

## Cox 2 inhibitors: NICE guidance

The recent withdrawal of rofecoxib due to an increased risk in cardiovascular events has raised questions as to the cardiovascular safety of the Cox 2 inhibitors as a class. There is as yet no definitive evidence of a class effect, but as a recent NEJM commentator noted "Absence of evidence is not evidence of absence"<sup>1</sup>. Until the safety issue is clarified, be cautious when prescribing Cox-2 inhibitors to those with CVD.

When considering whether to prescribe a Cox 2 inhibitor for rheumatoid or osteoarthritis the guidance below from The National Institute of Clinical Excellence (NICE)\* may be useful. This advice has been reviewed following the withdrawal of rofecoxib and remains unchanged:

1. Cox 2 selective inhibitors and other NSAIDs are indicated for pain and stiffness in inflammatory rheumatoid arthritis and for the short-term management of pain in osteoarthritis. All NSAIDs are associated with adverse events and should only be prescribed when there is a demonstrable clinical need and in accordance with their summary of product characteristics. Long-term use should be avoided without appropriate monitoring and re-evaluation of the clinical need.
2. Of particular concern is the propensity of NSAIDs, including the Cox 2 selective agents, to cause gastro-intestinal adverse events, which can include life threatening gastro-intestinal perforations, ulcers or bleeds. These agents should therefore only be prescribed after careful consideration of their risks and benefits, especially in patients who may be at increased risk of such adverse events.
3. Cox 2 selective inhibitors are not recommended for routine use in patients with rheumatoid arthritis (RA) or osteoarthritis (OA). They should be used, in preference to standard NSAIDs, when clearly indicated as part of the management of RA or OA only in patients who may be at 'high risk' of developing serious gastrointestinal adverse effects.
4. Patients at 'high risk' of developing serious gastrointestinal adverse events include those of 65 years of age and over, those using concomitant medications known to increase the likelihood of upper gastrointestinal adverse events, those with serious co-morbidity or those requiring the prolonged use of maximum recommended doses of standard NSAIDs. The risk of NSAID-induced complications is particularly increased in patients with a previous clinical history of gastroduodenal ulcer, gastrointestinal bleeding or gastroduodenal perforation. The use of even a Cox 2 selective agent should therefore be considered especially carefully in this situation.
5. In all patients with cardiovascular disease, there remains uncertainty over the use of Cox 2 selective inhibitors and they should not therefore be prescribed routinely in preference to standard NSAIDs where these are indicated in this group of patients. Furthermore, many patients with cardiovascular disease receive low dose aspirin and this carries an increased risk of gastro-intestinal events. In patients who are taking low dose aspirin, the benefit of using Cox 2 selective agents (to decrease gastrointestinal toxicity) is reduced. Prescribing Cox 2 selective agents preferentially over standard NSAIDs in this situation is therefore not justified on current evidence.
6. There is no evidence to justify the simultaneous prescription of gastro protective agents with Cox 2 selective inhibitors as a means of further reducing potential gastrointestinal adverse events. \*\*

NICE guidance on the use of Cox-2 selective inhibitors in osteoarthritis and rheumatoid arthritis. (TA27) Reviewed May 2004 and Sep. 2004 <http://www.nice.org.uk/page.aspx?o=18035> accessed 26 Oct 04

## Reference

1. FitzGerald, G. Coxibs and Cardiovascular Disease. *N Engl J Med* 2004 Oct; 351(17) 1709-10

## Notes

\* About NICE: "The National Institute for Clinical Excellence (NICE) is part of the NHS. It is the independent organisation responsible for providing national guidance on treatments and care for people using the NHS in England and Wales. Our guidance is intended for healthcare professionals, patients and their carers to help them make decisions about treatment and healthcare.

NICE guidance is developed using the expertise of the NHS and wider healthcare community including NHS staff, healthcare professionals, patients and carers, industry and the academic community." (From NICE website; <http://www.nice.org.uk/page.aspx?o=aboutnice>)

\*\* Note point 6 in the NICE guidance refers to co-prescribing gastroprotectants with Cox 2 inhibitors only. Co-prescribing gastroprotectants in high risk users of non-selective NSAID may be justified.