Prescribing Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in Inflammatory Arthritis and Osteoarthritis in Adults
Prescribing Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in Inflammatory Arthritis and Osteoarthritis in Adults

Failure of response to non-pharmacological management and regular dosing of paracetamol (1g four times a day)

Inflammatory arthritis

Osteoarthritis (OA)

Consider addition of topical NSAID for hand or knee arthritis eg Ibuprofen 5% gel, Piroxicam 0.5% gel or ‘Movelat gel’. Then consider adding moderate opioid analgesia, then consider addition of Capsaicin 0.025% cream for hand or knee arthritis

NSAID INDICATED (refer to guidance note 1)

Consider contra-indications and cautions (see below)

Risk assess for gastrointestinal (GI) and cardiovascular (CV) risk

Avoid NSAIDs if possible in renal and hepatic impairment

Avoid long term use where possible and always aim to use lowest effective dose for shortest possible duration

Contra-indications and Cautions

- Recent or active peptic ulcer disease
- Inflammatory bowel disease
- Gastrointestinal and/or cardiovascular risk factors. (Refer to guidance notes 2 & 3)

- Previous hypersensitivity to other NSAIDs
- Sulphonamide sensitivity (celecoxib only)
- Asthma and elderly patients

Assess GI and CV risk

Consider if benefit of NSAID treatment outweighs risk

No GI or CV risk factors

Ibuprofen or Naproxen (refer to guidance note 4)

For gout use: Naproxen or Etoricoxib

When duration of use becomes long term or repeated add in PPI

GI risk factors

No NSAID without risk (refer to guidance note 3)

CV risk factors

No NSAID without risk (refer to guidance note 2)

Both GI & CV risk factors

No NSAID without risk (refer to guidance note 2 & 3)

Celecoxib

+ Omeprazole

20mg daily

or

Ibuprofen (refer to guidance note 4)

+ Omeprazole

20mg daily

For gout use: Etoricoxib

+ Omeprazole

20mg daily

or

Naproxen

+ Omeprazole

20mg daily

When duration of use becomes long term or repeated add in PPI

Avoid long term use where possible and always aim to use lowest effective dose for shortest possible duration

May need to use on an intermittent basis

No NSAID without risk (refer to guidance note 3)

For gout use: Naproxen or Etoricoxib – consider CV risks

Naproxen (refer to guidance note 4)

or

Celecoxib (refer to guidance note 2)

For gout use: Naproxen or Etoricoxib – consider CV risks

When duration of use becomes long term or repeated add in PPI
1. NSAID Selectivity

1. NSAIDs vary in their selectivity for inhibiting different types of cyclo-oxygenase. The term NSAID includes non-selective NSAIDs and selective NSAIDs (COX 2 inhibitors).

2. Always use the lowest effective dose for the shortest duration possible. All patients must have a gastrointestinal, cardiovascular and renal risk assessment done and the appropriate anti-inflammatory agent selected following a risk versus benefit discussion with the patient. Consider documenting in patient’s clinical notes.

2. Cardiovascular Disease (CV) Risk Factors

- Ischaemic heart disease
- Cerebrovascular disease
- Peripheral artery disease
- Moderate to severe congestive heart failure
- Hypertension
- Hyperlipidaemia
- Diabetes
- Smoking

Patients with cardiovascular risks:

(i) COX-2 selective inhibitors.

The European Medicines Agency (EMEA) concluded COX-2 inhibitors must not be used in patients with established ischaemic heart disease, cerebrovascular disease, moderate-severe congestive heart failure (NYHA II-IV) or peripheral arterial disease. When prescribed in accordance with their cautions, the benefits versus risks remain positive for COX-2 inhibitors when used in their target populations. Etoricoxib has higher rates of cardiorenal events than celecoxib and is also contraindicated in patients with hypertension whose BP is persistently above 140/90mmHg and has not been adequately controlled.

(ii) Non-selective NSAIDs.

