

## NEWSLETTER

Supporting the Derbyshire Health Community

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### JAPC Update

The Joint Area Prescribing Committee (JAPC) is a countywide group covering Derbyshire County PCT and Derby City PCT. It provides recommendations on drugs and medicines management issues.

RED drugs are those where prescribing responsibility lies with a hospital consultant or a specialist. AMBER drugs are those that are initiated within a hospital/specialist setting but are suitable for shared care with a GP under a shared care agreement. GREEN drugs are regarded as suitable for primary care prescribing.

BROWN drugs are those that JAPC does not recommend for use, except in exceptional circumstances, due to lack of data on safety, effectiveness, and/or cost-effectiveness.

The most recent updates are in the table below; the full list is available at

<http://www.derbyshirecountyinternet.nhs.uk/guidelines/default.asp>

The guidelines, formulary chapters, newsletters, etc can now be found via this link. The old PACEF and PAG websites have now been shut down.

Drug	Date considered	Decision
Aripiprazole injection	August 2008	RED
Deferasirox	August 2008	RED
Methylnaltrexone	August 2008	RED
Micardis plus (telmisartan + hydrochlorothiazide)	August 2008	BROWN
Ambrisentan	July 2008	RED
Aripiprazole tablets	July 2008	GREEN (only on consultant recommendation)
Olanzapine tablets	July 2008	GREEN (only on consultant recommendation)
Quetiapine tablets	July 2008	GREEN (only on consultant recommendation)
Fesoterodine	July 2008	BROWN
Melatonin prolonged-release (Circadin)	July 2008	BROWN
Rimonabant	July 2008	GREEN (as per NICE guidance)

### Colesevelam

MTRAC (Midlands Therapeutics Review and Advisory Committee) have reviewed colesevelam and this is their verdict<sup>1</sup>: colesevelam cannot be recommended for prescribing. Its place in therapy is uncertain because of the availability of a number of alternative effective lipid-lowering agents and the absence of trials comparing colesevelam with such agents. No long term studies (>24 weeks) of colesevelam, or trials studying its effect on patient-orientated outcomes, have been published. There is concern about its potential to bind other drugs in the gut.

JAPC agree with this and have designated **colesevelam as a BROWN drug** and it is not recommended for prescribing.

1. [www.keele.ac.uk/schools/pharm/MTRAC/ProductInfo/verdicts/C/Colesevelam.pdf](http://www.keele.ac.uk/schools/pharm/MTRAC/ProductInfo/verdicts/C/Colesevelam.pdf)

### **Modified-release melatonin**

A licensed form of modified-release (m/r) melatonin (Circadin®) has been launched by Lundbeck for the short-term monotherapy treatment of primary insomnia in patients aged 55 years or older. The recommended dose is 2 mg, 1-2 hours before bedtime and after food, for 3 weeks and it is available in a 21-tablet blister pack priced at £10.77.

The NPCi blog on this product<sup>1</sup> suggests the following action points:

- Practitioners who consider m/r melatonin for an older person need to ensure that the patient has primary insomnia, through robust questioning and physical and mental assessment. This is a minority of insomnia patients.
- Before considering medication, all patients with insomnia should review their life-style and behaviour to improve “sleep hygiene” – see ‘The Good Sleep Guide’<sup>2</sup>.
- Only a small proportion of patients are likely to benefit from m/r melatonin and its effects appear small.
- Due to the short-term nature of the trials, m/r melatonin is not suitable for repeat prescription. Sleep hygiene measures should be continued after the 3-week course of m/r melatonin.
- It is difficult to place m/r melatonin in the current management of primary insomnia because of the lack of comparative data with other treatments, including prescription hypnotics.

There are two ‘pivotal’ published trials<sup>3,4</sup>. These two trials have demonstrated that some older people treated with m/r melatonin for 3 weeks will have an improvement in quality of sleep and morning awakeness, but only a minority will benefit (NNT of 9 or 5) over 3 weeks. A small improvement in sleep latency (about 9 minutes) was found, as a secondary end-point, which is a similar magnitude to that found in trials of benzodiazepines and Z-drugs.

Day-time functioning, fatigue, mood and quality of life are important to patients who are suffering from insomnia, however, these two trials provide little or no evidence that m/r melatonin produces a significant improvement on these patient-oriented outcomes. One trial did show a statistically significant improvement in quality of life, as a secondary end-point<sup>3</sup>. However, the effect appears small.

