UKMi UK Medicines Information MIDLANDS

TRENT MEDICINES INFORMATION SERVICE

NHS

QIPP Detail Aid

Providing support for quality in prescribing

NSAIDs- ibuprofen or naproxen preferred

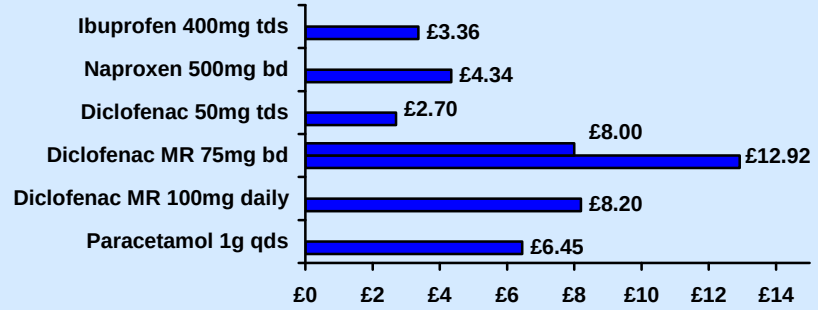
WHAT IS THE PROBLEM?

- Over the last 8 years there have been several warnings from the MHRA regarding the cardiovascular risks with some non-steroidal anti-inflammatory agents (NSAIDs), specifically diclofenac.
- Despite this, there continues to be significant prescribing of diclofenac; it accounts for 21% of all NSAID items in the East Midlands. In some areas nearly a third of prescriptions for NSAIDs in primary care are for diclofenac.
- Ibuprofen and naproxen make up 64% of all NSAID prescriptions in the East Midlands. However, in some areas only half of all NSAID prescriptions are for these preferred agents.

WHAT IS THE EVIDENCE?

- In 2005 the European Committee for Medicinal Products for Human Use (CHMP) identified an increased risk of thrombotic events, such as myocardial infarction (MI) or stroke with COX-2 inhibitors. In 2006, they advised that a similar link may exist with non-specific NSAIDs, in particular diclofenac, particularly if used at high doses for long-term treatment.
- In October 2012, the MHRA confirmed the previous findings, based on a more recent review of the evidence. The currently available data consistently indicate that the risk of MI, stroke or other thrombotic events is higher for diclofenac than other widely used non-selective NSAIDs and similar to selective COX-2 inhibitors.
- Two meta-analyses have both estimated that, compared with placebo, a COX-2 inhibitor or diclofenac causes around three additional major vascular events per 1000 patients per year, with one such event causing death. The risk was increased regardless of the patient's background vascular risk. High-dose ibuprofen (2400mg daily) also significantly increased the risk of major coronary events, but its safety requires further study as there were many fewer relevant vascular events. Naproxen did not seem to increase the risk of major vascular events.
- Ibuprofen (1200mg per day or less) and naproxen (1000mg per day or less) are considered to have the most favourable cardiovascular safety profiles of all non-selective NSAIDs. All NSAIDs increased the risk of heart failure and of gastro-intestinal (GI) events; naproxen having a higher risk of GI events than ibuprofen or diclofenac.
- Results from a Danish cohort study of patients who had suffered a MI suggested that even short-term use of NSAIDs (in some cases for as little as one week) was associated with an increased risk of death or recurrent MI. Consistent with other studies, diclofenac was found to have the highest risk, and naproxen the lowest.

WHAT ARE THE COSTS?



Costs for 28 days supply. Taken from Drug Tariff June 2013
Doses are a guide and do not imply therapeutic equivalence.

KEY MESSAGES

- **Recent cohort data have confirmed previous safety warnings that diclofenac has a higher risk of thrombotic events (including MI and stroke) than naproxen or low-dose ibuprofen. Even a few days of treatment may increase risk, both in healthy individuals and those with cardiovascular disease. High doses of ibuprofen may also have an increased risk.**
- **Two meta-analyses have both estimated that, compared with placebo, diclofenac causes around three additional major vascular events per 1000 patients per year, with one such event causing death.**
- **Diclofenac continues to be widely prescribed; in some areas of the East Midlands nearly a third of NSAID prescribing is for diclofenac.**
- **Ibuprofen (1200mg per day or less) or naproxen (1000mg per day or less) are recommended first-line agents, combined with gastro-protection if at high risk for gastrointestinal adverse events. NSAIDs should be prescribed for the shortest time and lowest dose necessary to control symptoms.**

References: **Date of Preparation: June 2013**

1. MHRA Drug Safety Update October 2012, vol 6, issue 3: S1 (http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON199570)
2. NICE Medicines Evidence Commentary 30th Nov 2012 (www.evidence.nhs.uk)