PRESCRIBING NEWS

NHS Milton Keynes

September 2010

Key therapeutic topics 2010/11 – Medicines management options for local implementation
The National Prescribing Centre and Department of Health have provided evidence on specific cost saving opportunities in their document **"Key therapeutic topics 2010/11 – Medicines management options for local implementation."** The list currently covers 15 medicines or classes of medicines. None of the topics listed will be new to local clinicians; they have been targeted in the incentive schemes and work undertaken with you by the Pharmaceutical Advisers. The publication of this list is an opportunity to redouble our efforts to ensure cost-effective prescribing. Please contact us if you would like further information on the evidence behind these key areas.

National Key therapeutic area	Local actions
1. Renin angiotensin system drugs	Review and, where appropriate, revise prescribing to ensure it is in line with NICE guidance. **First choice – ramipril capsules (losartan only if A2RA is indicated)**
2. Statins	Review and, where appropriate, revise prescribing of high cost statins to ensure it is in line with NICE guidance. **First choice – simvastatin tablets 40mg**
3. Newer hypoglycaemics	Review and, where appropriate, revise prescribing to ensure that it is in line with NICE guidance. **First choice – metformin** (NB See article on page 2 about rosiglitazone)
4. Proton pump inhibitors	Review and, where appropriate, revise prescribing of PPIs to ensure it is in line with NICE guidance and, if a PPI is required, that a low cost PPI is used unless it is ineffective or not tolerated. **First choice - omeprazole or lansoprazole capsules**
5. NSAIDs	Review the appropriateness of NSAID prescribing widely and on a routine basis. **First choice – Ibuprofen or naproxen**
6. Antipsychotics in dementia	Review, and where appropriate revise, prescribing of low dose antipsychotics in people with dementia. **Risperidone is licensed for short term use.**
7. Long acting insulin analogues	Review, and where appropriate revise, prescribing of long acting insulin analogues to ensure that it is in line with NICE guidance. **First choice – human NPH insulin**
8. Self monitoring of blood glucose	Review and, where appropriate, revise local use of SMBG in type 2 diabetes mellitus to ensure that it is in line with NICE guidance.
9. Clopidogrel	Review, and where appropriate revise, prescribing of clopidogrel to ensure it is in line with NICE guidance. Prescribe generically.
10. Ezetimibe	Review and, where appropriate, revise prescribing to ensure it is in line with NICE guidance.
11. Antibiotics	Review and, where appropriate, revise current prescribing practice and use implementation techniques to ensure prescribing is in line with local guidance.
12. Hypnotics	Review and, where appropriate, revise prescribing of hypnotics to ensure that it is in line with national guidance.
13. Orlistat	Review and, where appropriate, revise prescribing to ensure it is in line with the Summary of Product Characteristics (SPC) and NICE guidance.
14. High dose inhaled corticosteroids	Review the use of inhaled corticosteroids (ICS) routinely in patients with asthma and COPD. Step down the dose and use of ICS whenever possible. **First choice – beclometasone**
15. Alendronate	Promote the use of generic alendronate (as once a week preparation) as first line bisphosphonate for osteoporosis.

Safety Hot Topics – Safety advice from the MHRA

a) Long-acting-beta-agonists

The September 2010 edition of the MHRAs Drug Safety Update has featured a discussion on the use of long-acting-beta-agonists (LABA) in the treatment of adults, adolescents, and children with asthma. This follows a review on the use of LABAs, specifically in children younger than 12 years, which has concluded that the benefits of these medicines used in conjunction with inhaled corticosteroids (ICS) in the control of asthma symptoms in children outweigh any apparent risks.