JAPC has reviewed the evidence for this product and designated it as BROWN due to insufficient evidence i.e. **melatonin (Circadin®) is not recommended for prescribing.**

1. [www.npci.org.uk/blog/?p=137](http://www.npci.org.uk/blog/?p=137)
2. [www.npc.co.uk/MeReC\\_Briefings/2001/good\\_sleep\\_guide.pdf](http://www.npc.co.uk/MeReC_Briefings/2001/good_sleep_guide.pdf)
3. Curr Med Res Opinion 2007; 23: 2597-605
4. J Sleep Res 2007; 16: 372-80

### **Dipyridamole**

Only dipyridamole modified-release 200mg capsules are licensed for secondary prevention of ischaemic strokes and TIAs. Standard-release tablets and oral suspension do not have this licence, nor is there evidence to support their use for this indication. Indeed, there is some evidence that standard-release tablets are not effective<sup>1</sup>.

NICE says that the combination of m/r dipyridamole and aspirin is recommended for people who have had an ischaemic stroke or TIA for a period of 2 years from the most recent event (and aspirin alone thereafter)<sup>2</sup>. This is based on the evidence from the ESPS-2 study<sup>3</sup>. This was a two-year, double-blind, placebo-controlled RCT that compared aspirin 25mg, m/r dipyridamole 200mg and the combination, all taken twice daily, in 6,602 people who had recently suffered a TIA or ischaemic stroke.

ESPS-2 found a significant reduction in stroke at two years with the combination of aspirin plus m/r dipyridamole compared with aspirin alone (strokes with combination 9.5% vs. aspirin 12.5%;  $P < 0.001$ ; NNT=34). However, there was no statistically significant reduction in death from all causes, or the combined endpoint of stroke and/or death with the combination compared with aspirin. However, more people stopped dipyridamole-based therapy than aspirin because of adverse effects (aspirin 8.6%, dipyridamole 15.1%, combination 15.9%;  $P < 0.001$  for all comparisons; NNH=14), especially GI events (particularly diarrhoea) and headache. Because dipyridamole is a vasodilator, patients might also develop hot flushes, hypotension, dizziness, or worsening of unstable angina.

The NICE guidance says that if m/r dipyridamole is not tolerated just use low-dose aspirin. There would seem to be little justification for using dipyridamole standard release tablets or oral solution in this situation. Chesterfield Royal Hospital and Derby Hospitals now only use m/r dipyridamole. If there are swallowing difficulties, it is acceptable to open the capsules and mix the granules with yoghurt, as long as the patient does not crush the granules. If m/r dipyridamole cannot be used do not substitute clopidogrel i.e. prescribe aspirin + clopidogrel, as this combination causes more harm than good<sup>4,5</sup>.

Since the NICE guidance was issued the ESPRIT study has been published<sup>6</sup>. This suggests that the combination of m/r dipyridamole and aspirin should not be stopped after 2 years, as it appears to be effective for at least 5 years. It would seem reasonable to continue with the combination for as long as it is tolerated and then revert to aspirin alone.

1. DTB 1998; 36 (2): 10
2. NICE TA 90, May 2005
3. J Neurol Sci 1996; 143: 1-13
4. Lancet 2004; 364: 331-7
5. N Engl J Med 2006; 354: 1706-17
6. Lancet 2006; 367: 1665-73

### **Treating hypertension in the elderly**

Two recent publications provide support for the use of blood pressure lowering drugs in elderly people with hypertension.

A meta-analysis for the Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC) evaluated data from 31 trials, involving more than 190,000 people with hypertension.<sup>1</sup> They compared results between the two age groups <65 and ≥65 years. Reducing blood pressure with drugs reduced CV risk to a similar degree in both groups, irrespective of which drug regimen was used. Because the absolute risk of CV events is higher in older people than in younger ones, for a similar relative risk reduction, far fewer patient-years of treatment are needed to prevent one major CV event in an elderly person.

Until recently, there was little direct evidence around the management of hypertension in people aged 80 and older. The HYVET study has addressed this.<sup>2</sup> 3845 people who were 80 years of age or older (mean 83.6 years) and had a sustained systolic BP of 160mmHg or more were randomly assigned to receive either indapamide SR 1.5mg or matching placebo daily. Perindopril (2-4mg) or matching placebo was added if necessary to achieve the target blood pressure of 150/80mmHg. The primary endpoint was fatal or nonfatal stroke.

