

## NICE publishes guidance on management of RA

A new NICE guideline<sup>1</sup> covers the management of rheumatoid arthritis (RA) of recent onset and more established disease. It includes sections on diagnosis and referral, pharmacological and surgical management, monitoring and the role of the multidisciplinary team.

### Action

The quick reference guide is worth reading by all who have any involvement in the care of people with RA. Specialist staff will need to become familiar with the whole guideline.

### Disease-modifying drugs

NICE advises the following on use of disease-modifying anti-rheumatic drugs (DMARDs):

- In people with newly diagnosed active RA, offer a combination of DMARDs (including methotrexate and at least one other DMARD, plus short term glucocorticoids) as first-line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms.
- In people with newly diagnosed RA for whom combination DMARD therapy is not appropriate, start DMARD monotherapy,

placing greater emphasis on fast escalation to a clinically effective dose rather than on the choice of DMARD.

- In people with recent-onset RA (less than 2 years since diagnosis) receiving combination DMARD therapy and in whom sustained and satisfactory levels of disease control have been achieved, cautiously try to reduce drug doses to levels that still maintain disease control.

This guideline and the NICE guideline on osteoarthritis update previous NICE guidance on COX-2 inhibitors. For more details see *MeReC Stop Press Blog No. 284*.

### References

1. NICE. Rheumatoid arthritis: the management of rheumatoid arthritis in adults. Clinical Guideline 79. February 2009



## Increased CV risk with NSAIDs, but prescribing trends encouraging

In the February edition<sup>1</sup> of Drug Safety Update, the MHRA and CHM reported that all users of non-steroidal anti-inflammatory drugs (NSAIDs) may be at some increased thrombotic cardiovascular (CV) risk, although the absolute risk for 'healthy' users is low. Reassuringly, since November 2007, primary care prescribing data in England indicates that there has been a significant decrease in diclofenac prescribing, accompanied by a significant increase in naproxen prescribing. This coincides with our initiatives here at the NPC to encourage medication review and more appropriate prescribing of NSAIDs with better risk profiles, taking into account both their CV and gastrointestinal risks and individual patient risk factors.

Results of two recently published epidemiological studies lend support to the view that some increase in thrombotic CV risk may apply to all NSAID users, irrespective of their baseline risk, and not only to chronic users. However, the absolute increase in risk for 'healthy' users (defined, in this instance as those with no hospital admissions in the last 5–10 years and no prescriptions for specific concomitant medications) is very low. The greatest concern relates to chronic use of high doses (especially for coxibs and diclofenac).<sup>1</sup>

The need for long-term treatment should be reviewed periodically. Current advice remains that patients should use the lowest effective dose and the shortest duration of treatment necessary to control symptoms. Overall, evidence continues to indicate that naproxen is associated with a lower thrombotic risk than coxibs. For ibuprofen, no significant increase

in risk has been identified for doses of up to 1200mg daily.<sup>1</sup> Prescribing should take into consideration the overall safety profile of NSAIDs and each patient's risk factors. For more details see *MeReC Stop Press Blogs No. 272* and *No. 293*.

Further information on the CV risk of NSAIDs is available in *MeReC Extra No. 30*, which was also summarised in *MeReC Stop Press Blog No. 42*. Additional resources, such as eLearning materials and a patient decision aid, are available on the musculoskeletal floor of NPCi. Implementation resources are also provided to help healthcare professionals ensure NSAID prescribing is in line with national guidance and to facilitate the review of patients taking NSAIDs.

This publication was correct at the time of preparation: April 2009

### References

1. MHRA. Non-steroidal anti-inflammatory drugs: cardiovascular risk. Drug Safety Update; Vol 2: Issue 7. February 2009

## New antidepressant meta-analysis has limitations

A meta-analysis,<sup>1</sup> which considered the comparative efficacy of 12 second-generation antidepressants, has concluded that sertraline may be the best choice when starting treatment for moderate to severe major depression in adults because it showed the most favourable balance between benefits, acceptability and acquisition cost. However, the meta-analysis has many limitations: the statistical significance of the results is uncertain and the clinical difference between antidepressants is likely to be small.

