

# Prescribing and Clinical Effectiveness Bulletin

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## What's new this month?

- Lower cost generic pioglitazone tablets are now available in all strengths; prescribers should ensure that all prescribing of pioglitazone is by generic name. Some community pharmacies have been asking prescribers to prescribe *Actos* by brand where generic products do not hold appropriate marketing authorisations; prescribers are advised to refuse these requests and prescribe all pioglitazone generically (see page 3).
- An adrenaline tartrate auto-injector device (*Jext*) has been approved for use as an alternative to *Epipen* (see page 4).
- Very low cost generic donepezil 5mg and 10mg tablets are now available and currently constitute the lowest cost option in the treatment of Alzheimer's disease (see page 6).
- Following patent expiry, generic latanoprost 50mcg per ml eye drops are now significantly lower in cost than any alternative branded prostaglandin analogue preparation for the treatment of chronic open angle glaucoma (COAG) and ocular hypertension (OHT). Prescribers should ensure that all latanoprost eye drops are prescribed generically. The generic reimbursement price of latanoprost 50mcg/ timolol 5mg per ml eye drops is also beginning to fall; prescribers are urged to ensure that all prescriptions for *Xalacom* are genericised to maximize potential savings (see page 7).
- Low cost generic standard release olanzapine tablets are now available in a wide range of strengths; prescribers should ensure that all olanzapine is prescribed generically. Where orodispersible olanzapine tablets are indicated they should be prescribed generically and not as *Zyprexa Velotabs*. The reimbursement prices of generic orodispersible olanzapine formulations are beginning to fall, but prices remain significantly higher than standard release alternatives (see page 8).
- Low cost generic standard release quetiapine tablets are now available in a wide range of strengths; prescribers should ensure that all quetiapine is prescribed generically. When the use of quetiapine is clinically indicated, the standard release preparation should be preferred first line as quetiapine MR tablets (*Seroquel XL*) are now extremely expensive in comparison to generic standard release equivalents (see page 9).
- There are now three low cost generic Angiotensin Receptor Blockers (ARBs) available: candesartan tablets, losartan tablets and valsartan capsules. Prescribers are urged to standardize first line ARB choice around one of these three products; many practices have already undertaken therapeutic switches away from long patent life high-cost branded ARBs (e.g. olmesartan (*Olmetec*) and telmisartan (*Micardis*)) to lower cost generic alternatives. Any practices that have yet to undertake this work are encouraged to do so in response to this further round of patent expiries (see page 10).

- Generic sumatriptan remains the first line triptan of choice for the treatment of migraine, although the emergence of low cost generic zolmitriptan in both standard and orodispersible formulations offers a useful alternative. Prescribers should ensure that all zolmitriptan is prescribed generically and that patients currently taking *Zomig Rapimelt* are switched to the generic orodispersible alternative (see page 10).
- Early in year estimates of potential savings related to these patent expiries totalled £5.6M across the healthcare community. This figure includes nearly £3M linked to the atorvastatin patent expiry alone. Since these figures were calculated, *Drug Tariff* prices for many of these medicines have fallen again and these estimates are likely to be under-estimates. Prescribers are urged to maximise these savings still further by making the prescribing changes detailed above and continuing to focus on switching away from rosuvastatin (*Crestor*) where appropriate (see page 12).
- Calcitonin nasal spray (200 units per actuation) (*Miacalcic*) is to be withdrawn from the European market and should no longer be prescribed for the treatment of postmenopausal osteoporosis (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](http://www.lincolnshire.nhs.uk)). Click on 'Commissioning' and follow the links to PACEF.

## SUMMARY OF PACEF DECISIONS: JULY-SEPTEMBER 2012 UPDATE

Drug	Indication(s)	Traffic Light Status
Adrenaline tartrate single use pre-filled pen 150 microgram and 300microgram ( <i>Jext</i> )	Licensed for the emergency treatment of acute anaphylaxis in adults and children (of 15kg and above)	GREEN
Alfentanil sublingual spray 5mg in 5ml (140 micrograms per spray) (unlicensed)	Used in acute or breakthrough pain in renal impairment (eGFR <30/mL/min).	RED Should not be prescribed by GPs in primary care for any indication.
Calcitonin nasal spray (200 units per actuation) ( <i>Miacalcic</i> )	Licensed for the treatment of postmenopausal osteoporosis to reduce the risk of vertebral fractures	RED-RED This product is to be withdrawn from the European market due to safety concerns
Ulipristal 30mg tablets ( <i>Ellaone</i> )	Emergency contraception within 120 hours (5 days) of unprotected intercourse or contraceptive failure.	GREEN NB Up to 72 hours after UPSI or contraceptive failure, levonorgestrel ( <i>Levonelle 1500</i> ) is preferred first line. Ulipristal ( <i>Ellaone</i> ) should be preferred in patients presenting between 72 and 120 hours after UPSI or contraceptive failure.