At two years, the mean BP while sitting was 15.0/6.1 mmHg lower in the active-treatment group than in the placebo group.

The study found that, at two years, antihypertensive treatment with indapamide SR 1.5mg with/without perindopril 2-4mg daily significantly reduced deaths from any cause by 21% compared with placebo (95% confidence intervals[CI] 4 to 35, p=0.02). Deaths from stroke were significantly reduced by a relative risk of 39% (95%CI 1 to 62, p=0.05). In the active treatment group, fatal or non-fatal heart failure was reduced by a relative risk of 64% (95%CI 42 to 78, p<0.001) and the rate of any cardiovascular event was reduced by a relative risk of 34% (95% CI 18 to 47, p<0.001).

There were significantly more adverse events in the placebo group compared with the antihypertensive group (448 vs. 358, p=0.001). Only five events were considered to be treatment-related (3 in the placebo group vs 2 in the active treatment group).

The decrease in the risk of the primary endpoint, fatal or non-fatal stroke, did not reach statistical significance, nor did the secondary endpoints reduction in deaths from CV or cardiac (MI, heart failure and sudden death) causes. However, the study was stopped early for ethical reasons on the recommendations of an independent monitoring committee, owing to the significant benefit of antihypertensive treatment on death from any cause. To prevent one death only 40 elderly people had to be treated for 2 years (NNT = 40).

So antihypertensive treatment with a thiazide-like diuretic and/or an ACE inhibitor has now been shown to reduce the risk of death from stroke or any cause in patients aged 80 years or older. It is unclear whether other classes of antihypertensive will have the same benefits. Also, the patients in HYVET were generally

healthier than those aged 80 years and over in the general population. The results of this study may not apply to frail elderly people.

The NPC blog<sup>3</sup> recommends that clinicians should offer people over 80 years of age treatment for hypertension. Treatment should be individualised and take into account the preferences and general health of the individual, including co-morbidities and their current drug regimen, which may already be complex.

1. BMJ 2008, 336:1121-3
2. N Engl J Med 2008; 358:1887-98
3. [www.npci.org.uk/blog/?p=104](http://www.npci.org.uk/blog/?p=104)

## **Update on gout**

### *Confirm diagnosis<sup>1</sup> – is it really gout?*

A typical history of rapid onset, severe, self limiting joint pain reaching its maximum over 6-12 hours, with swelling and erythema, suggests gout, particularly if it involves the first metatarsophalangeal joint at some point. (This joint is affected in 90% of cases and is the first joint affected in 70%). The presence of tophi supports the diagnosis. Previous evidence of monosodium urate crystals from a joint aspirate (during or between attacks) would be the gold standard. A concentration of serum uric acid (SUA) of  $\leq 380 \mu\text{mol/l}$  at least one month after an acute attack or  $\leq 330 \mu\text{mol/l}$  during an attack makes gout an unlikely diagnosis. Common risk factors include beer or spirit consumption, use of drugs (e.g. thiazides), and male gender.

### *Drug treatment<sup>1</sup>*

- Stop or change any precipitating treatment, such as a thiazide diuretic, where this is appropriate.
- If tophi or urate nephropathy are present, or he/she often has attacks of gout (more than three a year), consider treatment with allopurinol: 100 mg daily initiated one month after an acute episode. Increase by 100 mg every four weeks, depending on his SUA concentration (as indicated in the BNF). Aim for a concentration of  $\leq 360 \mu\text{mol/l}$ . Such a “go slow” regimen reduces the risk of allopurinol induced gout and toxicity. In cases of renal impairment start at 50 mg and titrate to a maximum of 100 mg. When starting allopurinol warn him/her that it may precipitate gout but that he/she should continue taking it and seek advice on a prescription for an anti-inflammatory drug (such as an NSAID), colchicine, or a corticosteroid; that it may take many months for gout attacks to settle, even after urate concentrations normalise; and that he/she should come back if a rash appears.

