

## IBUPROFEN and NAPROXEN (oral formulations)

**The Pan Mersey Area Prescribing Committee recommends the prescribing of IBUPROFEN (low dose) and NAPROXEN (low dose) as the non-steroidal anti-inflammatory drugs (NSAIDs) of choice, if an NSAID is appropriate.<sup>1</sup>**

### GREEN

There are long-standing and well-recognised gastrointestinal and renal safety concerns with all NSAIDs. There is also substantial evidence confirming an increased risk of cardiovascular events with many NSAIDs, including COX-2 inhibitors and some traditional NSAIDs such as diclofenac and high-dose ibuprofen.<sup>1</sup>

**If an NSAID is needed, use ibuprofen (1200 mg a day or less) or naproxen (1000 mg a day or less). Use the lowest effective dose and the shortest duration of treatment necessary to control symptoms.<sup>1</sup>**

- The decision to prescribe an NSAID should be based on an assessment of a person's individual risk factors, including any history of cardiovascular and gastrointestinal illness.<sup>1</sup>

- Naproxen (1000 mg a day or less) and low-dose ibuprofen (1200 mg a day or less) are considered to have the most favourable thrombotic cardiovascular safety profiles of all NSAIDs.<sup>1</sup>

- The lowest effective dose should be used for the shortest duration necessary to control symptoms. A person's need for symptomatic relief and response to treatment should be re-evaluated periodically.<sup>1</sup>

All NSAID use (including cyclo-oxygenase-2 selective inhibitors) can, to varying degrees, be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of baseline cardiovascular risk factors or duration of NSAID use; however, the greatest risk may be in those receiving high doses long term.<sup>2</sup>

- Cyclo-oxygenase-2 selective inhibitors, diclofenac (150 mg daily) and ibuprofen (2.4 g daily) are associated with an increased risk of thrombotic events. The increased risk for diclofenac is similar to that of licensed doses of etoricoxib. Naproxen (1 g daily) is associated with a lower thrombotic risk, and low doses of ibuprofen (1.2 g daily or less) have not been associated with an increased risk of myocardial infarction.<sup>2</sup>

**Review the appropriateness of non-steroidal anti-inflammatory drug (NSAID) prescribing widely and on a routine basis, especially in people who are at higher risk of gastrointestinal, renal and cardiovascular morbidity and mortality (for example, older people).<sup>1</sup>**

There are specific indications where other Pan Mersey approved NSAIDs are more effective and preferred.

Co-prescribe a proton pump inhibitor with NSAIDs for people who have osteoarthritis or rheumatoid arthritis, and think about the use of gastro-protective treatment when prescribing NSAIDs for low back pain, axial spondylo-arthritis, psoriatic arthritis and other peripheral spondylo-arthritis.<sup>1</sup>

**Paediatrics:** The risk of cardiovascular events secondary to NSAID use is undetermined in children. A small increased thrombotic risk cannot be excluded in children. Children appear to tolerate NSAIDs better than adults and gastro-intestinal side-effects are less common although they do still occur and can be significant; use of gastro-protective drugs may be necessary.<sup>3</sup>

**Note:** Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

## IBUPROFEN and NAPROXEN (oral formulations)

### Effectiveness

NSAIDs reduce the production of prostaglandins by inhibiting the enzyme cyclo-oxygenase. They vary in their selectivity for inhibiting different types of cyclo-oxygenase; selective inhibition of cyclo-oxygenase-2 is associated with less gastrointestinal intolerance. In single doses NSAIDs have analgesic activity comparable to paracetamol, but paracetamol is preferred, particularly in the elderly. In regular full dosage, NSAIDs have a lasting analgesic and anti-inflammatory effect. About 60% of patients will respond to any NSAID, of the others, those who do not respond to one may well respond to another. Pain relief starts soon after taking the first dose and a full analgesic effect should normally be obtained within one week, whereas an anti-inflammatory effect may not be achieved (or may not be clinically assessable) for up to 3 weeks. If appropriate responses are not obtained within these times, another NSAID should be tried.<sup>2</sup>

NICE has issued advice on NSAIDs for people with osteoarthritis, rheumatoid arthritis, and low back pain & sciatica and spondyloarthritis (NICE guidelines 177<sup>4</sup>, 100<sup>5</sup>, 59<sup>6</sup> & 65<sup>7</sup>).

