

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.derbyshirecountypct.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
Hyaluronic acid injection	September 2008	BROWN
Leuprorelin injection	September 2008	BROWN
Aripiprazole injection	August 2008	RED
Deferasirox	August 2008	RED
Methylnaltrexone	August 2008	RED
Micardis plus (telmisartan + hydrochlorothiazide)	August 2008	BROWN
Ambrisentan	July 2008	RED
Fesoterodine	July 2008	BROWN
Melatonin prolonged-release (Circadin)	July 2008	BROWN
Rimonabant	July 2008	GREEN (as per NICE guidance)

Guidelines update

The following guidelines and shared care agreements have recently been ratified by JAPC for use across Derbyshire:

- COPD management
- Policy for appropriate statin use
- Use of clopidogrel
- Shared care of VSL#3 for pouchitis

You can obtain copies of these from your Medicines Management team, from me, or from the website address above.

More on bleeding risk with SSRIs

Further to the article in the April 08 edition, a large case-control study has been published¹. This study provides further support for an increased risk of upper gastrointestinal bleeding with SSRI antidepressants. It also suggests that venlafaxine also increases risk (but to a lesser extent), indicates an interaction with other drugs that increase the risk (e.g. NSAIDs), and that acid-suppressant therapy may possibly reduce the risk.

There were 1321 cases for evaluation, matched with 10,000 controls. There were more current users of SSRIs in the cases compared to controls (5.3% vs. 3.0%, adjusted odds ratio 1.6; 95% CI, 1.2 to 2.1) and also more current venlafaxine users in the cases compared to controls (1.1% vs. 0.3%, OR 2.9; 95% CI, 1.5 to 5.6).

There was an interaction with NSAID use: risk with concurrent use of either SSRI or SNRI with a NSAID was greater than the sum of the individual effects (OR, 4.8; 95% CI, 2.8 to 8.3). There was also indication of an added risk with systemic corticosteroids (OR, 4.0; 95% CI, 1.3 to 12.3) however concurrent use of antiplatelet drugs and oral anticoagulants did not appear to be associated with increased risk.

Numbers needed to harm (NNH) calculations indicate that the absolute risk is low: for all SSRI/SNRI combined, 2000 patients would need to be treated for one additional case of upper gastrointestinal bleeding. However, in combination with an NSAID, the NNH is 250. Concurrent use of acid-suppressing drugs would appear to reduce the risk to give an estimated NNH of 5000.

The authors conclude that their results confirm that antidepressant drugs blocking serotonin reuptake increase the risk of upper gastrointestinal bleeding. They note that the results add to anecdotal evidence that SNRIs (venlafaxine) also have this effect. A positive interaction was seen with NSAIDs and systemic corticosteroids; however concurrent use of acid suppressing drugs seems to reduce the risk - especially the increased risk shown with concurrent NSAID use. No indication of increased risk was seen with other antidepressant drug groups.

This is an epidemiological study, so the figures will not be as robust as from a randomised controlled trial. Nevertheless, they follow the weight of evidence so far available and further support this being a real effect. The effect of concurrent acid-suppressing drug use would be intuitively expected, but we've had little data in support up to now. Given that a randomised controlled trial in this area is (regrettably) unlikely, this study could reasonably support such use in at-risk patients taking an SSRI or SNRI - especially if also taking another drug that increases risk.

1. Arch Gen Psychiatry 2008; 65: 795-803

Intensive blood glucose-lowering

Further to the article in the March 08 edition, the ACCORD study has now been published¹. ACCORD was a randomised, controlled, non-blinded study. Eligible participants had type 2 diabetes and glycated haemoglobin (HbA1c) levels of 7.5% or more; they were either aged between 40 and 79 years and had cardiovascular disease, or were aged between 55 and 79 and had atherosclerosis, albuminuria, left ventricular hypertrophy, or at least two additional risk factors for cardiovascular disease.

Target HbA1c level in the intensive control group was less than 6.0%, and in the standard control group was 7.0 to 7.5%. Medications came primarily from a study formulary – any other marketed anti-hyperglycaemic therapy could be prescribed if clinically indicated, but was not provided by the study investigators. All patients were provided with instructional materials and behavioural counselling related to their diabetes. The primary outcome was first occurrence of non-fatal myocardial infarction, non-fatal stroke, or death from cardiovascular causes. Secondary outcomes included death from any cause.