### *Reducing the risk of further attacks<sup>1</sup>*

- Advise him/her to lose weight. Dieting and exercise may reduce his/her serum urate concentration by around  $100 \mu\text{mol/l}$  and will lessen his risk of developing metabolic syndrome. He/she should drink 2litres of fluid a day (especially if he/she has a history of renal stones). Restricting purine rich foods is difficult and usually less effective than weight loss where this is appropriate; dietary advice is available from UK Gout Society ([www.ukgoutsociety.org](http://www.ukgoutsociety.org)).
- Advise him/her to reduce his alcohol intake. He/she should avoid beer (rich in purine) and, ideally, spirits. Wine is not a major risk factor.

### *Ongoing care<sup>1</sup>*

- While he/she is taking allopurinol measure his/her renal function annually and monitor risk factors for metabolic syndrome or cardiovascular adverse events.
- Refer him/her to a specialist if he/she has urate renal stones or nephropathy or is intolerant to allopurinol.

Previous studies have looked at the association of obesity, alcohol, and diet with the onset of gout. A new analysis considers the role of non-alcoholic drinks and fruit on the first onset of gout<sup>2</sup>. It found a strong association between sugar sweetened soft drinks, usually containing fructose, and gout.

Regular drinking of sweetened soft drinks, but not diet soft drinks, was associated with an increased likelihood of developing gout, with an almost doubling of risk with 2 or more soft drinks per day (RR 1.85; 95% CI 1.08 to 3.16). A high intake of naturally occurring fructose also increased the risk of developing gout; consuming two or more glasses of fruit juice each day increased the risk by 81% (RR 1.81; 1.12 to 2.93) and eating an apple or orange a day increased the risk by 64% (RR 1.64; 1.05 to 2.56).

The traditional treatments for the acute phase of gout are an NSAID or colchicine, but these have the potential for adverse events. The use of oral corticosteroids might provide an equally effective and safer method to treat gout. This has been tested in a randomised controlled trial<sup>3</sup>.

The trial tested the equivalence of prednisolone and naproxen for the treatment of monoarticular gout. Primary-care patients with gout confirmed by presence of monosodium urate crystals were eligible. 120 patients were randomly assigned with computer-generated randomisation to receive either prednisolone (35 mg once a day; n=60) or naproxen (500 mg twice a day; n=60), for 5 days. Treatment was masked for both patients and physicians. The primary outcome was pain measured on a 100 mm visual analogue scale and the priori margin for equivalence set at 10%.

Data were incomplete for one patient in each treatment group, so per-protocol analyses included 59 patients in each group. After 90 hours the reduction in the pain score was 44.7 mm and 46.0 mm for prednisolone and naproxen, respectively (difference 1.3 mm; 95% CI -9.8 to 7.1), suggesting equivalence. Adverse effects were similar between groups, minor, and resolved by 3 week follow-up.

The authors concluded that oral prednisolone and naproxen are equally effective in the initial treatment of gout arthritis over 4 days and that the study provides a strong argument to consider prednisolone as a first-line treatment option. However, the accompanying editorial, whilst recognising that the study is high-quality, well designed, generisable, and the largest trial of its type, comments that it is fairly small and done in one centre.<sup>4</sup> The authors suggest “the general clinician might not be convinced that studies with only 120 patients should change long-established practice”.

1. BMJ 2008; 336:329
2. BMJ 2008; 336:309-12
3. Lancet 2008; 371:1854-60
4. Lancet 2008; 371:1816-18

### **Antioxidants and zinc for age-related macular degeneration**

For patients who do not have AMD or who have early disease, there is no evidence from randomised controlled trials to support the use of nutritional supplements. Epidemiological evidence for benefit of a high dietary intake of antioxidants and zinc in preventing the development of AMD is conflicting. However, it would seem reasonable to advise people without AMD or with only mild signs of the disease to follow Department of Health dietary guidelines and increase consumption of fruit and vegetables.

Dietary sources of antioxidants include orange, yellow and green fruit, and dark green leafy vegetables; spinach and cabbage are particularly good sources of lutein and zeaxanthin. Dietary advice should be supplemented with smoking cessation advice if relevant, as smoking is a risk factor for AMD.

For patients with intermediate AMD or advanced AMD in one eye, there is evidence from one study (AREDS) that the specific combination of zinc 80mg, vitamin E 400 units, vitamin C 500mg and beta-carotene 15mg daily may be modestly beneficial in slowing disease progression. Products available in the UK that most closely match this combination are *PreserVision* and *Viteyes Original*. However, as these products contain beta-carotene, people who smoke or are recent ex-smokers should not take them. Similar formulations in which beta-carotene has been substituted with lutein (*PreserVision Lutein*, *Viteyes Smoker's Formula plus Lutein*) lack the evidence base of the original formulation.