### Cost per annum<sup>8</sup>

Ibuprofen 200mg tabs three times a day £35  
 Ibuprofen 400mg tabs three times a day £38  
 Naproxen 250mg tabs twice a day £26  
 Naproxen 500mg tabs twice a day £54

Ibuprofen, naproxen and diclofenac % items (total number of items prescribed as a proportion of all NSAID items) in the Pan Mersey area excl Wirral (ePACT report Nov 2018-Oct 2018): Ibuprofen 18% Naproxen 62%, Diclofenac 5% Others 15%

### Safety

#### Adverse effects<sup>9</sup>

Dyspepsia and other upper gastrointestinal (GI) complications are the most common adverse effects of NSAIDs — for example, ulcer, perforation, obstruction or bleeding.

Cardiovascular and renal complications are less common but serious NSAID adverse effects — for example, myocardial infarction, stroke, cardiac failure, hypertension, and renal failure.

All NSAID use is associated with a small increased risk of thrombotic events independent of baseline cardiovascular risk factors or duration of NSAID use. Other adverse effects include:

Prolonged bleeding (for example, after surgery) as a result of inhibition of platelet aggregation; bronchospasm; severe skin reactions and angioedema. Very rarely, NSAIDs can precipitate severe hepatic reactions (such as hepatitis, liver necrosis, or hepatic failure).

#### Contra-indications<sup>2</sup>

Active gastro-intestinal bleeding; active gastro-intestinal ulceration; history of gastro-intestinal bleeding related to previous NSAID therapy; history of gastro-intestinal perforation related to previous NSAID therapy; history of recurrent gastro-intestinal haemorrhage (two or more distinct episodes); history of recurrent gastro-intestinal ulceration (two or more distinct episodes); severe heart failure; patients with a history of hypersensitivity to aspirin or any other NSAID—which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID.

For detailed information on specific medicines, see the summary of product characteristics, available at the electronic Medicines Compendium (eMC) ([www.medicines.org.uk](http://www.medicines.org.uk)).

### Patient factors<sup>2</sup>

Hepatic impairment: Use with caution; there is an increased risk of GI bleeding and fluid retention. Avoid in severe liver disease. Renal impairment: Avoid if possible or use with caution. Avoid if eGFR less than 30 mL/minute/1.73 m<sup>2</sup>. In renal impairment monitor renal function; sodium and water retention may occur and renal function may deteriorate, possibly leading to renal failure. Long-term use of some NSAIDs is associated with reduced female fertility, which is reversible on stopping treatment.

Pregnancy: avoid unless the potential benefit outweighs the risk. Avoid during the third trimester (risk of closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn); onset of labour may be delayed and duration may be increased.

### Prescribing information & Implementation notes

Review the appropriateness of NSAID prescribing widely and on a routine basis, especially in people who are at higher risk of both gastrointestinal (GI) and cardiovascular (CV) morbidity and mortality (e.g. older patients). If initiating an NSAID is obligatory, use ibuprofen (1200mg per day or less) or naproxen (1000mg per day). Review patients currently prescribed NSAIDs. If continued use is necessary, consider changing to ibuprofen (1200mg per day or less) or naproxen (1000mg per day). Co-prescribe a proton pump inhibitor with NSAIDs for people who have osteoarthritis or rheumatoid arthritis, and think about the use of gastro-protective treatment when prescribing NSAIDs for low back pain, axial spondylo-arthritis, psoriatic arthritis and other peripheral spondylo-arthritides. Take account of drug interactions when co-prescribing NSAIDs with other medicines (see Summaries of Product Characteristics). For example, co-prescribing NSAIDs with angiotensin converting enzyme (ACE) inhibitors or angiotensin-2 receptor antagonists (A2RAs) may pose particular risks to renal function; this combination should be especially carefully considered and regularly monitored if continued.

## Supporting information

### References

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4. National Institute for Health & Care Excellence. Osteoarthritis care & management. CG177 Feb 2014. <https://www.nice.org.uk/guidance/cg177>
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9. Clinical Knowledge Summaries (CKS). NSAIDs- Prescribing Issues Summary. Last revised Aug 2018. Accessed 10<sup>th</sup> January 2019. <https://cks.nice.org.uk/nsaids-prescribing-issues#!topicsummary>