Choice of NSAIDs

Risk factors direct the choice of NSAID to be used:

<table>
<thead>
<tr>
<th>Gastrointestinal risk factors</th>
<th>Cardiovascular risk factors</th>
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<tbody>
<tr>
<td>&gt;65 years</td>
<td>65 years (especially if male)</td>
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<tr>
<td>Previous GI history</td>
<td>Established cardiovascular disease (CVD)</td>
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<td>Concomitant antiplatelets, anticoagulants, SSRIs, oral steroids</td>
<td>Hypertension</td>
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<td>Serious co-morbidity, e.g. CVD, diabetes</td>
<td>Heart failure</td>
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<tr>
<td>Long term use (&gt;2 weeks), e.g. rheumatoid arthritis (RA), osteoarthritis (OA) or &gt;45 years and low back pain</td>
<td>Diabetes</td>
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Diclofenac is contraindicated in patients with serious underlying heart conditions, e.g. heart failure, heart disease, circulatory problems or a previous heart attack or stroke.\(^{(1)}\)

**Fig 1. NSAID choice**

- **FIRST CHOICE**
  - No GI and CV risk factors: Ibuprofen PO 400 mg 8 hrly
  - CV risk factors only: Ibuprofen PO 400 mg 8 hrly
  - GI risk factors only: Ibuprofen PO 400 mg 8 hrly
  - CV and GI risk factors: Ibuprofen PO 400 mg 8 hrly

- **SECOND CHOICE**
  - Naproxen PO 250 - 500 mg\(^*\) 12 hrly
  - Naproxen PO 250 - 500 mg\(^*\) 12 hrly plus PPI\(^*\)

- **THIRD CHOICE**
  - Diclofenac PO 50 mg 8 hrly
  - No further option
  - Diclofenac PO 50 mg 8 hrly plus PPI\(^*\)

\(\text{* Lansoprazole 15 mg daily for duration of NSAID treatment. Stop thereafter if not normally taken.}\(^{(2,3)}\)

**Ibuprofen doses**

Maximum dose is 2.4 g. However, doses >1.2 g are associated with similar CV risk to diclofenac 50 mg.

**Diclofenac and naproxen doses:** In this guideline are quoted at the higher end of the licensed ranges.

**Diclofenac\(^{(11)}\):**
- For milder cases, 75 to 100 mg daily in 2 or 3 divided doses may be sufficient.
- For migraine see BNF.
- Maximum dose in 24 hours: 150 mg.

**Naproxen\(^{(14)}\):**
- RA, OA, ankylosing spondylitis: 500 mg PO 12 hourly.
- Acute gout: 750 mg stat followed by 250 mg 8 hourly.
- Musculoskeletal disorders and dysmenorrhea: 500 mg stat followed by 250 mg 6 to 8 hourly as required. Maximum daily dose after first day: 1250 mg daily.
Advice regarding specific patient groups

Post-operative pain
- 1st choice NSAID is ibuprofen PO 400 mg 8 hourly.
- When the oral route is not available, IV or PR diclofenac may be used until oral administration of ibuprofen or naproxen is possible.
- Do not prescribe “Diclofenac PO/IV/PR”.

Breastfeeding
- 1st choice NSAID is ibuprofen.
- 2nd choice is naproxen.

Pregnancy
- NSAIDs should not be used in the third trimester of pregnancy.
- Patients in the first or second trimesters can take ibuprofen or naproxen for short term use.

Long term treatment, e.g. of rheumatological conditions
- If patients on long term diclofenac have not already tried ibuprofen and naproxen, they should be switched to one of these safer alternatives.
- If patients on long term diclofenac have already tried ibuprofen and naproxen and they have been found ineffective, the patients should remain on diclofenac treatment.

Comparative efficacy
Ibuprofen 400 mg, diclofenac 50 mg and naproxen 500 mg have shown similar pain relief over 4 to 6 hours in randomised controlled trials (RCTs) of patients with moderate to severe acute pain when compared to placebo.

Diclofenac tablets 50 mg = diclofenac injection 50 mg = diclofenac suppositories 75 mg (based upon their pharmacokinetic profiles described in their summary of product characteristics (SPCs)).

There are only small differences in anti-inflammatory activity between the various NSAIDs and choice based upon efficacy is largely empirical. Responses of individual patients vary widely.

Comparative safety

<table>
<thead>
<tr>
<th>Gastrointestinal risk (11)</th>
<th>Cardiovascular risk (12,13)</th>
<th>Renal risk (11)</th>
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| All NSAIDs are associated with GI toxicity. The risk is greatest in the elderly. | See below | All NSAIDs increase the risk of renal events. Highest risk patients are:  
- The elderly  
- Those with pre-existing renal impairment  
- Those on ACE inhibitors and angiotensin 2 antagonists  
- Those on long term use |
| **High risk NSAID**  
Diclofenac (all doses)  
Naproxen (all doses)  
Indomethacin (all doses)  
Ibuprofen 2.4 g daily | Increased thrombotic risk (MI or stroke) in patients without CV risk factors even after short term use (<30 days) of approx. 3 events per 1000 patients for:  
- COX-II inhibitors  
- Diclofenac 150 mg daily  
- Ibuprofen 2.4 g daily | NSAIDs should be avoided in kidney disease and patients at high risk of renal impairment. |
| **Low risk NSAID**  
No increased upper GI events risk for:  
Ibuprofen 1.2 g daily (or less) | No increased thrombotic risk for:  
- Ibuprofen 1.2 g daily (or less)  
- Naproxen (1 g daily) | |

Avoid prescribing NSAIDs unless absolutely necessary. Wherever possible, prescribe paracetamol first (see dose in **algorithm** on page 1). If an NSAID is needed, prescribe the lowest effective dose for the shortest possible duration.
References

2. BHNHST Guideline 656 Use of Proton Pump Inhibitors.
7. Diclofenac tablets 50 mg (Adacium Rapid®) SPC, last updated September 14th 2016.
13. European Medicines Agency review of recent published data on the cardiovascular safety of NSAIDs, October 2012, and Non-steroidal anti-inflammatory drugs (NSAIDs): Further evidence that the cardiovascular risk with diclofenac is higher than other non-selective NSAIDs and similar to the selective COX-2 inhibitors. Drug Safety Update October 2012.

See also:
Guideline 49FM Post-Operative Analgesic Ladder for Adults
Guideline 656 Guidelines on the Use of Proton Pump Inhibitors
Guideline 721FM Buckinghamshire Headache Management Guidelines for Adults