**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**.

## **GUIDANCE ON THE PRESCRIBING OF GENERIC PIOGLITAZONE**

Generic pioglitazone tablets are now available in the UK, but do not hold all of the marketing authorisations of *Actos* and the pioglitazone/metformin combination product, *Competact*. Specifically, *Actos* is licensed for the treatment of type 2 diabetes mellitus (DM) as:

- monotherapy in adult patients (particularly those who are overweight) inadequately controlled by diet and exercise for whom metformin is inappropriate because of contraindications or intolerance.
- dual oral therapy in combination with metformin or a sulfonylurea
- triple oral therapy in combination with metformin and a sulfonylurea.

*Actos* is also licensed for use in combination with insulin in type 2 DM inadequately controlled by insulin in patients with an intolerance or contraindication to metformin.

In comparison, generic pioglitazone tablets 15mg, 30mg and 45mg are only licensed for monotherapy, dual oral therapy with a sulfonylurea (some generics, but not all) and in combination with insulin in type 2 DM.

As a result of this, some community pharmacies are requesting branded prescribing of *Actos* to cover those indications for which the new generic formulations are unlicensed (i.e. dual therapy in combination with metformin and triple oral therapy in combination with metformin and a sulfonylurea).

### **Cost Comparison**

	Dose	Cost 28 days supply
<b>Pioglitazone 15mg tablets (generic)</b>	<b>15mg once daily</b>	<b>£6.61</b>
<b>Pioglitazone 30mg tablets (generic)</b>	<b>30mg once daily</b>	<b>£8.96</b>
<b>Pioglitazone 45mg tablets (generic)</b>	<b>45mg once daily</b>	<b>£10.67</b>
Pioglitazone 15mg tablets (Actos)	15mg once daily	£25.83
Pioglitazone 30mg tablets (Actos)	30mg once daily	£35.89
Pioglitazone 45mg tablets (Actos)	45mg once daily	£39.55

### **PACEF Recommendation**

**The licensing authorities have assessed all of the generic pioglitazone formulations and are satisfied that generic pioglitazone products are bioequivalent with Actos. Current differences in licensed indications have arisen as a result of patent protection issues. It is acknowledged that the use**

of unlicensed medicines or off-label use of licensed medicines rests with the prescriber, who remains professionally accountable for their judgement and may be called upon to justify their actions. However, due to the demonstrated bioequivalence of these products and the existence of the EMEA marketing authorisations, the risk associated with off-label prescribing of generic pioglitazone for all indications is low. Prescribers will be aware of other generics (e.g. omeprazole) that do not carry all of the licensed indications of the originator molecule, but are nonetheless widely prescribed interchangeably. In order to maximise cost-effectiveness, prescribers are asked to refuse all community pharmacy requests to prescribe the Actos brand and to ensure that all prescribing of pioglitazone is by non-proprietary or approved name.

**RAPID DRUG ASSESSMENT: ALFENTANIL SUB-LINGUAL SPRAY 5MG/5ML 140 MICROGRAMS PER SPRAY (UNLICENSED)**

Alfentanil sublingual spray 5mg in 5ml (140 micrograms per spray) is an unlicensed medication used in acute or breakthrough pain in renal impairment (eGFR <30mL/min). The dose is 2 to 8 sprays sublingually every hour when required. Sublingual alfentanil provides rapid onset of pain relief (within 10 to 15 minutes) and has a short duration of action (30 to 40 minutes). The sublingual route avoids first pass metabolism and has fewer opioid related side effects. Alfentanil is useful in patients with renal impairment as it is metabolised by the cytochrome p450 3A3/4 system and does not accumulate in the same way as morphine. One bottle lasts for 2 to 4 weeks and costs £11.55. It is estimated that it will be used in around 3 patients per year.