The following recommendations have been made for healthcare professionals:

• Prescribers are reminded to follow the advice on the management of asthma from the Commission on Human Medicines, consistent with the guideline from The British Thoracic Society and Scottish Intercollegiate Guidelines Network. In particular, always prescribe LABA with concomitant ICS and only when ICS alone are not sufficient to control asthma symptoms
• LABA should not be initiated in patients with rapidly deteriorating asthma
• Review LABA therapy regularly, prescribe the lowest effective dose, and stop if there is no benefit
• Stepping-down therapy should be considered when good long-term asthma control has been achieved
• LABA should not be prescribed for the relief of exercise-induced asthma symptoms in the absence of regular ICS (a short-acting beta-2-agonist should be used in this situation)
• Combination inhalers should be prescribed when appropriate to aid compliance in line with NICE Guidance

b) Rosiglitazone

The UK Commission on Human Medicines (CHM) has reviewed the available data and has concluded that there is an increased cardiovascular risk for rosiglitazone which outweigh its benefits.

Unfortunately there is not a "one-size-fits-all" solution to what patients who were previously taking rosiglitazone should be offered now; this really does need to be an individual decision for each patient depending on their circumstances. These are some options.

- Given the recent studies looking at HbA1c targets and the proposed revision to the QOF targets, consider whether the patient actually needs an alternative to rosiglitazone at all. If the patient's HbA1c on rosiglitazone was below 8% and other CV risk factors are well controlled (stop smoking, BP, lipids) and they do not have any evidence of microvascular disease, consider trying without it for a few months and then review the need for an additional intervention.
- It's not advisable to simply switch all patients to pioglitazone. Pioglitazone carries the same risk of heart failure and probably a higher risk of fracture as rosiglitazone. In addition, just this week an observational study has identified a possible link between pioglitazone and bladder cancer. See http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm226244.htm
- Could the patient tolerate an increased dose of metformin? If not of the standard formulation, maybe m/r metformin might be better tolerated and is worth considering. The evidence base that the m/r formulation is better tolerated is weak but if it helps an individual patient to tolerate a higher dose of metformin, rather than adding another drug, then it would seem worth a try.
- If rosiglitazone was being used as a second-line treatment with metformin, then consider substituting a sulphonylurea if not previously contra-indicated or not tolerated. A sulphonylurea is the recommended usual second line choice according to NICE CG87.
- NICE CG87 advises that insulin is the usual 3rd line treatment, after metformin and a sulphonylurea. NICE also advises that this should be human NPH (isophane) insulin with analogues reserved only for certain patients.
- If gliptins are considered, remember that they do not have any microvascular or macrovascular outcome data nor do they have long-term safety data.
- Patients could be referred for consideration for exenatide if they fit the NICE criteria. However exenatide also does not have any microvascular or macrovascular outcome data or any long-term safety data. Patients on exenatide must be reviewed at 6 months.

c) Quinine

The MHRA has warned that quinine should not be used routinely for nocturnal leg cramps. It should only be used when leg cramps regularly disrupt sleep. Before use of quinine for nocturnal leg cramps, the risks should be carefully considered relative to the potential benefits. After a trial of at least 4 weeks, treatment should be stopped if there is no benefit. If treatment continues, the benefits should be assessed around every 3 months. Practices are advised to consider whether quinine is still needed when reviewing medication.

Can bisphosphonates be stopped? Dr Jenkins has advised that most experts now recommend 5 years treatment with bisphosphonates then a break without therapy. There is no evidence of an increased rate of fracture in the following 5 years off treatment. She adds that she takes people off treatment after 10years because of the risk of adynamic bone disease and increased fracture risk.

Watch out for the launch of the RED BAG scheme – coming soon!