Levels of HbA1c fell rapidly in each arm after randomisation, from a mean baseline of 8.1% to mean levels of 6.7% in the intensive group and 7.5% in the standard therapy group: at one year, they were 6.4% and 7.5% respectively. These levels were maintained throughout the study. The primary outcome was numerically less frequent in the intensive group, starting to diverge from the standard group at three years, however when the study was stopped the difference was not statistically significant (6.9% vs. 7.2%; hazard ratio [HR] 0.90; 95% confidence interval [CI], 0.78 to 1.04; p=0.16).

The rate of death from any cause was higher in the intensive therapy group (5.0% vs 4.0%; HR 1.22; 95% CI, 1.01 to 1.46; p=0.04; NNH=100). This difference was stable to various sensitivity analyses: death rates in the two groups started to diverge after the first year with the difference persisting throughout follow-up.

Another study investigating intensive blood glucose-lowering, ADVANCE, has also been published². The ADVANCE trial was designed to assess the effects on major vascular outcomes of lowering the glycated haemoglobin value to a target of 6.5% or less in a broad cross-section of patients with type 2 diabetes. Eligibility criteria were a diagnosis of type 2 diabetes mellitus at 30 years of age or older, an age of at least 55 years at the time of study entry, and a history of major macrovascular or microvascular disease or at least one other risk factor for vascular disease.

Participants were randomised to undergo either a strategy of intensive blood glucose control (target glycated haemoglobin value, $\leq 6.5\%$) or a strategy of standard glucose control (with target glycated haemoglobin levels defined on the basis of local guidelines). Those who were assigned to undergo intensive glucose control were given gliclazide (modified release, 30 to 120 mg daily) and were required to discontinue any other sulfonylurea. Although the timing, selection, and doses of all other treatments were at the discretion of the treating physician, a treatment protocol was suggested. On the basis of the glycated haemoglobin level at each visit, this protocol initially advised increasing the dose of gliclazide mr, with the sequential addition or increase in dose of metformin, thiazolidinediones, acarbose, or insulin. Patients in the standard-control group who were using gliclazide mr when they entered the study were required to substitute this drug with another sulfonylurea, if continued therapy was required.

The primary study outcomes were a composite of macrovascular events and a composite of microvascular events, considered both jointly and separately. Macrovascular events were defined as death from cardiovascular causes, non-fatal myocardial infarction, or non-fatal stroke. Microvascular events were defined as new or worsening nephropathy (i.e. development of macroalbuminuria, defined as a urinary albumin:creatinine ratio of more than 300 μg of albumin per milligram of creatinine, or doubling of the serum creatinine level to at least 200 μmol per litre, the need for renal-replacement therapy, or death due to renal disease) or retinopathy (i.e., development of proliferative retinopathy, macular oedema or diabetes-related blindness or the use of retinal photocoagulation therapy).

Pre-specified secondary outcomes were numerous and included death from any cause, death from CV causes, major coronary events, major cerebrovascular events, heart failure, nephropathy, retinopathy, neuropathy, and development of microalbuminuria. Hypoglycaemia was defined as a blood glucose level of less than 2.8 mmol per litre or the presence of typical symptoms and signs of hypoglycaemia without other apparent cause. Patients with transient dysfunction of the central nervous system who were unable to treat themselves (requiring help from another person) were considered to have severe hypoglycaemia.

The mean baseline glycated haemoglobin was 7.5%. At the end of follow-up (median 5 years), the mean values were 6.5% in the intensive-control group and 7.3% in the standard-control group. A total of 2125 participants had a major macrovascular or microvascular event: 18.1% in the intensive-control group and 20.0% in the standard-control group (hazard ratio, 0.90; 95% confidence interval (CI), 0.82 to 0.98; $p=0.01$). Thus, it was estimated that such an event would be averted during a 5-year period in 1 of every 52 participants (95% CI, 30 to 213) undergoing intensive control, i.e. NNT=52.