**PACEF Recommendation:**

**Alfentanil sub-lingual spray 5mg/5ml (140 micrograms per spray) has been approved for limited use in acute or breakthrough pain in renal impairment (eGFR <30mL/min) by consultant nephrologists within United Lincolnshire Hospitals Trust. PACEF have designated the product as RED. It should not be prescribed by GPs in primary care for any indication.**

**RAPID DRUG ASSESSMENT: ADRENALINE TARTRATE AUTO-INJECTOR DEVICE (JEXT)**

*Jext* is an auto-injector device containing adrenaline tartrate available in 150 microgram and 300 microgram strengths. It is licensed for the emergency treatment of acute anaphylaxis in adults and children (of 15kg and above); the product is unlicensed for children less than 15kg. *Jext* has a number of advantages over the brand leader *Epipen* including:

- a longer expiry date of 2 years for *Jext* compared to 18 months with *Epipen*. This is likely to result in patients requiring fewer adrenaline pens over a lifetime.
- the storage requirements for *Jext* are slightly less complex than *Epipen*. *Jext* should not be frozen; *Epipen* must not be refrigerated or stored above 25°C.
- although *Jext* is more expensive per device than *Epipen* in primary care, there are potential cost efficiencies linked to the longer shelf-life of *Jext* and the need to replace expired unused pens less frequently than with *Epipen*.

**PACEF Recommendation**

**Adrenaline tartrate single-use pre-filled pens 150 microgram and 300microgram (*Jext*) are designated GREEN and should be considered as an alternative to the *Epipen* device.**

## **UPDATED NEW DRUG ASSESSMENT: ULIPRISTAL 30MG TABLETS (ELLAONE)**

This is an updated version of a New Drug Assessment originally published in *PACE Bulletin*, Vol 4, No 1 (January/February 2010). New text is highlighted in italics.

Ulipristal (*Ellaone*) is the first oral emergency contraceptive licensed for use up to 120 hours (five days) after unprotected sexual intercourse (UPSI) or contraceptive failure. It is a progesterone receptor modulator and acts by delaying ovulation and follicular development; *it has been shown to inhibit or significantly delay follicular rupture for over 5 days*. The alternative oral emergency contraceptive, levonorgestrel 1500 microgram (*Levonelle 1500*), should be taken as soon as possible after UPSI, preferably within 12 hours and definitely within 72 hours. The only other option for women requiring emergency contraception between 72 hours and 120 hours (3 to 5 days) post UPSI is to have an intra-uterine device (IUD) fitted. This is an invasive procedure that can only be undertaken by an appropriately trained healthcare professional.

Clinical evidence for ulipristal still rests on four trials. One trial compared the 50mg dose of ulipristal against levonorgestrel in the period 0 to 72 hours following UPSI. This is not the current licensed dose of ulipristal, nor does it reflect the drug's full licensed indication. Results from this trial showed that ulipristal has equivalent contraceptive efficacy to levonorgestrel in the period up to 72 hours following UPSI. Further trials have also shown that ulipristal reduces the number of expected pregnancies if administered between the periods 72 to 120 hours post UPSI. There are still no studies comparing the efficacy of ulipristal against the only other licensed alternative in the period 72 hours to 120 hours post UPSI, the IUD. The phase 2 trials used a 50mg capsule of ulipristal rather than the 30mg micronized form that has been brought to market as *Ellaone*. The Committee for Human Medicinal Products (CHMP) have confirmed that plasma levels reached with the 30mg micronized tablet formulation are approximately equivalent to those reached with the 50mg standard formulation used in trials. On this basis, PACEF have made the assumption that results obtained from trials where the 50mg dose was used, can be extrapolated to apply to the 30mg micronized formulation.

Side effects recorded with ulipristal are similar to those seen with levonorgestrel (*Levonelle*) (i.e. nausea, vomiting, abdominal pain and disruption to the subsequent menstrual cycle). Existing arrangements for post-coital emergency contraception centre on the provision of levonorgestrel (*Levonelle*) either on prescription or supplied direct from family planning clinics or community pharmacies according to a patient group direction. An over the counter preparation known as *Levonelle One Step* can also be purchased from community pharmacies.

Ulipristal is significantly higher in price than levonorgestrel (see cost comparison below):

Drug	Daily dose range	Cost (£)pa
Ulipristal 30mg tablets ( <i>Ellaone</i> )	30mg	£16.95
Levonorgestrel ( <i>Levonelle 1500</i> )	1500mcg	£5.20
Copper Intrauterine devices	Insert device, replace after 5 years	£8.00-13.08 per device

Since the original PACE Bulletin, the Drug and Therapeutics Bulletin (DTB) have published their own review and concluded that:

- Ulipristal is effective for up to 5 days after UPSI and is no less effective than levonorgestrel within the first 72 hours.
- Ulipristal and levonorgestrel are similarly well tolerated.
- Ulipristal is likely to delay the subsequent menstrual period.
- Levonorgestrel remains the preferred product within the first 72 hours after UPSI.

The Faculty of Sexual and Reproductive Healthcare have updated their clinical guidance on emergency contraception and have recommended ulipristal as an option within 0 to 120 hours (0 to 5 days) following UPSI. FSRH guidance does not suggest that ulipristal should be used in preference to levonorgestrel, although some sexual health services have started to recommend first line ulipristal in women presenting mid-cycle in an attempt to delay ovulation; estimates suggest that approximately 40% of women presenting for emergency contraception would fall into this category.

