Prescribing guidelines for NSAIDs (including COX II selective inhibitors)

Oral NSAIDs

The potential for reduced pain and inflammation with NSAIDs must be weighed against the well established multiple risks of treatment. They include: hypersensitivity reactions e.g. asthma. Severe dyspepsia, GI bleeds and ulceration, precipitating and enhancing hypertension & heart failure, functional and intrinsic renal toxicity and thrombosis are all well established risks. These adverse effects lead to a wide range of absolute and relative contraindications. Side effects, in combination with a range of drug interactions; makes oral NSAIDs difficult to prescribe safely in accordance with National guidance.

Osteoarthritis is probably a reasonable model for the long-term prescription of NSAIDs in primary care (as distinct from acute strains and sprains). Recent NICE OA Guidance¹ has recognised the shifting balance of evidence between toxicity and efficacy of long-term oral NSAIDs and recommends them fourth line to non-drug interventions, high dose regular paracetamol & topical NSAIDs (for which there is now more evidence to support their use).

The Prescribing Reference Group at NHS Anglia CSU suggests a cautious and conservative approach to the prescribing of oral NSAIDs – see below.

GI side effects

All NSAIDs (including COX-IIs) increase the risk of serious GI bleeds. NICE OA¹ and RA Guidance² advocate co-prescription (usually a PPI - to reduce risk of GI damage) in ALL patients IF an NSAID has to be prescribed. This applies to all NSAIDs including COX-II inhibitors.

Ibuprofen up to 1200mg daily carries the lowest risk of GI injury followed by diclofenac and naproxen.

COX-II NSAIDs have a marginally lower risk of GI damage BUT evidence does not support the advantage of COX-IIs being maintained when either a COX-II or “standard NSAID” are co-prescribed with a PPI³.

COX-II NSAIDs should not be prescribed with aspirin.

Cardiovascular toxicity

Thrombotic risk is slightly increased with COX-II inhibitors and diclofenac (especially at doses of 150mg daily). This small increased risk is shared with ibuprofen at doses above 1200mg daily.

Low dose ibuprofen – less than 1200mg daily and Naproxen up to 1000mg daily have a minimal risk.

Whilst the absolute increase in risk is small, the very widespread use of NSAIDs in the UK, means, for example that high dose diclofenac alone may result in 2000 premature or additional thrombotic events annually.

Renal toxicity

All NSAIDs can precipitate functional renal insufficiency, especially in patients with existing renal impairment; this is usually dose dependent. NSAIDs are also directly reno-toxic, causing (rarely) renal papillary necrosis and interstitial fibrosis leading to renal failure (which may be irreversible)⁴.

Topical NSAIDs and Rubifacients

Topical NSAIDs must be systemically absorbed to have an effect. They cause similar systemic adverse effects to oral NSAIDs but only rarely and usually when used to excess.

Hypersensitivity reactions e.g. asthma do occur with topical NSAIDs

Photosensitivity reactions can occur with all topical NSAIDs – being more common with ketoprofen - occurring in between 1-2 cases per 10,000 patients. Patients should be advised against excessive exposure to direct sunlight⁵,⁶.

There is more evidence to support the effectiveness of topical NSAIDs for chronic pain conditions when compared to rubifacients e.g. Algesal. There are very few data to support the use of capsaicin (which is expensive)⁶.

The order of preference for efficacy in chronic conditions such as OA is thus – topical NSAIDs, then rubifacients then capsaicin⁶.
Summary - Formulary Choices:
The majority of patients who MUST be prescribed an ORAL NSAID (including those where enhanced CV risk is a concern), should first be tried with ibuprofen (up to 1200mg daily). Naproxen (up to 1000mg daily) is the next logical choice. Prescribing of a low dose PPI to reduce GI damage is required IF an NSAID is to be taken regularly.

Diclofenac and COX IIs have been removed from the formulary, due to their increased cardiovascular risk over other NSAIDs and the lack of proven advantage of COX-IIs when prescribed with a PPI to reduce GI damage.

To avoid oral NSAIDs first try non-drug interventions, then high dose regular paracetamol, then topical ketoprofen or piroxicam gel, then a rubifacient e.g. Algesal, then Capsaicin (which is expensive).

2. NICE Rheumatoid Arthritis Clinical Guideline CG079 February 2009.
4. BNF March 2014.
5. MHRA Drug Safety Up-date 2009;2(11):5

NICE Clinical Guideline 59: Osteoarthritis, Feb 2008

Guidelines for prescribing NSAIDs
1. Don't use them unless you have to
   - The only way to avoid NSAID side effects is not to use them
   - Paracetamol works for many - use regular dosing
   - Employ non-drug interventions routinely - as above
   - Consider topical NSAIDs ahead of oral NSAIDs for OA

2. If you have to use them, use them wisely
   - The balance of benefits and risks needs to be carefully assessed; think about CV, GI and renal issues routinely
   - Use a safer drug (ibuprofen, then Naproxen) in the lowest effective dose for the shortest period
   - NSAID users should be a high priority for medication review: are all NSAIDs still needed and effective?
   - Consider Drug holidays? Don’t issue repeat prescriptions without review

3. Consider gastroprotection in those taking regular oral NSAIDs of any type
   - PPIs are the treatment of choice
   - Double-dose H2RAs (less evidence) or misoprostol (effective but poorly tolerated) are alternatives