As compared with standard control, intensive control resulted in a significant reduction in the incidence of major microvascular events (hazard ratio, 0.86; 95% CI, 0.77 to 0.97; $p=0.01$; NNT = 63) but not in the incidence of major macrovascular events (hazard ratio, 0.94; 95% CI, 0.84 to 1.06; $p=0.32$). The reduction in microvascular events was primarily because of a reduction in the incidence of nephropathy (HR, 0.79; CI 0.66 to 0.93; $p=0.006$; NNT = 91).

The component of new or worsening nephropathy most clearly reduced through intensive glucose control was the development of macroalbuminuria (2.9%, vs. 4.1% with standard control; hazard ratio, 0.70; 95% CI, 0.57 to 0.85; $p<0.001$; NNT = 83). There was no reduction in the need for renal-replacement therapy or death from renal causes (0.4% vs. 0.6%; hazard ratio, 0.64; 95% CI, 0.38 to 1.08; $p=0.09$) and no effect on the doubling of serum creatinine level (1.2% vs. 1.1%; hazard ratio, 1.15; 95% CI, 0.82 to 1.63; $p=0.42$). A total of 1031 participants died: 8.9% in the intensive-control group and 9.6% in the standard control group (hazard ratio, 0.93; 95% CI, 0.83 to 1.06; $p=0.28$). There were no significant differences between the two groups for any of the other pre-specified secondary outcomes.

More patients undergoing intensive control were hospitalised for any cause (44.9%, vs. 42.8% of those in the standard-control group; hazard ratio, 1.07; 95% CI, 1.01 to 1.13; $p=0.03$; NNH=48), with some of the excess of hospitalisations due to severe hypoglycaemia (1.1% vs. 0.7%; odds ratio, 1.52; 95% CI, 1.01 to 2.28; $p=0.04$).

Severe hypoglycaemia occurred more frequently in the intensive-control group than in the standard-control group: 150 patients (2.7%) undergoing intensive control had at least one severe hypoglycaemic episode, as compared with 81 patients (1.5%) undergoing standard control (hazard ratio, 1.86; 95% CI, 1.42 to 2.40; $p < 0.001$; NNH=83).

The ADVANCE trial did not show a significant effect of intensive glucose control on the risk of major macrovascular events. Intensive glucose control resulted in a reduction by one fifth in the development of new or worsening nephropathy, mainly due to a reduction in the development of macroalbuminuria. There was no reduction in the need for renal replacement therapy or death from renal causes. There was no reduction in new or worsening retinopathy, including retinal photocoagulation, or in neuropathy. Intensive glucose control was associated with an increased risk of hospitalisation and severe hypoglycaemia, as compared with standard control. Is an NNT over 5 years of 83 to prevent one person developing macroalbuminuria worth an NNH of 48 for hospitalisation or an NNH of 83 for severe hypoglycaemia?

The most significant message from ACCORD and ADVANCE is that in high-risk type 2 diabetics, intensive therapy intended to produce near-normal blood sugar levels does not improve cardiovascular outcomes over the 3.5 to 5 year time frame, and may worsen them. Neither trial showed a significant improvement in macrovascular outcomes with intensive therapy, and the increased risk of all-cause death in ACCORD is of concern. In both studies, patients in the intensive treatment groups had higher incidences of hypoglycaemia – around twice that of the standard treatment group in ADVANCE, and three times it in ACCORD.

The NPCi blog, ‘Putting blood glucose control in type 2 diabetes into perspective’³, suggests the following action: “Managing cardiovascular (CV) risk factors are the priority for patients with type 2 diabetes. Although interventions (e.g. metformin and diet/lifestyle) will often be required to control the symptoms associated with having high blood glucose levels, clinicians should not become over-focussed on intensive strategies to achieve HbA1c targets. These are often unnecessary and can put patients at risk of adverse drug-related events. Clinicians should give priority to reducing the risk of macrovascular events with evidence-based interventions (e.g. smoking cessation, blood pressure control and the use of metformin/aspirin/simvastatin).”