**PACEF Recommendation:**

***PACEF can find no evidence that ulipristal (Ellaone) is superior in terms of clinical efficacy to levonorgestrel within the first 72 hours after UPSI; both products are also similarly well tolerated. As a result of this, taking into account comparative cost, levonorgestrel remains the first line emergency hormonal contraceptive of choice within the first 72 hours after UPSI. Ulipristal (Ellaone) is licensed for up to 120 hours (five days) after UPSI or contraceptive failure and presents a preferable alternative to unlicensed levonorgestrel use or the use of an intrauterine contraceptive device (IUD) in patients presenting for emergency oral contraception between 72 and 120 hours after UPSI or contraceptive failure. Within this context only, ulipristal (Ellaone) continues to be designated GREEN. Patients presenting before 72 hours should continue to receive levonorgestrel 1500mcg (Levonelle 1500) either on prescription or through family planning clinics or community pharmacies.***

**NEW LOW COST GENERICS: DRUG TARIFF (OCTOBER 2012)**

In addition to the *Lipitor* (atorvastatin) patent expiry, a number of other key patents expire in 2012/13 and are likely to generate significant fortuitous savings for Lincolnshire Clinical Commissioning Groups. The following low cost generic medicines are already available. Care should be taken to ensure that all prescriptions for these medicines are prescribed generically and that consideration is given towards more prominent first line use where appropriate. Patent expiries and price reductions around new generics do not just create fortuitous savings, but also create new opportunities for more cost-effective first and second line prescribing choices. All prices quoted are from the *Drug Tariff* October 2012.

Generic donepezil (plain and orodispersible) versus other oral treatments for Alzheimer's Disease)

**PACEF Recommendation: Very low cost generic donepezil 5mg and 10mg tablets are now available and currently constitute the lowest cost option in the treatment of Alzheimer's disease. NICE Technology Appraisal 217: *Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease* (March 2011) specifies that when prescribing an acetylcholinesterase (AChE) inhibitor, treatment should be started with the drug of lowest acquisition cost (subject to adverse event profile, expectations about adherence, medical co-morbidity, possibility of drug interactions and dosing**

profiles). As a result of this, generic donepezil tablets are likely to be consolidated as a prominent first line treatment choice within this disease area. The standard release formulation is preferred; while generic orodispersible tablets are available at a lower cost than the *Aricept Evess* product they still constitute an expensive treatment option more comparable in cost to alternative branded medicines such as galantamine (*Reminyl XL*), memantine (*Ebixa*) and rivastigmine (*Exelon*). Patent expiries around galantamine and rivastigmine have already occurred with the expectation that lower cost generic products will be available soon; the October *Tariff* revealed modest falls in the reimbursement prices of the various strengths of generic rivastigmine although prices still remain only marginally less than the originator brand. The memantine (*Ebixa*) patent is not due to expire until April 2014.

	Dose	Cost (28 days)
Donepezil 5mg tablets (generic)	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£2.19
Donepezil 10mg tablets (generic)	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£2.89
Donepezil 5mg tablets ( <i>Aricept</i> )	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£59.85
Donepezil 10mg tablets ( <i>Aricept</i> )	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£83.89
Donepezil 5mg orodispersible tablets (generic)	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£39.03
Donepezil 10mg orodispersible tablets (generic)	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£54.41
Donepezil 5mg orodispersible tablets ( <i>Aricept Evess</i> )	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£59.85
Donepezil 10mg orodispersible tablets ( <i>Aricept Evess</i> )	Initially 5mg once daily at bedtime increased if necessary after one month to a maximum of 10mg daily	£83.89

Generic latanoprost 50microgram per ml eye drops and latanoprost/timolol 50microgram/5mg per ml eye drops

**PACEF Recommendation:** Following patent expiry, generic latanoprost 50mcg per ml eye drops are now significantly lower in cost than any alternative branded prostaglandin analogue preparation. As a result of this, the treatment of chronic open angle glaucoma (COAG) and ocular hypertension (OHT) is the subject of a review with ULH ophthalmologists with revised local guidance expected soon. At present, prescribers should ensure that all latanoprost eye drops are prescribed generically. The generic reimbursement price of latanoprost 50mcg/ timolol 5mg per ml eye drops is also beginning to fall; prescribers are urged to ensure that all prescriptions for *Xalacom* are genericised to maximize potential savings.