Some of the interactions of theophylline including aminophylline

Aciclovir	Plasma concentration of theophylline possibly increased by aciclovir
Azithromycin	Plasma concentration of theophylline possibly increased by azithromycin
Calcium-channel Blockers	Plasma concentration of theophylline possibly increased by calcium-channel blockers (enhanced effect)
Carbamazepine	Metabolism of theophylline accelerated by carbamazepine (reduced effect)
Cimetidine	Metabolism of theophylline inhibited by cimetidine (increased plasma concentration)
Ciprofloxacin	Plasma concentration of theophylline increased by ciprofloxacin
Clarithromycin	Metabolism of theophylline inhibited by clarithromycin (increased plasma concentration)
Corticosteroids	Increased risk of hypokalaemia when theophylline given with corticosteroids
Diltiazem	Plasma concentration of theophylline increased by diltiazem
Erythromycin	Metabolism of theophylline inhibited by erythromycin (increased plasma concentration), if erythromycin given by mouth, also decreased plasma-erythromycin concentration
Fluconazole	Plasma concentration of theophylline possibly increased by fluconazole
Ketoconazole	Plasma concentration of theophylline possibly increased by ketoconazole
Phenytoin	Plasma concentration of both drugs reduced when theophylline given with phenytoin
Quinolones	Possible increased risk of convulsions when theophylline given with quinolones
St John's Wort	Plasma concentration of theophylline reduced by St John's wort —avoid concomitant use
Tobacco	Metabolism of theophylline increased by tobacco smoking (reduced plasma concentration)
Verapamil	Plasma concentration of theophylline increased by verapamil (enhanced effect)

These interactions need to be considered in a patient taking theophylline or aminophylline regularly who then starts a course of antibiotics or other medication. For complete list of interactions refer to current BNF or SPC

Does General Practice need Patient Group Directions?

Yes – if you don't want to write Patient Specific Directions for all your immunisations!

The BMA has recently revised its guidance on the use of PGDs in general practice and now recommends their use where non-prescribing healthcare professionals are to administer a medicine without a patient specific direction (PSD) being in place.

The Medicines Act 1968 does not permit nurses who are not qualified prescribers to administer or supply prescription only medicines (POMs) unless one of three types of instruction is in place:

1. A signed prescription
2. A signed Patient Specific Direction (PSD)
3. A Patient Group Direction (PGD)

If non-prescribing healthcare professionals are to administer a medicine on the instruction of a GP, the GP must be able to show that they have appropriate mechanisms in place to ensure that their practice meets statutory requirements.

If a Patient SPECIFIC Direction is used, it must state the name of the patient, the name and dose of the medicine to be administered and evidence to confirm the patient has been considered as an individual. It can be a written or electronic instruction in the patient record, or a list of individually named patients to be treated with a named POM signed by the prescriber, providing that each patient on the list has been considered individually by the prescriber. The practice should have a protocol in place for staff to follow when administering using a PSD.

Patient Group Directions are developed locally and must be authorised by the PCT. Practices can then adopt the PGDs for their use. There should be robust systems in place within the practice to ensure nurses working to the PGDs are competent in the assessment of patients, use of the medicine and legal aspects of PGDs. The system should ensure that all nurses working to the PGDs are signed up to them and authorised by the practice on an individual basis. It must also ensure only current PGDs are in use. No variation from the PGD is allowed and records must be kept to demonstrate a PGD has been used.

PGDs cannot be used by healthcare assistants or for training purposes – Patient Specific Directions must be used in both cases.

The full guidance is available on the BMA website: http://www.bma.org.uk/images/pgdpatientspecificdrectionsgeneralpracticeaug2010_tcm41-199271.pdf

If you would like further information about PGDs please contact us.

Withdrawal of Mixtard 30

NovoNordisk has announced the withdrawal of insulin Mixtard 30, and stock will cease to be available after 31/12/10

- Humulin M3 will probably be an appropriate alternative for a significant proportion of patients. However it is important to remember a change in pen device will also be needed. Humulin M3 is compatible with HumaPen Luxura or Autopen Classic
- For some patients with inadequate control this may also be an opportunity for review of their diabetes management.
- Some patients with poor dexterity and eyesight may currently be using Mixtard 30 with the Innolet device. Humulin M3 is not compatible with this device and these patients will need review.
- Alternatives for these patients with dexterity / eyesight problems are to continue with same device (Innolet) and change to a more complex insulin regime or move to a twice daily regime
- It is important to identify these patients now in anticipation of this change.