These supplements are not licensed medicinal products and so they have not undergone regulatory assessment. They contain doses that are significantly higher than recommended daily allowances and the safety profile of these products when used long-term is unknown.

**JAPC recommend that products such as PreserVision/Viteyes/ICaps should not be prescribed.**

### **Metformin SR**

Metformin was shown in UKPDS to be effective in reducing diabetic complications and is the only hypoglycaemic agent with evidence of reducing all cause mortality. To reduce the potential for side effects with metformin, slowly titrate the dose upwards. If standard metformin is poorly tolerated then it is recommended to try metformin SR.

Until recently metformin SR was only available as 500mg tablets but now 750mg tablets are also available. These have the potential to reduce both the tablet burden and the cost of treatment. Both the 500mg and 750mg tablets cost £3.20 for 28. So a daily dose of 1500mg daily will cost £125.14 per year with the 500mg tablets as opposed to £83.43 with the 750mg tablets, a one-third reduction.

### **Choice of angiotensin II receptor blocker**

The first-line angiotensin II receptor blocker (ARB) in the formulary, should one be required, is candesartan as it is the current most cost-effective choice for this class of drugs. Irbesartan has been approved for the limited group of patients with type 2 diabetes, hypertension and nephropathy, should an ARB be indicated.

### **Drug safety update**

This can be found at [www.mhra.gov.uk/drugsafetyupdate](http://www.mhra.gov.uk/drugsafetyupdate). Here are some of the key points from the July issue.

### ***Varenicline: suicidal thoughts and behaviour***

Suicidal thoughts and behaviour have been reported in users of varenicline who have no known pre-existing psychiatric conditions, and while they continue to smoke. Anyone taking varenicline who develops depression or suicidal thoughts should stop their treatment and contact their doctor immediately.

#### *Suicidal thoughts and behaviour*

Stopping smoking – with or without medication – may be associated with various psychiatric symptoms, such as depressed mood, irritability, anxiety, frustration, or anger. Moreover, stopping smoking may exacerbate an underlying psychiatric condition.

Recently, concerns have arisen about reports of suicidal ideation and suicidal behaviour associated with the use of varenicline. Up to March 18, 2008, the MHRA have received 129 reports of suicidal thoughts or behaviour associated with the use of varenicline. These reports mainly involved people who had pre-existing psychiatric conditions or other psychosocial risk factors. However, a detailed review of UK Yellow Card data found that suicide-related events have been reported in patients taking varenicline who have no known pre-existing psychiatric conditions and in patients who continued to smoke.

### **Advice for healthcare professionals:**

- Patients should be told to stop treatment and contact their doctor immediately if they develop suicidal thoughts or behaviour.
- Varenicline should be stopped immediately if agitation, depressed mood, or changes in behaviour are observed that are of concern to the patient, family, or caregivers.
- The safety and efficacy of varenicline in people with serious psychiatric illness have not been established. Patients who have a history of psychiatric illness should be monitored closely while taking varenicline.

### ***Bisphosphonates: atrial fibrillation***

Clinical trial results have suggested an increased risk of atrial fibrillation for zoledronic acid (Aclasta ▼), pamidronic acid, and possibly for alendronic acid. The balance of risks and benefits for bisphosphonates remains favourable.

### **Information for healthcare professionals:**

- The risk of atrial fibrillation in association with bisphosphonate treatment seems to be low, and the balance of risks and benefits for bisphosphonates remains favourable.
- To date, clinical trial results have suggested an increased risk of atrial fibrillation for zoledronic acid (Aclasta ▼), pamidronic acid, and possibly for alendronic acid.
- The product information for zoledronic acid has been updated to include atrial fibrillation as a possible side-effect (both for Aclasta ▼ and Zometa, a product that contains zoledronic acid that is given every 3-4 weeks as part of cancer treatment). Atrial fibrillation is also being added to the product information for pamidronic acid.
- The risk of atrial fibrillation with alendronic acid will be kept under close review. Should further evidence accumulate, the product information for alendronic acid will be updated accordingly.