Prostaglandin analogues	Licensed indications	Recommended dose	Cost
<b>Latanoprost 50mcg per ml drops (generic)</b>	<b>COAG and OHT</b>	<b>One drop into the affected eye once daily in the evening</b>	<b>2.5ml £3.89</b>
Latanoprost 50mcg per ml drops ( <i>Xalatan</i> )	COAG and OHT	One drop into the affected eye once daily in the evening	2.5ml £12.48
Bimatoprost 0.1mg per ml drops ( <i>Lumigan</i> )	As monotherapy or as an adjunct to BBs in COAG or OHT	One drop into the affected eye once daily in the evening	3ml £12.43
Bimatoprost 0.3mg per ml drops ( <i>Lumigan</i> )	As monotherapy or as an adjunct to BBs in COAG or OHT	One drop into the affected eye once daily in the evening	3ml £10.30 Patent expiry March 2017
Tafuprost 15mcg per ml drops ( <i>Saftutan</i> )	As monotherapy or as an adjunct to BBs in COAG or OHT	One drop into the affected eye once daily in the evening	30 x 0.3ml single use vials £17.41
Travoprost 40mcg per ml drops ( <i>Travatan</i> )	OHT and COAG	One drop into the affected eye once daily in the evening	2.5ml £9.98 Patent expiry August 2014

Prostaglandin analogues/beta-blocker combinations	Licensed indications	Recommended dose	Cost
<b>Latanoprost 50mcg/ timolol 5mg per ml drops (generic)</b>	<b>OHT and COAG insufficiently responsive to BBs or prostaglandin analogues</b>	<b>One drop into the affected eye once daily</b>	<b>2.5ml £10.88</b>
Latanoprost 50mcg/ timolol 5mg per ml ( <i>Xalacom</i> )	OHT and COAG insufficiently responsive to BBs or prostaglandin analogues	One drop into the affected eye once daily	2.5ml £14.32
Bimatoprost 0.3mg/ timolol 5mg per ml eye drops ( <i>Ganfort</i> )	OHT and COAG insufficiently responsive to BBs or prostaglandin analogues	One drop into the affected eye once daily in the morning	3ml £13.95 Patent expiry March 2017
Travoprost 40mcg/ timolol 5mg per ml drops ( <i>DuoTrav</i> )	OHT and COAG insufficiently responsive to BBs or prostaglandin analogues	One drop into the affected eye once daily	2.5ml £12.55 Patent expiry August 2014

Olanzapine: generic olanzapine tablets versus branded Zyprexa

**PACEF Recommendation: Low cost generic standard release olanzapine tablets are now available in a wide range of strengths; prescribers should ensure that all olanzapine is prescribed generically. Where orodispersible olanzapine tablets are indicated they should be prescribed generically and not as *Zyprexa Velotabs*. The reimbursement prices of generic orodispersible olanzapine formulations are beginning to fall, but prices remain significantly higher than standard release alternatives.**

	Dose	Cost (28 days)
<b>Olanzapine tablets 2.5mg (generic)</b>	<b>2.5mg daily</b>	<b>£1.17</b>
Olanzapine tablets 2.5mg ( <i>Zyprexa</i> )	2.5mg daily	£21.85
<b>Olanzapine tablets 5mg (generic)</b>	<b>5mg daily</b>	<b>£1.81</b>
Olanzapine tablets 5mg ( <i>Zyprexa</i> )	5mg daily	£43.70
<b>Olanzapine orodispersible tablets 5mg (generic)</b>	<b>5mg daily</b>	<b>£16.61</b>
<b>Olanzapine orodispersible tablets 5mg sugar free (generic)</b>	<b>5mg daily</b>	<b>£25.26</b>
Olanzapine orodispersible tablets 5mg ( <i>Zyprexa Velotab</i> )	5mg daily	£48.07
<b>Olanzapine tablets 7.5mg (generic)</b>	<b>7.5mg daily</b>	<b>£2.31</b>
Olanzapine tablets 7.5mg ( <i>Zyprexa</i> )	7.5mg daily	£65.55
<b>Olanzapine tablets 10mg (generic)</b>	<b>10mg daily</b>	<b>£2.85</b>