Both of these studies have been reviewed and discussed at JAPC. **JAPC concluded that the current QoF target of HbA1c <7.5 is reasonable but chasing the NICE target of <6.5 is not advised and may cause harm. Prescribers are advised to follow the diabetes ‘hand’.**



1. N Engl J Med 2008; 358: 2545-59
2. N Engl J Med 2008; 358:2560-72
3. www.npci.org.uk/blog/?p=147

Efcortelan discontinued

Unfortunately it is true. Chemidex, who took over production of Efcortelan cream and ointment from GSK, have announced that these products are being discontinued. Patients on these products will now have to be prescribed generic hydrocortisone cream/ointment at considerably more cost. Bizarre!

However please don't prescribe the 50g tubes – 30g of hydrocortisone 1% ointment costs £4.74 and the 50g tube is £27.91! (£4.32 and £19.13 respectively for 1% cream).

More data on the safety of salmeterol in asthma

In 2006, Salpeter and co-workers¹ reported the results of a meta-analysis that examined questions about the safety of long-acting beta-agonists (LABAs). They found that LABAs significantly increased asthma-related hospital exacerbations, life-threatening exacerbations, and asthma deaths (see PACE Newsletter of July 2006).

An analysis of data from RCTs conducted by GSK has recently been published² in attempt to alleviate concerns regarding the safety of salmeterol when used in the recommended manner in combination with inhaled corticosteroids (ICS). They found no clinically significant effect of salmeterol on asthma-related hospitalisations. In a subgroup of trials that provided information on severe asthma exacerbations, this outcome was less frequent by a statistically significant – albeit small – amount in patients taking salmeterol. Asthma-related death in either group was too infrequent to provide useful guidance.

The NPCi blog³ that accompanies the paper comments:

“In view of the limitations of the study, the results should be interpreted cautiously. The study suggests that if salmeterol is used in combination with inhaled corticosteroids according to British Guidelines, then the incidence of serious adverse events arising from the use of salmeterol in asthma are likely to be very small, at least over the short term. The study does not by itself alleviate the concerns over the long-term safety of LABAs when used in routine clinical practice, and clinicians should continue to bear in mind the possibility of serious adverse events arising from their use, and to advise patients of the risks and monitor them accordingly. LABAs should only be used in patients with asthma whose symptoms are uncontrolled by inhaled corticosteroids alone. Stepping-down therapy should be considered when good long-term asthma control has been achieved”.

The editorial⁴ that accompanies the paper comments:

“Because we cannot expect any more new data, how should physicians and patients use combination therapy? Perhaps the best advice is to consider using combination therapy only for indications that accord with nationally accepted clinical guidelines. Specifically, long-acting β -agonists with or without inhaled corticosteroids should not be used as first-line treatment and especially not for persons with mild asthma. In addition, the prudent course would be to use this treatment only when the physician is confident that the patient will adhere to close monitoring and instructions to seek care when asthma is out of control.

Ultimately, nearly all drugs have therapeutic windows within which physicians and patients must function. Like insulin and oral anticoagulation, long-acting β -agonists have a particularly narrow therapeutic window. They deserve the same caution and meticulous attention to detail that physicians expect of themselves when they prescribe potentially harmful drugs.”

A Cochrane review of serious adverse events of regular treatment with salmeterol for chronic asthma has recently been published.⁵

Main results

All-cause mortality was higher with regular salmeterol than placebo but the increase was not significant, Odds Ratio 1.33 [95% CI: 0.85 to 2.10]. Non-fatal serious adverse events were significantly increased when regular salmeterol was compared with placebo, Odds Ratio 1.14 [95% CI: 1.01 to 1.28]. One extra serious adverse event occurred over 28 weeks for every 188 people treated with regular salmeterol [95% CI: 95 to 2606]. There is insufficient evidence to assess whether the risk in children is higher or lower than in adults. No significant increase in fatal or non-fatal serious adverse events was found when regular salmeterol was compared with regular salbutamol.

Individual patient data from the SNS study have been combined with the results of the SMART study; in patients who were not taking inhaled corticosteroids, compared to regular salbutamol or placebo, there was a significant increase in risk of asthma-related death with regular salmeterol, Odds Ratio 9.52 [95% CI: 1.24 to 73.09]. The confidence interval for patients taking inhaled corticosteroids is too wide to rule out an increase in asthma mortality in this group.