### Action

Prescribers should continue to follow the NICE guideline for the management of depression. The choice of antidepressant, or indeed any drug, should be based on efficacy, side-effect profile, patient preference, past experience with treatment, and cost. NICE recommends that selective serotonin re-uptake inhibitors (SSRIs) are an appropriate first-line choice for most people where the prescribing of an antidepressant is appropriate. NICE is currently updating their guidance on depression in adults and publication is anticipated in September this year.

### What does this study claim?

This meta-analysis (117 RCTs), which included 25,928 adults with unipolar major depression, found statistically significant differences between the efficacy and acceptability of 12 second-generation antidepressants over a mean duration of 8.1 weeks. In terms of response rate (the proportion of patients with a reduction of at least 50% from the baseline score on a depression rating scale), multiple-treatments meta-analysis showed that mirtazapine, escitalopram, and venlafaxine, were statistically significantly more efficacious than duloxetine, fluoxetine, fluvoxamine, paroxetine, and reboxetine. Sertraline was more effective than fluoxetine, paroxetine and reboxetine. Based on dropout rates in the first 8 weeks of treatment, escitalopram and sertraline appeared to be better tolerated than several other second-generation antidepressants. Escitalopram and sertraline showed the best balance between efficacy and acceptability, but the higher cost of escitalopram is an important consideration. Also, it is

important to consider this meta-analysis in the context of its many limitations (below).

### What are the limitations of this study?

There are few large, high quality, independently sponsored comparative trials of antidepressants and the meta-analysis has many limitations relating to the poor quality of the included studies. Most studies comparing many of the antidepressants were done by the pharmaceutical companies marketing these compounds, which might be a source of bias. Indeed the results of the study show that discrepancies existed between some of the results of the multiple-treatments meta-analysis and those in the direct comparisons. Also, the quality of most studies was rated as unclear, the mean sample size was small, the mean duration of studies was only about 8 weeks and the clinical significance of the definition of response rate was unclear. The multiple treatments meta-analysis procedure that was used in this study has additional limitations; and the statistical significance of the results is uncertain because adjustments were not made for multiple testing.

Although some statistically significant differences in efficacy and acceptability were found between agents, it is possible that any differences are of limited clinical significance. For more details see *MeReC Rapid review Blog No. 283*.

### References

1. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* 2009;373:746-58

## MHRA warns against cough and cold medicines in young children

In the absence of robust evidence for their effectiveness, and some evidence of harm, the MHRA has warned against the use of many commonly used over-the-counter cough and cold medicines for children under six years of age. Supply of these medicines for children aged 6-12 years will be restricted to pharmacies.<sup>1</sup>

### Action

Parents and carers should no longer give over-the-counter (OTC) cough and cold medicines containing certain ingredients (see below) to children less than six years of age. This extends MHRA advice to avoid OTC cough and cold medicines for children aged under 2 years, which was issued in 2008. Advice on relieving symptoms is outlined in Chapter 6 of the Department of Health's 2007 guidance 'Birth to Five'. For 6 to 12 year olds, these medicines will continue to be available but will only be sold in pharmacies, with clearer advice on the packaging.

### Which medicines are affected?

OTC cough and cold medicines containing the following active ingredients are affected by the advice:<sup>2</sup>

- **Antitussives:** dextromethorphan and pholcodine
- **Expectorants:** guaifenesin and ipecacuanha
- **Nasal decongestants:** ephedrine, oxymetazoline, phenylephrine, pseudoephedrine and xylometazoline
- **Antihistamines:** brompheniramine, chlorphenamine, diphenhydramine, doxylamine, promethazine and triprolidine.

A list of branded products affected is available on the MHRA website.

For more details see *MeReC Stop Press Blog No. 311*.

### References

1. MHRA. Press release: Better medicines for children's coughs and colds. February 2009
2. MHRA. Healthcare professional letter: Over-the-counter cough and cold medicines for children. February 2009

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