Olanzapine tablets 10mg ( <i>Zyprexa</i> )	10mg daily	£87.40
<b>Olanzapine orodispersible tablets 10mg (generic)</b>	<b>10mg daily</b>	<b>£30.00</b>
<b>Olanzapine orodispersible tablets 10mg sugar free (generic)</b>	<b>10mg daily</b>	<b>£45.72</b>
Olanzapine orodispersible tablets 10mg ( <i>Zyprexa Velotab</i> )	10mg daily	£87.40
<b>Olanzapine tablets 15mg (generic)</b>	<b>15mg daily</b>	<b>£4.17</b>
Olanzapine tablets 15mg ( <i>Zyprexa</i> )	15mg daily	£119.18
<b>Olanzapine orodispersible tablets 15mg (generic)</b>	<b>15mg daily</b>	<b>£45.17</b>
<b>Olanzapine orodispersible tablets 15mg sugar free (generic)</b>	<b>15mg daily</b>	<b>£68.69</b>
Olanzapine orodispersible tablets 15mg ( <i>Zyprexa Velotab</i> )	15mg daily	£131.10
<b>Olanzapine tablets 20mg (generic)</b>	<b>20mg daily</b>	<b>£5.62</b>
Olanzapine tablets 20mg ( <i>Zyprexa</i> )	20mg daily	£158.90
<b>Olanzapine orodispersible tablets 20mg (generic)</b>	<b>20mg daily</b>	<b>£60.01</b>
<b>Olanzapine orodispersible tablets 20mg sugar free (generic)</b>	<b>20mg daily</b>	<b>£91.49</b>
Olanzapine orodispersible tablets 20mg ( <i>Zyprexa Velotab</i> )	20mg daily	£174.79

Quetiapine: generic quetiapine tablets versus branded Seroquel and Seroquel XL

**PACEF Recommendation: Low cost generic standard release quetiapine tablets are now available in a wide range of strengths; prescribers should ensure that all quetiapine is prescribed generically. When the use of quetiapine is clinically indicated, the standard release preparation should be preferred first line as quetiapine MR tablets (Seroquel XL) are now extremely expensive in comparison to generic standard release equivalents.**

	Dose	Cost (30 days)
<b>Quetiapine tablets 25mg (generic)</b>	<b>25mg twice daily</b>	<b>£2.93</b>
Quetiapine tablets 25mg ( <i>Seroquel</i> )	25mg twice daily	£40.50
Quetiapine MR tablets 50mg ( <i>Seroquel XL</i> )	50mg once daily	£33.83
<b>Quetiapine tablets 25mg (generic)</b>	<b>50mg twice daily</b>	<b>£5.86</b>
Quetiapine tablets 25mg ( <i>Seroquel</i> )	50mg twice daily	£81.00
<b>Quetiapine tablets 100mg (generic)</b>	<b>100mg twice daily</b>	<b>£7.89</b>
Quetiapine tablets 100mg ( <i>Seroquel</i> )	100mg twice daily	£113.10
Quetiapine MR tablets 200mg ( <i>Seroquel XL</i> )	200mg once daily	£56.55
<b>Quetiapine tablets 150mg (generic)</b>	<b>150mg twice daily</b>	<b>£8.05</b>
Quetiapine tablets 150mg ( <i>Seroquel</i> )	150mg twice daily	£113.10
Quetiapine MR tablets 300mg ( <i>Seroquel XL</i> )	300mg once daily	£85.00
<b>Quetiapine tablets 200mg (generic)</b>	<b>200mg twice daily</b>	<b>£8.52</b>
Quetiapine tablets 200mg ( <i>Seroquel</i> )	200mg twice daily	£113.10
Quetiapine MR tablets 400mg ( <i>Seroquel XL</i> )	400mg once daily	£113.10
<b>Quetiapine tablets 300mg (generic)</b>	<b>300mg twice daily</b>	<b>£11.42</b>
Quetiapine tablets 300mg ( <i>Seroquel</i> )	300mg twice daily	£170.00

**Candesartan and valsartan: generic versus other Angiotensin Receptor Blockers**

**PACEF Recommendation:** There are now three low cost generic ARBs available: candesartan tablets, losartan tablets and valsartan capsules. Prescribers are urged to standardize first line ARB choice around one of these three products; many practices have also undertaken therapeutic switches away from long patent life high-cost branded ARBs to lower cost generic alternatives. Any practices that have yet to undertake this work are encouraged to do so in response to this further round of patent expiries. Specifically, switches away from olmesartan (Olmotec) and telmisartan (Micardis) are encouraged.

