could benefit as many as 1 in 5 patients with OA of the knee and calculated a Number Needed to Treat (NNT) of 4.9. An accompanying editorial stressed the relatively small improvements with

glucosamine in comparison to other interventions, the importance of individual patient perception and experience, the poor design of many of the published trials and the difficulties in assessing the clinical effectiveness of interventions like glucosamine from such evidence.

(4) More recently still, NICE Clinical Guideline 59: *Osteoarthritis - The care and management of osteoarthritis in adults* (February 2008) recommended that glucosamine or glucosamine/chondroitin products should not be used in the treatment of OA. NICE stated that the evidence for glucosamine sulphate was not strong enough to justify prescribing on the NHS; they also emphasized the poor quality of the evidence for glucosamine hydrochloride (Alateris).

The Products

In addition to an overall review of the evidence for glucosamine sulphate and glucosamine/chondroitin preparations, PACEF has also evaluated two licensed glucosamine preparations: glucosamine sulphate (Dolenio) and glucosamine hydrochloride (Alateris).

Dolenio (glucosamine sulphate 1500mg tablets) is the first licensed formulation of glucosamine sulphate. It is licensed for the treatment of mild to moderate osteoarthritis of the knee. The trial evidence associated with the product consists solely of placebo controlled efficacy studies that contribute little to the wider evidence base reviewed above. Compared to commonly prescribed alternatives, glucosamine sulphate (Dolenio) is comparable in cost to a branded coxib.

Alateris (glucosamine hydrochloride 625mg tablets) is the first licensed formulation of glucosamine hydrochloride. All other formulations of glucosamine are unlicensed food supplements and do not have to comply with pharmaceutical standards. Alateris is licensed for the relief of symptoms in mild to moderate OA of the knee. There is very little specific evidence available to justify the use of glucosamine hydrochloride over glucosamine sulphate. The vast majority of the research detailed above refers to glucosamine sulphate. Compared to commonly prescribed alternatives, glucosamine hydrochloride (Alateris) is comparable in cost to a branded coxib.

Glusartel (glucosamine sulphate 1500mg sachets) is the first licensed powder formulation; it is licensed for mild to moderate OA of the knee.

Alternative glucosamine formulations, although unlicensed, contain glucosamine sulphate, the salt utilized in many of the key studies. Examples include Valupak, Natrahealth and Lifespan.

PACEF Recommendations:

The evidence base in support of glucosamine is relatively weak and often conflicted. There is some evidence of benefit linked to the use of glucosamine sulphate 1500mg daily in the symptomatic relief of OA of the knee. Within this context, glucosamine may reduce pain in some people to a modest degree. However, such marginal benefit from such relatively expensive products does not represent a compelling case for continued NHS investment. The recent emergence of licensed formulations of glucosamine sulphate (Dolenio and Glusartel) and glucosamine hydrochloride (Alateris) has not helped to strengthen the case for glucosamine on prescription. The premium prices of both licensed and unlicensed formulations (often comparable to the price of coxibs), renders them extremely poor value for money. As a result of this, all glucosamine and glucosamine/chondroitin preparations, both licensed and

unlicensed, are designated RED-RED. Practices are advised to identify and review all patients currently receiving prescriptions for glucosamine and glucosamine/chondroitin preparations. Where the patient appears to be deriving little or no benefit from the treatment, glucosamine should be stopped and, where indicated, alternative therapy considered as defined in NICE CG 59. Where the patient appears to be deriving some benefit from glucosamine, they should be advised to purchase future supplies from their local health food shop, community pharmacy or supermarket. As evidenced above, glucosamine sulphate 1500mg daily may be of benefit to some patients suffering from OA of the knee. If a patient is advised to undertake a trial of glucosamine it should be as purchased self-care; a three month trial of 1500mg daily should be sufficient to demonstrate real or perceived benefit. The Prescribing and Medicines Management Team have devised a range of materials including patient letters and a FAQ sheet to help to support such a change. PACEF are fully in support of practices stopping all glucosamine prescribing; NHS Lincolnshire will be supportive of the practice if patient complaints arise. Prescribers are reminded that discontinuing all glucosamine prescribing in Lincolnshire will save approximately £760,000pa. This will contribute significantly to containing prescribing cost growth overall; it will also help those practices with significant use of glucosamine to realise substantial savings against their prescribing allocation and contribute significantly to the NHS savings target for 2010/11.