Authors' conclusions

In comparison with placebo, we have found an increased risk of serious adverse events with regular salmeterol. There is also a clear increase in risk of asthma-related mortality in patients not using inhaled corticosteroids in the two large surveillance studies. Although the increase in asthma-related mortality was smaller in patients taking inhaled corticosteroids at baseline, the confidence interval is wide, so it cannot be concluded that the inhaled corticosteroids abolish the risks of regular salmeterol. The adverse effects of regular salmeterol in children remain uncertain due to the small number of children studied.

The authors offer the following advice:

“For patients whose asthma is not well-controlled on moderate doses of inhaled corticosteroids, additional salmeterol can give symptomatic benefit but this may be at the expense of an increased risk of serious adverse events and asthma related mortality; risks which are not clearly abolished by inhaled corticosteroids. Therefore, the risks as well as the benefits of regular salmeterol should be discussed with patients, the drug should be discontinued if no symptomatic benefit is achieved and the manufacturers' advice not to increase the dose of salmeterol during exacerbations should be made clear”.

Are LABAs overused in asthma? The NPC states that most patients can be managed successfully at step 2 (regular ICS plus reliever inhaler when required), at least most of the time.⁶ Weiss⁴ notes that the number of patients receiving the combination of ICS + LABA exceeds the number of patients with moderate to severe asthma, making it likely that physicians are prescribing it for patients who do not fit the guideline-recommended indication of moderate asthma (that is, asthma not controlled by anti-inflammatory medications alone).

Recommendations

- It is important to follow current guidelines and emphasise the use of ICS as the first-line treatment for patients with mild to moderate asthma symptoms. LABAs should not be used as initial therapy for any asthmatic patient.
- Make sure individuals are receiving an adequate dose of ICS. Escalate the dose of ICS to the levels recommended in the British Asthma Guideline (800mcg/day beclometasone equivalent in adults and 400mcg/day in children aged 12 and under) before considering a LABA. Do not jump to step 3 too early. If satisfactory control is not obtained at these doses then a LABA should be added.
- Do not move to step 3 without assessing inhaler technique and compliance. Encourage the use of spacer devices.
- If a step 3, review regularly as recommended by the British Asthma Guideline, and consider stepping down back to step 2, i.e. stop the LABA.
- It is important to carefully monitor patients on LABAs to identify those who do not respond or whose condition deteriorates in response to LABA therapy. Health professionals should be prepared to provide an alternative medication for patients in whom LABA therapy fails.
- Remember that the step 3 recommendation for children aged under 5 in the British Asthma Guideline is not a LABA.

1. Salpeter SR et al, Ann Intern Med 2006; 144:904-12

2. Bateman E et al, Ann Intern Med 2008; 149: early online publication

3. www.npci.org.uk/blog/?p=156

4. Weiss KB, Ann Intern Med 2008; 149:early online publication

5. Cates CJ et al, Cochrane Database of Systematic Reviews 2008, Issue 3

6. www.npci.org.uk/blog/?p=114

Drug safety update

This can be found at www.mhra.gov.uk/drugsafetyupdate. Here are some of the key points from the August issue.

Moxifloxacin: restricted use

Oral moxifloxacin (Avelox, a fluoroquinolone antibiotic) is now restricted for use only when other medicines cannot be prescribed, or have failed, for treatment of acute bacterial sinusitis, acute exacerbation of chronic bronchitis, or community acquired pneumonia. This restriction is based on evidence of an increased risk of life threatening liver reactions and other serious risks associated with moxifloxacin.

Antiepileptics: risk of suicidal thoughts and behaviour

Concern about a possible risk of suicidal thoughts and behaviour associated with antiepileptics led to a Europe-wide review of data from clinical trials, published literature, and postmarketing spontaneous reports of adverse drug reactions. This review has concluded that any antiepileptic drug may rarely be associated with a small increased risk of suicidal thoughts and behaviour.

Advice for healthcare professionals:

- Antiepileptic treatment is associated with a small risk of suicidal thoughts and behaviour; available data suggest that the increased risk applies to all antiepileptics and is seen as early as 1 week after starting treatment.
- Patients should be alert to any mood changes, distressing thoughts, or feelings about suicide or harming themselves at any point during treatment. They should be advised to seek medical advice if they develop such thoughts or behaviour, and should be referred for appropriate treatment if necessary.
- The available evidence does not define whether the risk of suicidal thoughts and behaviour differs between antiepileptics. Patients should not stop or switch treatment on the basis of this information and without speaking to a healthcare professional.