	Dose	Cost for 28 tabs / caps
Candesartan tablets (generic)	<b>4mg once daily</b>	<b>£4.40</b>
	<b>8mg once daily</b>	<b>£2.80</b>
	<b>16mg once daily</b>	<b>£3.43</b>
	<b>32mg once daily</b>	<b>£4.71</b>
Candesartan tablets ( <i>Amlas</i> )	2mg once daily	£14.32
	4mg once daily	£9.78
	8mg once daily	£9.89
	16mg once daily	£12.72
	32mg once daily	£16.13
Eprosartan tablets (Teveten)	300mg once daily	£7.31
	600mg once daily	£14.31
	800mg once daily	£15.77
Irbesartan tablets (Aprovel)	75mg once daily	£9.69
	150mg once daily	£11.84
	300mg once daily	£15.93
Losartan tablets (generic)	<b>12.5mg once daily</b>	<b>£5.95</b>
	<b>25mg once daily</b>	<b>£1.55</b>
	<b>50mg once daily</b>	<b>£1.66</b>
	<b>100mg once daily</b>	<b>£1.95</b>
Losartan tablets (Cozaar)	12.5mg once daily	£8.09
	25mg once daily	£16.18
	50mg once daily	£12.80
	100mg once daily	£16.18
Olmesartan tablets (Olmotec)	10mg once daily	£10.95
	20mg once daily	£12.95
	40mg once daily	£17.50
Telmisartan tablets (Micardis)	20mg once daily	£11.10
	40mg once daily	£13.61
	80mg once daily	£17.00
Valsartan tablets (generic)	40mg once daily	£9.80
	80mg once daily	£13.97
	160mg once daily	£18.41
	320mg once daily	£20.23
Valsartan capsules (generic)	<b>40mg once daily</b>	<b>£2.84</b>
	<b>80mg once daily</b>	<b>£2.86</b>
	<b>160mg once daily</b>	<b>£3.71</b>
Valsartan tablets (Diovan Tablets)	40mg once daily	£13.96
	320mg once daily	£20.23
Valsartan capsules (Diovan)	80mg once daily	£13.97
	160mg once daily	£18.41

**Zolmitriptan plain and orodispersible tablets versus other triptans**

**PACEF Recommendation:** Generic sumatriptan remains the first line triptan of choice for the treatment of migraine, although the emergence of low cost generic zolmitriptan in both standard and orodispersible formulations offers a useful alternative. Prescribers should ensure that all zolmitriptan is prescribed generically and that patients currently taking Zomig Rapimelt are switched to the generic orodispersible alternative.

	Dose	Cost and Cost per dose
Almotriptan 12.5mg tablets (Almogran)	12.5mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 25mg in 24 hours.	£9.07 (3 tabs) £18.14 (6 tabs) £27.20 (9 tabs) £3.02 per dose
Eletriptan 40mg tablets (Relpax)	40mg repeated after 2 hours if migraine recurs; maximum 80mg in 24 hours.	£22.50 (6 tabs) £3.75 per dose
Frovatriptan 2.5mg tablets (Migard)	2.5mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 5mg in 24 hours	£16.67 (6 tabs) £2.78 per dose
Naratriptan 2.5mg tablets (Naramig)	2.5mg as soon as possible after onset repeated after at least 4 hours if migraine recurs; maximum 5mg in 24 hours	£24.55 (6 tabs) £49.10 (12 tabs) £4.09 per dose
Rizatriptan 10mg tablets (Maxalt)	10mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 20mg in 24 hours	£13.37 (3 tabs) £26.74 (6 tabs) £4.46 per dose
Rizatriptan 10mg oral lyophilisate tablets (Maxalt Melt)	10mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 20mg in 24 hours	£13.37 (3 tabs) £26.74 (6 tabs) £53.48 (12 tabs) £4.46 per dose
<b>Sumatriptan 50mg tablets (generic)</b>	<b>50 to 100mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 300mg in 24 hours</b>	<b>£1.66 (6 tabs)</b> <b>£0.28 per dose</b>
<b>Sumatriptan 100mg tablets (generic)</b>	<b>50 to 100mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 300mg in 24 hours</b>	<b>£2.15 (6 tabs)</b> <b>£0.36 per dose</b>
Sumatriptan 50mg tablets (Imigran)	50 to 100mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 300mg in 24 hours	£26.54 (6 tabs) £50.43 (12 tabs) £4.20 to £4.42 per dose
Sumatriptan 100mg tablets (Imigran)	50 to 100mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 300mg in 24 hours	£42.90 (6 tabs) £85.80 (12 tabs) £7.15 per dose
Sumatriptan 50mg dispersible tablets (Imigran Radis)	50 to 100mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 300mg in 24 hours	£23.90 (6 tabs) £47.83 (12 tabs) £3.98 per dose
Sumatriptan 100mg dispersible tablets (Imigran Radis)	50 to 100mg as soon as possible after onset repeated after 2 hours if migraine recurs; maximum 300mg in 24 hours	£42.90 (6 tabs) £85.80 (12 tabs) £7.15 per dose
<b>Zolmitriptan 2.5mg tablets (generic)</b>	<b>2.5mg as soon as possible after onset repeated after at 2 hours if migraine recurs; maximum 10mg in 24 hours</b>	<b>£4.33 (6 tabs)</b> <b>£0.72 per dose</b>
Zolmitriptan 2.5mg tablets (Zomig)	2.5mg as soon as possible after onset repeated after at 2 hours if migraine recurs; maximum 10mg in 24 hours	£18.00 (6 tabs) £36.00 (12 tabs) £3.00 per dose
<b>Zolmitriptan 2.5mg orodispersible tablet sugar free (generic)</b>	<b>2.5mg as soon as possible after onset repeated after at 2 hours if migraine recurs; maximum 10mg in 24 hours</b>	<b>£4.35 (6 tabs)</b> <b>£0.73 per dose</b>
Zolmitriptan 2.5mg oral dissolving tablet (Zomig Rapimelt)	2.5mg as soon as possible after onset repeated after at 2 hours if migraine recurs; maximum 10mg in 24 hours	£17.90 (6 tabs) £2.98 per dose
Zolmitriptan 5mg orodispersible tablet sugar free (generic)	2.5mg as soon as possible after onset repeated after at 2 hours if migraine recurs; maximum 10mg in 24 hours	£22.80 (6 tabs) £3.80 per dose
Zolmitriptan 5mg oral dissolving tablet (Zomig Rapimelt)	2.5mg as soon as possible after onset repeated after at 2 hours if migraine recurs; maximum 10mg in 24 hours	£22.80 (6 tabs) £3.80 per dose

