

Selective and non-selective NSAIDs—Questions and answers

1. What are NSAIDs?

Non-steroidal anti-inflammatory drugs (commonly known as NSAIDs) are widely used effective medicines for treatment of arthritis and many other painful conditions. Most NSAIDs are available only on prescription; however, ibuprofen (Nurofen) is an NSAID that can be bought in shops and pharmacies. NSAIDs interfere with the body's inflammatory process by blocking enzymes called cyclo-oxygenases (COX-1 and COX-2). NSAIDs vary in their "selectivity" for cyclo-oxygenase enzymes. Selective inhibitors of COX-2 (coxibs) have a more targeted mechanism against COX-2 alone, and for this reason are thought to have fewer side-effects on the gastrointestinal system.

2. What is known about the safety of NSAIDs?

NSAIDs are generally well-tolerated, and most patients do not have side-effects. The most common side-effects are gastrointestinal irritation (eg, abdominal pain, heartburn, nausea, and vomiting). Rarely, serious side-effects such as gastrointestinal ulceration or bleeding may occur, which are more likely with high doses and prolonged use. NSAIDs can also cause allergic reactions, fluid retention, and various other rare side-effects, which are listed in the product information (including patient information leaflets). The cardiovascular risk with non-selective NSAIDs was considered last year by the UK and European expert committees (see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=227). Since then, further evidence has emerged, which suggests that some NSAIDs may be associated with a small increased risk of thrombotic events (eg, heart attack or stroke) when used at high doses and for a long time.

3. What are selective COX-2 inhibitors?

COX-2 selective inhibitors (commonly known as coxibs) are newer anti-inflammatory medicines developed to produce fewer gastrointestinal side-effects than NSAIDs. Coxibs are also used in the treatment of inflammatory and painful conditions such as arthritis.

4. What is known about the safety of coxibs?

Evidence suggests that patients treated with coxibs may be at a small increased risk of arterial thrombotic events such as heart attacks and strokes compared with non-users. In February 2005 the Committee on Safety of Medicines (CSM, which has been replaced by the Commission on Human Medicines or CHM) advised that coxibs should not be used in patients who have some types of cardiovascular disease. For other patients, doctors were advised to consider carefully in individual patients the potential balance of gastrointestinal benefits in terms of tolerability and cardiovascular risks associated with coxibs.

5. What is the concern about thrombotic reactions with NSAIDs and coxibs? Do they have the same thrombotic risk as each other?

The level of thrombotic risk for NSAIDs and coxibs is small, although it may vary between individual NSAIDs and coxibs. New evidence for the NSAID diclofenac suggests that it has a cardiovascular risk similar to that of at least one coxib—etoricoxib. Updated evidence for another NSAID, called naproxen, suggests this drug is associated with a lower thrombotic risk compared with coxibs; however, further studies of this drug are needed to establish fully its risk profile. Information for ibuprofen (an NSAID) suggests that high doses (2400 mg a day) might be associated with a small increased thrombotic risk, but studies do not suggest that low doses (1200 mg a day or less) are associated with increased risk of heart attack. Further studies are needed to define the thrombotic safety profile of other NSAIDs.

6. What is known about the level of thrombotic risk?

The level of thrombotic risk with NSAIDs and coxibs is small, especially for patients without other risk factors. At present, the exact level of risk for individual coxibs and NSAIDs is not known. Evidence from clinical trials of coxibs suggests that about 3 additional thrombotic events per 1000 patients per year may occur in the general population. In order to minimise risk, healthcare professionals are advised to prescribe the lowest dose for the shortest time to control symptoms.

7. What about other adverse effects, such as high blood pressure, fluid retention, and heart failure?

All NSAIDs and coxibs can have effects on the kidney, particularly at high doses, which increase the risk of fluid retention, high blood pressure, and (rarely) heart failure in at-risk patients. These risks are described in the patient information leaflet.

8. What is the most up-to-date prescribing advice for NSAIDs and coxibs?

All anti-inflammatory medicines (including NSAIDs and coxibs) should be **used at the lowest possible dose and for the shortest possible period necessary** to control symptoms.

There is no need to stop taking regular NSAID or coxib treatment. There is also no need for patients to switch between NSAIDs: the prescribing of NSAIDs and coxibs should be based on careful consideration of a patient's condition and risk factors for treatment, particularly with regard to the known effects of NSAIDs and coxibs on the gastrointestinal and cardiovascular systems.

9. I've been taking diclofenac regularly for some time. Do I need to change treatment?

Patients who gain effective pain relief by taking diclofenac regularly do not need to switch immediately to another NSAID based on current evidence. At the next routine review, the choice of NSAID can be reviewed as necessary.

10. Is ibuprofen still safe enough to be bought over the counter?

Yes. For doses available over the counter, ibuprofen has an established safety profile, particularly with regard to gastrointestinal adverse effects. Whereas there is some evidence for an increased thrombotic risk associated with prolonged treatment and **high** doses of ibuprofen, short-term use at doses that can be bought over the counter are unlikely to be associated with any significant increase in risk.

11. What should patients do if they are concerned?

Anyone who is concerned about the potential risks associated with a medicine should discuss the matter with their doctor at a routine appointment, who may reassess a patient to ensure they are taking the most appropriate anti-inflammatory. Such an assessment should consider a patient's need for pain relief and any particular treatment preference they have, as well as any risk factors they may carry.