More on insulin analogues

Last year the Cochrane Collaboration published a review of long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus (see May 07 issue of PACE Newsletter)¹. The overall conclusion of this Cochrane review was “our analysis suggests, if at all, only minor clinical benefit of treatment with long-acting insulin analogues for patients with diabetes mellitus type 2 treated with ‘basal’ insulin regarding symptomatic hypoglycaemic events. Until long-term efficacy and safety data are available, **we suggest a cautious approach to therapy with insulin glargine or detemir**”.

Cochrane have now published a review of intermediate acting versus long acting insulin for type 1 diabetes mellitus². The weighted mean difference (WMD) for the level of glycosylated haemoglobin was -0.08 (95% CI -0.12 to -0.04) in favour of the long acting insulin arm. This may have been statistically significant but as the authors point out this difference is clinically unremarkable.

There was no difference in the development of all types of hypoglycaemia combined. There was some reduction in nocturnal hypoglycaemic episodes, OR 0.70 (0.63 to 0.79). The WMD between the long and intermediate insulin groups for nocturnal hypoglycaemic episodes was -0.40 (-0.45 to -0.34). The authors conclude “Our analysis suggests only modest clinical benefit of treatment with long acting insulin preparations rather than intermediate acting preparations for patients with diabetes mellitus type 1. Their effect is more prominent for the control of nocturnal hypoglycaemia. **We suggest a cautious approach to their use in view of their potential mitogenic effect**”.

All the interventions we use or commission need to be a) effective, b) cost-effective, and c) affordable. If not, resources are used inappropriately and other interventions cannot be provided. The evidence shows us that for most people with diabetes the use of insulin analogues just doesn't stack up. A long acting insulin analogue may be appropriate for someone who suffers with significant nocturnal hypoglycaemia, but this is not common in people with type 2 diabetes. Of the total expenditure on insulins in Derbyshire, 57% in County PCT and 84% in City PCT is for insulin analogues. Is this justifiable? Consider the opportunity cost.

1. Horvath K et al. *Cochrane Database of Systematic Reviews* 2007, Issue 2
2. Vardi M et al. *Cochrane Database of Systematic Reviews* 2008, Issue 3

FDA safety warning for exenatide

Further to the MHRA warning about the risks of acute pancreatitis with exenatide (see June 08 issue of PACE Newsletter), The Food and Drugs Administration has issued an updated safety warning, following reports of six cases of haemorrhagic or necrotizing pancreatitis in patients taking exenatide (Byetta ▼). Of these six cases, all patients required hospitalisation, two patients died and four patients were recovering at time of reporting. Exenatide was discontinued in all six cases.

The FDA warning states:

“Byetta and other potentially suspect drugs should be promptly discontinued if pancreatitis is suspected. There are no signs or symptoms that distinguish acute hemorrhagic or necrotizing pancreatitis associated with Byetta

from the less severe form of pancreatitis. If pancreatitis is confirmed, initiate appropriate treatment and carefully monitor the patient until recovery. Byetta should not be restarted. Consider antidiabetic therapies other than Byetta in patients with a history of pancreatitis.”

Action¹:

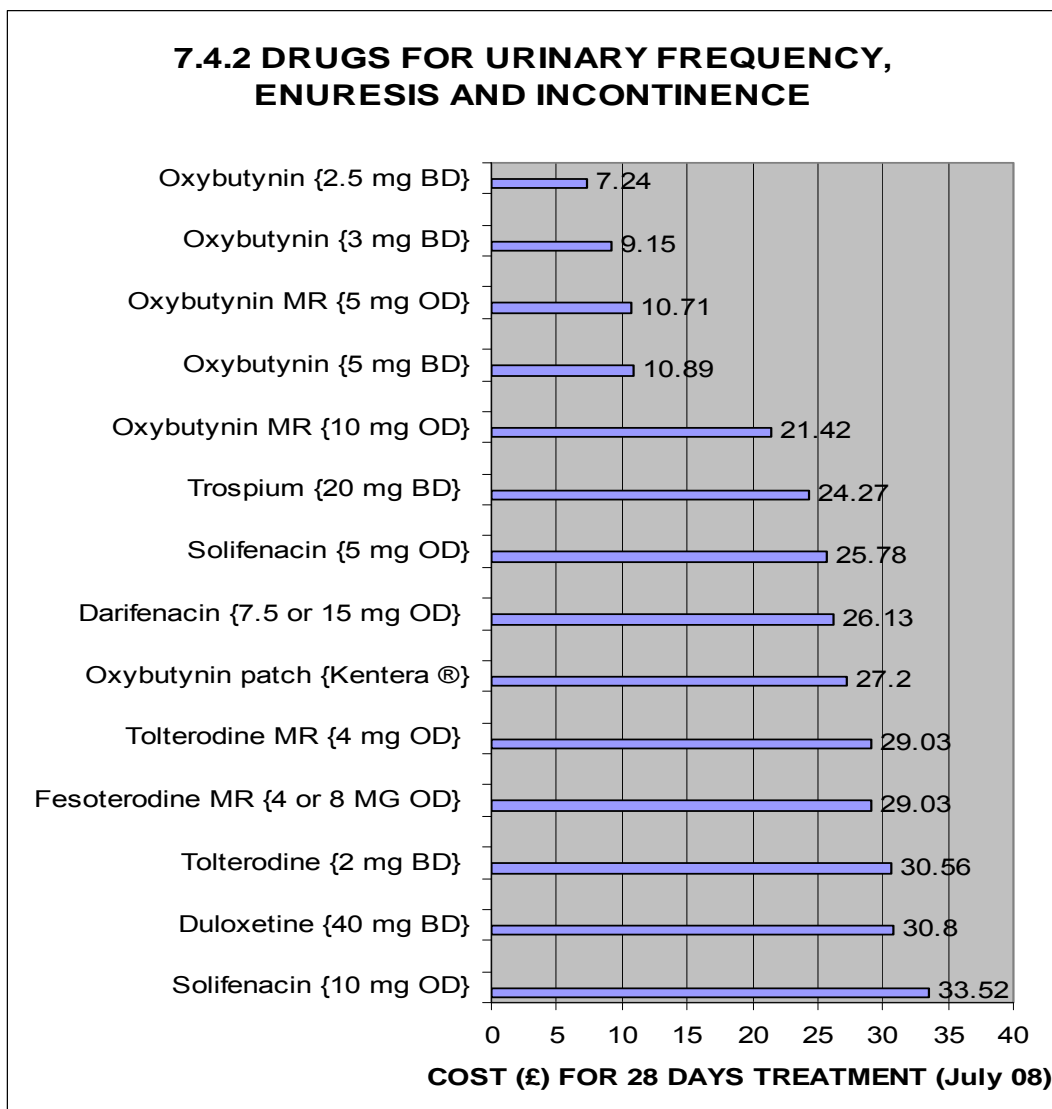
- Healthcare professionals should be alert for signs or symptoms of pancreatitis in patients prescribed exenatide (Byetta▼) in view of the rare, but potentially fatal, occurrences of haemorrhagic or necrotising pancreatitis.
- Where pancreatitis is suspected, exenatide (and other suspect drugs) should be immediately discontinued.
- Patients prescribed exenatide should be informed of the characteristic symptoms of acute pancreatitis (persistent, severe abdominal pain, with or without nausea and vomiting; back pain may also be present), and instructed to seek prompt medical care if they experience these symptoms.
- Any suspected adverse reactions should be reported to the MHRA through the Yellow Card scheme.

1. www.npci.org.uk/blog/?p=187

Drugs for urinary incontinence

NICE states that all the options are equally effective and choice should therefore be determined by cost. First choice recommendation is oxybutynin immediate-release. This has been endorsed by JAPC. JAPC does not recommend a specific second-line option but does agree that the choice should be based on picking the most cost-effective.

The following cost chart has been provided by the Regional Drug and Therapeutics Centre at Newcastle.



Fesoterodine is a BROWN drug in Derbyshire.