### ***Rotigotine patches: new prescribing and storage requirements***

Rotigotine (Neupro ▼) is a transdermal patch that is indicated for the treatment of the signs and symptoms of early-stage or advanced-stage idiopathic Parkinson's disease. The MHRA have recently become aware that the manufacture of rotigotine can result in an alternative crystalline structure of the active ingredient that is visible as a snowflake pattern. Although there is a theoretical possibility that clinical efficacy might be reduced,

to date there has been no change in the pattern of suspected adverse reactions reported with this medicine that could be attributed to crystal formation.

Refrigerated storage of the patches seems to reduce crystal development. The Marketing Authorisation Holder will be supplying refrigerated batches to replace products that remain in the distribution chain. Therefore, from the end of July 2008, only 2 mg and 4 mg 24-hour patches will be available for an interim period.

#### **Advice for healthcare professionals:**

- Healthcare professionals should be attentive to any signs that suggest lack of efficacy of rotigotine. Please report any cases of suspected lack of efficacy to the MHRA using a yellow card. Please report any defects to the Defective Medicines Report Centre.
- To prioritise supply for patients who currently take rotigotine, please limit every prescription to 1 month's supply and please do not initiate any new patients on rotigotine.
- Inform patients that the patches are currently available and can be used: patients must not stop using their current rotigotine patches, even if they notice snowflake patterns on the patch, without first speaking to a healthcare professional.
- Patients must not abruptly stop treatment. Abrupt withdrawal has been associated with a syndrome resembling neuroleptic malignant syndrome or akinetic crisis.
- Patients should be advised to store their rotigotine patches in the refrigerator; patches must not be stored in the freezer. Patients should apply and maintain gentle pressure with the palm on the hand for at least 1 minute for adhesion; there is no need to bring the patch to room temperature before use.

#### **Rimonabant**

NICE technology appraisal guidance 144 was recently issued. As a result, JAPC has had to move rimonabant from BROWN (not recommended) in the traffic lights list to GREEN (as per the NICE guidance). NICE sets strict criteria on the use of rimonabant:

- 1) Rimonabant, within its licensed indications, is recommended as an adjunct to diet and exercise for adults who are obese or overweight and who have had an inadequate response to, are intolerant\* of or are contraindicated to orlistat **and** sibutramine.

*\* steatorrhea as a consequence of not adhering to dietary advice should not be considered as intolerance to orlistat.*

- 2) Rimonabant treatment should be continued beyond 6 months only if the person has lost at least 5% of their initial body weight since starting rimonabant treatment.
- 3) Rimonabant treatment should be discontinued if a person returns to their original weight while on rimonabant treatment.
- 4) Rimonabant treatment should not be continued for longer than 2 years without a formal clinical assessment and discussion of the individual risks and benefits with the person receiving treatment.

Please remember that the MHRA issued a warning about depression and psychiatric adverse reactions with rimonabant in the May issue of "Drug Safety Update" (see June PACE Newsletter).

#### **Commonly used treatment options provide limited benefit but cost a lot of money**

This is the title of the recently published MeReC Monthly No. 3<sup>1</sup>. The NPC highlight two interventions; self-monitoring of blood glucose and the use of angiotensin II receptor blockers.

### Self-monitoring in type 2 diabetes

The view that routine self-monitoring of blood glucose (SMBG) is unlikely to be beneficial in patients with type 2 diabetes who are not treated with insulin has been reinforced by two recent studies. SMBG may also worsen quality of life and waste NHS resources.