SHARED CARE GUIDELINES

PACEF have reviewed and approved the following shared care guidelines for use:

- Lithium
- Cinacalcet in the management of secondary hyperparathyroidism in adult patients with end-stage renal disease on dialysis
- Lanthanum in the management of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis who did not respond to or were unable to tolerate treatment with sevelamer and for controlling hyperphosphataemia associated with chronic kidney disease (CKD)
- Sevelamer in the management of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis
- Fulvestrant in the management of postmenopausal women with oestrogen – receptor – positive, locally advanced or metastatic breast cancer for disease relapse on or after adjuvant anti-oestrogen therapy or disease progression on therapy with an anti-oestrogen

Approaches from specialists to GPs requesting participation in shared care should be accompanied by a copy of the relevant SCG. Any queries relating to shared care or interface related issues or requests for particular SCGs should be addressed to Cathy Johnson, Interface Lead Pharmacist at cathy.johnson@lpct.nhs.uk
All approved SCGs are now available through the PACEF section of the NHS Lincolnshire website.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY: *DRUG SAFETY UPDATE* (JUNE 2010)

Rivastigmine (Exelon) transdermal patch: risk of medication errors

- Case reports of medication errors and inappropriate use of the rivastigmine transdermal patch have been reported, some of which have resulted in overdose and hospital admission.
- The most frequently reported causes were lack of patch removal and application of more than one patch at a time. Other errors included: application of the patch to non-recommended sites, application to the same area for several weeks, cutting the patch into several pieces and dose errors in prescribing and dispensing.

Advice for healthcare professionals:

- Symptoms of rivastigmine overdose include nausea, vomiting, diarrhoea, hypertension, hallucinations, bradycardia and/or syncope, malaise and falls.
- In case of suspected overdose, remove all rivastigmine patches and apply no further patch for the next 24 hours.
- Instruct patients and caregivers on the proper use of the patch. Only one patch should be applied per day; apply to healthy skin on the upper or lower back, upper arm or chest. Remove the previous day's patch before applying a new one: apply the new patch to a different skin location.
- Avoid application to the same skin location for at least 14 days to minimise skin irritation.
- Do not cut patches into pieces.

Prescribers are reminded of existing PACEF guidance on the use of rivastigmine patches:

PACEF Recommendation:

PACEF acknowledge that rivastigmine transdermal patches offer an alternative for patients who would benefit from an acetylcholinesterase inhibitor, but who are unable to tolerate side effects linked to peak plasma levels of oral therapies (such as nausea and vomiting). The formulation is designated AMBER subject to the prescribing restrictions on the prescribing of treatments for AD published by NICE in TA111 (2007). The use of the patch should be restricted to those for whom rivastigmine is considered an appropriate therapy and the patch an appropriate formulation.

Quinine: Not to be used routinely for nocturnal leg cramps

- Quinine is not a routine treatment for nocturnal leg cramps; it should only be considered when: (1) cramps cause regular sleep disruption which is very painful and frequent; (2) other treatable causes of cramp have been ruled out; and (3) when non-pharmacological measures have not worked (e.g. passive stretching exercises).
- Where quinine is prescribed it should be given as an initial trial for 4 weeks and treatment stopped if there is no benefit. A reduction in frequency of leg cramps may take up to 4 weeks to become apparent. Treatment should be interrupted approximately every 3 months to reassess benefit.

- A meta-analysis of eight RCTs reported that the mean number of cramps in a 4 week period while taking placebo was 17.08 compared to 20% fewer cramps in the active quinine treatment arm.
- Adverse effects with quinine include tinnitus, impaired hearing, headache, nausea, disturbed vision, confusion, flushing and abdominal pain.
- Patients should be warned not to exceed the recommended dose. Overdose may cause irreversible blindness and even death.
- Thrombocytopenia is a rare but potentially life-threatening adverse reaction associated with quinine. Patients should be instructed to discontinue treatment if the signs of thrombocytopenia occur (e.g. unexplained petechiae, bruising, bleeding).
- Quinine should not be prescribed for patients who have previously experienced any adverse reaction to quinine, including that found in beverages (e.g. tonic water).

Bevacizumab (Avastin): hypersentivity and infusion reactions

- Infusion reactions and hypersensitivity reactions have been reported commonly (>1/100 to <1/10) during treatment with Avastin. The incidence of these reactions is estimated to be up to 5% in clinical trials.
- Symptoms reported include dyspnoea, flushing, rash, hypotension or hypertension, oxygen desaturation, chest pain, rigors, nausea and vomiting.
- These reactions normally resolve quickly if infusion is stopped immediately. Treatment with corticosteroids, antihistamines, oxygen and IV fluids may also be indicated.

Acknowlegements

Many thanks to Cathy Johnson, Interface Lead Pharmacist, NHSL, Stephen Jones, Pharmacist LPFT and Robyn Thompson, Senior Pharmacist, ULHT for their contributions to this edition of the *PACE Bulletin*.

August 2010