Please contact the Diabetes Specialists for advice on specific patients.

Opioids for chronic musculoskeletal pain

This article is adapted from one that appeared in the BMJ (ref BMJ2010:341:c3533). It notes that lack of evidence of benefit and the potential for harm should caution against the use of opioids for chronic musculoskeletal pain.

Chronic musculoskeletal pain is common. Up to half the adult population has chronic pain at any one time, and two thirds of these have musculoskeletal problems. Chronic musculoskeletal conditions are persistent, debilitating, often characterised by substantial pain, but are non-fatal. In the United Kingdom, this equates to as many as 16 million adults with chronic musculoskeletal pain, around five million of whom will seek healthcare advice. Treatments include analgesics and physiotherapy. The effects are often short lived, however, and the scope for preventing or alleviating long term pain is limited. Patients and clinicians continue to search for treatment that is safe and effective and alleviates short term and long term pain. Drug companies share the same goal, with the added motivation that such a treatment would have a huge potential in the worldwide market.

Opioids could be seen to fit the bill. The substantial, even dramatic, rise in prescriptions of opioids over recent years suggests that some groups believe this to be the case, although data exploring possible reasons for this are sparse. One recent survey from the UK reported that 83% of general practitioners believed that opioids were effective for chronic non-malignant pain. But is this group of drugs all it seems to be? Opioids are certainly justified in situations such as end of life pain, severe acute pain, and severe (short term) exacerbations of chronic pain. Evidence supports the effectiveness of opioids for short term pain relief, and they are often tolerated by patients despite common side effects such as dry mouth, nausea, and constipation. Crucially, though, gaps exist in the literature on both the effectiveness and the harms of long term use of opioids for chronic musculoskeletal and non-cancer pain.

The potential for risk has not been ignored. Treatment guidelines recommend considering the risks of side effects and opioid dependence when prescribing opioids, plus specialist referral if long term use is being considered. General practitioners have reported worries about addiction and other adverse events when prescribing opioids. In addition, the rise in opioid prescriptions has been paralleled by substantial increases in deaths from opioid related overdose. Overdoses were most common at the highest opioid doses, but importantly in public health terms, most overdoses occurred in the larger groups of people receiving lower doses.

The clinical community must ask itself why, in the face of inadequate evidence of effectiveness and emerging evidence of potential harms, such an increase in the use of opioids for chronic non-cancer pain has occurred? Long term use of particular types of opioids may be safe and effective for specific groups of people with chronic musculoskeletal pain. The challenge for future research is to identify who these people are, which opioids are best to treat them, which doses are most appropriate, and how long any effects last. Equally, alternative safe and effective treatments for people with chronic musculoskeletal pain are needed. Improved support for self management of long term pain conditions may also reduce requests for prescription pain relief.

Overall, the evidence of potential risks of long term opioid use combined with the lack of evidence of effectiveness is a public health concern, given the high prevalence of chronic musculoskeletal pain and the rising trends in opioid use.

Change in formulation and increased potency of some levothyroxine oral solutions

The manufacturer of all three strengths of levothyroxine oral solution marketed as Evotrox oral solution and Almus levothyroxine oral solution has announced that there has been a 10% increase in potency of the solutions.

Although for most patients this change in potency is unlikely to have significant clinical effects, there may be a small group for which it may be appropriate to ensure that TSH levels are monitored within 3 months of receiving this new formulation. This may include elderly patients and patients with pre-existing cardiac disease that are being maintained on relatively high doses or are already at the upper end of the range for TSH.

In a consensus statement published in July 2006 the Association for Clinical Biochemistry, the British Thyroid Association and the British Thyroid Foundation recommend that in adults TSH should be measured 2-3 months after a change in thyroxine dose and the dose titrated to achieve a serum TSH that is in the reference range. Once stabilised, patients should have their TSH checked annually. These guidelines additionally highlight the risk of over-treatment increasing the risk of adverse cardiac events in elderly patients and those with pre-existing cardiac disease.

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