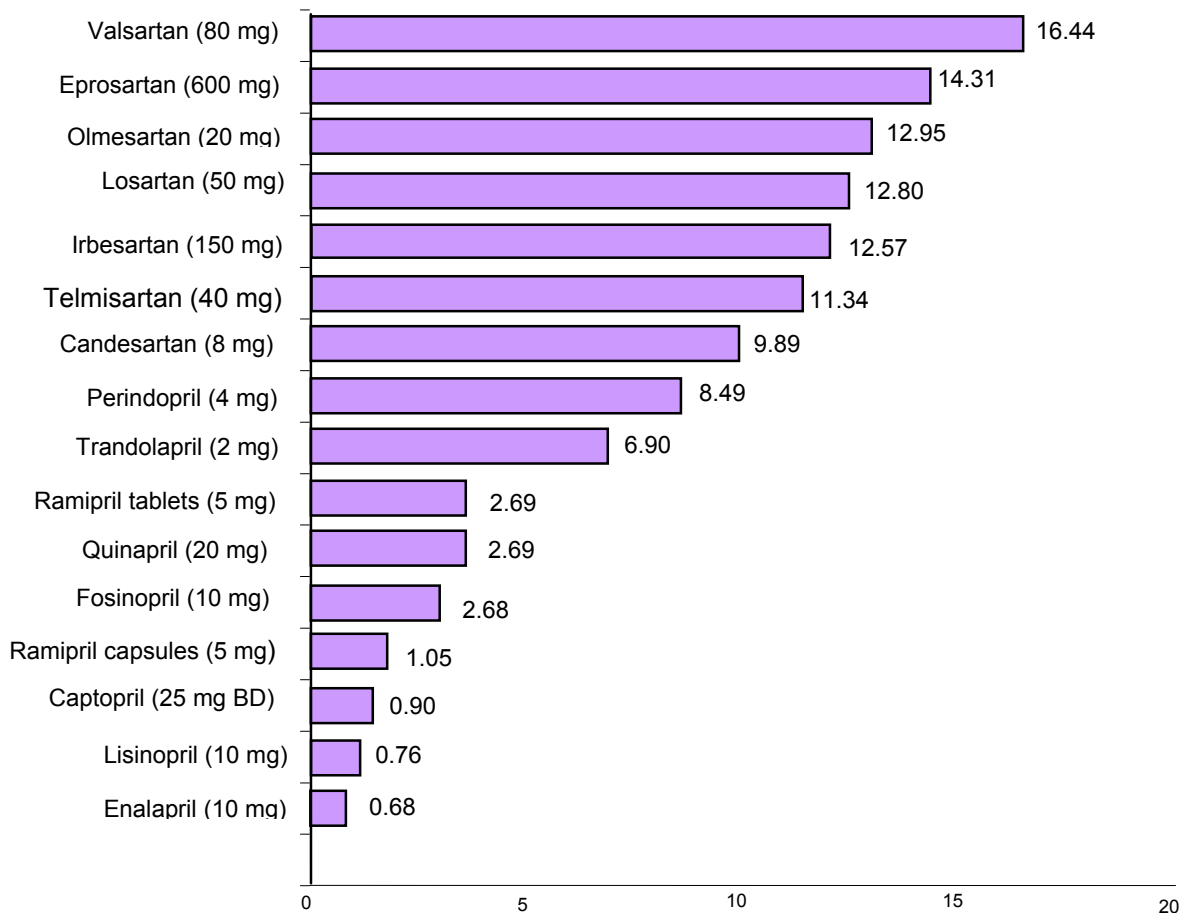
SMBG in patients with type 2 diabetes should be reserved for patients treated with insulin and for non-insulin treated patients in specific circumstances. NICE guidance on type 2 diabetes has recently been updated and recommends that SMBG should be offered to people newly diagnosed with type 2 diabetes as an integral part of self-management education, when the purpose is clear and the patient understands how results should be interpreted and acted upon. NICE advises that SMBG should be available to patients on insulin and to certain patients who require information on hypoglycaemia or hyperglycaemia (e.g. during intercurrent illness, due to changes in medication or lifestyle or to ensure safety during activities such as driving). The continued need for SMBG should be assessed at least annually.

### Angiotensin II receptor blockers

The first-choice renin-angiotensin system drug for people at high risk of CV disease, with or without heart failure, is an ACE inhibitor. Angiotensin II receptor blockers (ARBs) are an alternative in patients unable to tolerate ACE inhibitors due to cough, but note that cough can still occur with ARBs. The ONTARGET study suggests that adding an ARB to an ACE inhibitor in patients at high risk of CV events who do not also have heart failure does not prevent adverse CV events. Indeed, using the combination has been shown to increase the risk of adverse effects serious enough to cause patients to stop treatment.

1. [www.npc.co.uk/MeReC\\_Monthly/merec\\_monthly\\_no3\\_web.pdf](http://www.npc.co.uk/MeReC_Monthly/merec_monthly_no3_web.pdf)

### Drugs affecting the renin-angiotensin system



Doses given do not imply therapeutic equivalence

Cost (£) for 28 days treatment (August 2008)