



National Prescribing Service Limited

Australia's peak, independent, education and information provider about medicines

Fact sheet

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Switching patients from Vioxx

Merck Sharpe & Dohme has announced an immediate voluntary worldwide withdrawal of rofecoxib (Vioxx).

This follows analysis of the APPROVe study which was studying the effects of rofecoxib compared with placebo on recurrent colon polyps. The trial was stopped early for safety reasons.

There was an increased risk for confirmed cardiovascular events, such as heart attack and stroke in the patients taking rofecoxib compared to those taking placebo, beginning after 18 months of treatment. The results for the first 18 months of the APPROVe study did not show any increased risk of confirmed cardiovascular events on rofecoxib which is probably related to the frequency of the adverse event and the number of subjects in the trial, that is the statistical power.

New data

APPROVe was a multicentre, randomised, placebo-controlled, double-blind study to determine the effect of 156 weeks (three years) of treatment with rofecoxib on the recurrence of neoplastic polyps of the large bowel in patients with a history of colorectal adenoma. The trial enrolled 2,600 patients and compared rofecoxib 25 mg to placebo. The trial began enrolment in 2000.

In this study 25 patients taking placebo versus 45 patients taking rofecoxib experienced a confirmed serious thrombotic event such as myocardial infarction or stroke. The absolute event rates were approximately 3 per 400 patient years for placebo and 6 per 400 patient years for rofecoxib - an absolute increase in risk of approximately 3 thrombotic events per 400 patient years of treatment. This means that for every 100 patients treated for 4 years, three would have a serious thrombotic event over and above what would normally be expected. The difference in event rates was only apparent after 18 months of treatment.

Changing to an alternative

People taking rofecoxib are being advised to contact their doctor to discuss switching to alternative therapy. They will not be able to get repeat prescription for rofecoxib filled.

There is no evidence currently to suggest that other COX-2 selective inhibitors will have the same effects as rofecoxib but as these effects were not seen for 18 months it is important to look at long-term data with sufficient numbers of patients for the other agents. Long-term placebo-controlled studies are not currently available for other COX-2 selective inhibitors such as celecoxib and meloxicam.

The general advice from NPS regarding NSAIDs including COX 2 selective NSAIDs is to:

1. Use paracetamol as first line management when possible.
2. Use NSAIDs that are lower risk for serious gastrointestinal complications (eg celecoxib, diclofenac and ibuprofen) in preference to higher risk agents
3. Consider the adverse effect profile of the drugs in relation to the individual patient.
Potential adverse effects include:
 - gastrointestinal effects.
 - hypertension, heart failure and renal impairment: all NSAIDs can cause sodium and water retention, decreased glomerular filtration rate, increased blood pressure, peripheral oedema, and congestive heart failure. Caution is advised if NSAIDs or COX-2 selective NSAIDs are used in patients at risk of acute renal failure or heart failure, particularly the elderly. Assess renal function and blood pressure prior to prescribing and during therapy in those considered at risk.
 - acute renal failure and ‘triple whammy’: As with other NSAIDs, COX-2 selective NSAIDs are associated with acute renal failure, particularly when used in combination with ACE inhibitors and thiazide diuretics.
 - acute neuropsychiatric reactions, including confusion, insomnia, hallucinations, and depression, have been reported following celecoxib and rofecoxib use.

COX-2 selective NSAIDs are no more effective at relieving inflammation and pain than conventional NSAIDs.

It is important to report all suspected adverse effects to the Adverse Drug Reaction Advisory Committee (ADRAC) on their blue form.

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