**PACEF Conclusion:**

Early in year estimates of potential savings related to these patent expiries totalled £5.6M across the healthcare community. This figure includes nearly £3M linked to the atorvastatin patent expiry alone. Since these figures were calculated, *Drug Tariff* prices for many of these medicines have fallen again and these estimates are likely to be under-estimates. Prescribers are urged to maximise these savings still further by making the prescribing changes detailed above and continuing to focus on switching away from rosuvastatin (Crestor) where appropriate.

**MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY: DRUG SAFETY UPDATE (AUGUST 2012)****Calcitonin (*Miacalcic*): increased risk of cancer with long-term use – all intra-nasal formulations for osteoporosis to be withdrawn**

- Long-term use of calcitonin has been associated with an increased risk of cancer.
- Calcitonin-containing medicines should no longer be used in the treatment of osteoporosis.
- All intra-nasal calcitonin sprays (the only form of calcitonin licensed for osteoporosis) will be withdrawn from the European market. In the UK this refers to calcitonin nasal spray (200 units per actuation) (*Miacalcic*).
- Calcitonin will remain available as an injection and infusion for the short-term treatment of Paget's disease, acute bone loss prevention due to sudden immobilisation (up to 4 weeks only) and hypercalcaemia of malignancy.

Advice for healthcare professionals:

- Calcitonin-containing medicines should no longer be prescribed for the treatment of osteoporosis.
- Patients currently treated with intra-nasal calcitonin for osteoporosis should be reviewed at their next routine appointment or sooner and changed to another suitable alternative in line with NICE recommendations.

**PACEF Comment**

**Calcitonin nasal spray (200 units per actuation) (*Miacalcic*) is to be withdrawn from the European market and should no longer be prescribed.**

**Ondansetron (*Zofran*): risk of QTc prolongation – important new intravenous dose restriction**

- The new maximum single IV dose of ondansetron for the management of chemotherapy-induced nausea and vomiting (CINV) in adults is now 16mg (infused over at least 15 minutes).
- This restriction follows a review of new safety data which showed a greater risk of QTc prolongation (a known side effect of ondansetron) when used at the higher doses previously authorised for CINV. Prolongation of the QTc can lead to Torsade de Pointes, a potentially life threatening cardiac arrhythmia.
- Ondansetron should be avoided in patients with congenital long QT syndrome.
- Caution must be used if administering ondansetron to patients with risk factors for QT interval prolongation or cardiac arrhythmias. These include: electrolyte abnormalities, use of medicines that prolong the QT interval (including cytotoxic drugs) or may lead to electrolyte abnormalities, congestive heart failure, bradyarrhythmias and use of medicines which lower the heart rate.

- Hypokalaemia and hypomagnesaemia should be corrected prior to ondansetron administration.
- The maximum recommended IV dose of ondansetron for the prevention and treatment of post-operative nausea and vomiting in adult patients remains at 4mg.

**Doripenem (Doribax): current dosing regimen is insufficient in some patients – updated dosing recommendations**

- The recommended dose of doripenem (Doribax) to treat nosocomial pneumonia in patients with augmented renal function and/or infections with pathogens with possible decreased susceptibility has been increased to 1g every 8 hours given as a 4 hour infusion. Previous dosing regimens for doripenem in such patients were found to be insufficient.

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Stephen Gibson  
Head of Prescribing and Medicines Management  
NHS Lincolnshire

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