The EMEA concluded that the benefit-risk balance for non-selective NSAIDs remains favourable when prescribed in accordance with patients risk factors. It cannot be excluded that non-selective NSAIDs may be associated with a small increase in the absolute risk for thrombotic events (such as heart attack or stroke), especially when used at high doses for long term treatment.

Concomitant aspirin and/or clopidogrel

See advice under gastro-intestinal risk factors – guidance note 3

3. Gastrointestinal risk factors

- Past history of gastrointestinal disease
  - peptic ulcer disease (PUD), GI bleed, GORD
- Patients > 65 years with one of the following additional risk factors:
  - concomitant corticosteroids
  - long term NSAID treatment / maximal dose
  - concomitant anticoagulant
  - concomitant aspirin and/or clopidogrel (refer to guidance note regarding concomitant clopidogrel)
  - concomitant serotonin re-uptake inhibitor
- Patients > 75 years with no additional risk factors
- Inflammatory bowel disease (all NSAIDs including COX 2 inhibitors)

Concomitant Aspirin

There is no consensus in the literature regarding the co prescribing of low dose aspirin and NSAIDs. Opioid analgesics should be considered before NSAID or COX-2. If NSAID or COX-2 is deemed necessary, this combination can increase the risk of gastro-intestinal side effects therefore, add PPI (omeprazole 20mg daily).

Note: ibuprofen may reduce the cardioprotective effects of aspirin.

Concomitant Clopidogrel

The co-prescribing of NSAIDs and clopidogrel increases the risk of gastro-intestinal side effects and recent advice from the EMEA and MHRA is that clopidogrel and PPIs should not be used together unless considered essential, as concomitant use reduces the efficacy of clopidogrel. Consider alternative GI cover eg: H2 antagonist or misoprostol

Proton Pump Inhibitors (PPIs)

NICE Guidance (Management of osteoarthritis 2008) suggests the use of PPI’s with COX-2 selective inhibitors or non-selective NSAIDs should be considered in all patients with GI risk factors. This combination offers the lowest potential risk of GI adverse events.

PPI cover should only be used for the duration of NSAID use.
4. Formulary NSAIDs

Patients not responding to one NSAID may well respond if changed to another NSAID

**Non-selective NSAIDs**
- **Naproxen:** 250mg to 500mg orally twice a day
- **Ibuprofen:** 400mg orally three times daily
  (No significant thrombotic risk has been identified for doses up to 1200mg daily, however, dose can be increased to 2.4g daily in 3 to 4 divided doses if necessary)

**COX-2 selective inhibitor** (refer to guidance note 2)
- **Celecoxib:** 200mg orally daily in one to two divided doses (maximum 200mg twice daily)
- **Etoricoxib:** 120mg daily in acute gout

5. Common Drug Interactions with NSAIDs

This is not a comprehensive list. For further information please see BNF appendix 1

Stockleys Drug Interactions or contact your ward/practice pharmacist

- **SSRIs** – increased risk of bleeding
- **Ciclosporin** – increased risk of nephrotoxicity
- **Diuretics** – increased risk of nephrotoxicity
- **Lithium** – NSAIDs probably reduce excretion of lithium (increased risk of toxicity). NSAIDs should be avoided if possible
- **Methotrexate** – NSAIDs reduce excretion of methotrexate (increased risk of toxicity), however many patients are taking this combination safely through regular monitoring of their renal function and FBC
- **Tacrolimus** – increased risk of nephrotoxicity
- **Warfarin** – increased risk of GI haemorrhage with all NSAIDs. Avoid unnecessary concurrent use, when concurrent use is necessary extra care is needed. All NSAIDs can increase INR – increased monitoring recommended after initiating or changing the dose

References

1. European Medicines Agency Concludes Action on COX-2 Inhibitors, June 2005
2. European Medicines Agency review concludes positive benefit-risk balance for non-selective NSAIDs, October 2006
4. European Medicines Agency Public statement on possible interaction between clopidogrel and proton pump inhibitors, May 2009
5. MHRA Drug safety update June 2009. Clopidogrel and proton pump inhibitors: possible interaction
9. I Stockley, Drug Interactions, accessed online via www.medicinescomplete.com on 30/06/09

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