

## **NSAIDs & coxibs: GI and CVD safety** MeReC 2007, Extra No. 30

This review of the safety of NSAIDs comes from the National Prescribing Centre.

- **As you read this, don't forget that ibuprofen is a weaker anti-inflammatory (even at 2.4g/day) than most other NSAIDs and is therefore not the treatment of choice where inflammation is prominent (eg. gout).**
- **Naproxen is a good anti-inflammatory and has a low incidence of side effects** (although not quite as low as ibuprofen). This is discussed in more detail in the BNF.

### **GI risk**

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- Ibuprofen (at  $\leq 1200$ mg/day) has a lower GI risk than diclofenac or naproxen. But at higher doses (max 2.4g/day) there is much less evidence around the risk and benefits).
- Use of PPI significantly reduces the GI risks.
- Benefits of gastric protection are dependant on the **patient's underlying GI risk, not the NSAID you choose**. There seems to be no added benefit in using a coxib+PPI compared with a standard NSAID+PPI.
- Coxibs are generally associated with lower GI risk (perforation, ulcer, bleeding) than traditional NSAIDs BUT this advantage is lost when co-prescribed with aspirin or a PPI.

### **Cardiovascular risk**

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- **Coxibs:** small excess risk of thrombotic events (MI, CVA): 3 additional events /1000 users treated for one year compared with placebo. Contraindicated in established CVD.
- **NSAIDs** (ibuprofen, diclofenac) are also associated with a small increased risk of thrombotic events (eg. MI, CVA).
  - Diclofenac 150mg/day seems to have similar risk of coxibs
  - Ibuprofen ( $\leq 1200$ mg/d) and naproxen (1000mg/d) are associated with lower risks.
- And don't forget NSAIDs are associated with an increased risk of heart failure. This risk was lowest for naproxen (MeReC Monthly 2009;number 14).

### **What does this mean in practice?**

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The National Prescribing Centre's conclusions were that we should:

- **Use all NSAIDs at lowest effective dose and for the shortest period necessary.**
- **Naproxen (1g/day) is a good 1<sup>st</sup> line agent with lower GI and CVD risks than the others.**
- **Consider co-prescribing a PPI in those at increased risk of GI events, particularly:**
  - All those over 65yrs
  - Long term NSAID users
  - Those with a high baseline GI risk.
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- **There is no good evidence to support the use of Coxibs over and above NSAIDs+PPI, even in those with increased GI risk. *So little place for coxibs in our formularies!***

### **Take home messages**

- **Use naproxen first line for lowest GI and CV risks. Co-prescribe with a PPI if necessary.**
- **Coxibs have a very limited role. They have an increased CV risk and have no GI benefits compared to an NSAID with a PPI.**

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