# Nonsteroidal anti-inflammatory drugs

**Nonsteroidal anti-inflammatory drugs are members of a drug class that reduces pain, decreases fever, prevents blood clots, and in higher doses, decreases inflammation. Side effects depend on the specific drug but largely include an increased risk of gastrointestinal ulcers and bleeds, heart attack, and kidney disease. The term nonsteroidal distinguishes these drugs from steroids, which while having a similar eicosanoid-depressing, anti-inflammatory action, have a broad range of other effects. First used in 1960, the term served to distance these medications from steroids, which were particularly stigmatized at the time due to the connotations with anabolic steroid abuse. NSAIDs work by inhibiting the activity of cyclooxygenase enzymes. In cells, these enzymes are involved in the synthesis of key biological mediators, namely prostaglandins, which are involved in inflammation, and thromboxanes, which are involved in blood clotting. There are two types of NSAIDs available: non-selective and COX-2 selective. Most NSAIDs are non-selective and inhibit the activity of both COX-1 and COX-2. These NSAIDs, while reducing inflammation, also inhibit platelets aggregation (especially aspirin) and increase the risk of gastrointestinal ulcers/bleeds. COX-2 selective inhibitors have less gastrointestinal side effects but promote thrombosis and substantially increase the risk of heart attack. As a result, COX-2 selective inhibitors are generally contraindicated due to the risk of undiagnosed vascular disease. These differential effects are due to the different roles and tissue localizations of each COX isoenzyme. By inhibiting physiological COX activity, in all NSAIDs increase the risk of kidney disease and through a related mechanism, heart attack. In addition, NSAIDs can blunt the production of erythropoietin resulting in anemia, since hemoglobin needs this hormone to be produced.**

**Prolonged use is dangerous and prominent NSAIDs are aspirin, ibuprofen, and naproxen. Paracetamol is generally not considered as NSAID because it has only minor anti-inflammatory activity. It treats pain mainly by blocking COX-2 and inhibiting endocannabinoid reuptake almost exclusively within the brain, but not much in the rest of the body.**

## Administration

**Most commonly, NSAIDs are available as oral tablets. According to the package insert, the dosage for most common over-the-counter NSAIDs are as follows:**

- **Ibuprofen – for 200mg tablets, 1 to 2 tablets every 4 to 6 hours while symptoms persist. The daily limit for ibuprofen is 1200 mg.**
- **Aspirin regular strength: for 325 mg tablets, 1 or 2 tablets every 4 hours or 3 tablets every 6 hours. The daily limit for aspirin is 4000mg.**
- **Naproxen sodium: for 220 mg tablets, 1 to 2 tablets every 8 to 12 hours. The daily limit for naproxen sodium is 660 mg.**

**Topical NSAIDs are also available. They are most useful for treating pain due to soft-tissue injuries and osteoarthritis.**

## Adverse Effects

**NSAIDs have well-known adverse effects affecting the gastric mucosa, renal system, cardiovascular system, hepatic system, and hematologic system.**

**Gastric adverse effects are likely due to inhibition of COX-1, preventing the creation of prostaglandins that protect the gastric mucosa.**

**Renal adverse effects are because COX-1 and COX-2 facilitate the production that play a role in renal hemodynamics. In a patient**

**with normal renal function, inhibition of prostaglandin does not pose a large problem.**

**Cardiovascular adverse effects can also be increased with NSAID use; these include MI, thromboembolic events, and atrial fibrillation. Diclofenac seems to be the NSAID with the highest reported increase in adverse cardiovascular events.**

**Hepatic adverse effects are less common; NSAID-associated risk of hepatotoxicity is not very common, and liver-related hospitalization is very rare.**

**Hematologic adverse effects are possible, particularly with nonselective NSAIDs due to their antiplatelet activity.**

**Other minor adverse effects include anaphylactoid reactions that involve the skin and pulmonary systems, like urticarial and aspirin-exacerbated respiratory disease.**

**Contraindications**

**According to the package insert NSAIDs are contraindicated in patients:**

- **With NSAID hypersensitivity or salicylate hypersensitivity, as well as in patients who have experienced an allergic reaction after taking NSAIDs**
- **Who have undergone coronary artery bypass graft surgery**
- **During the third trimester of pregnancy**

**Monitoring**

**Recommended monitoring includes a CBC, renal tests, and hepatic panel. Monitoring is less common in patients not considered high risk for NSAID toxicity. However, NSAIDs are either contraindicated, or their use requires monitoring, in patients with liver or renal problems.**

**Toxicity**

**NSAID toxicity can manifest as GI bleeding, hypertension, and renal damage. Typically, acute NSAID overdose is asymptomatic or has negligible gastrointestinal symptoms. However, other symptoms of toxicity complications may include anion gap metabolic acidosis, coma, convulsions, and acute renal failure. Also, NSAIDs can confer gastrointestinal damage by inhibiting COX-1, which causes decrease gastric mucosa production. Nephrotoxicity can also occur with NSAID use because these medications reduce prostaglandin levels, which are essential for the vasodilation of the renal arterioles. Lastly, neurologic toxicity can present with drowsiness, confusion, nystagmus, blurred vision, diplopia, headache, and tinnitus.**

**Answer the questions:**

1. **Give a definition of NSAIDs.**
2. **What is the mechanism of the action of the NSAIDs?**
3. **What is the dosage for the most common over-the-counter NSAIDs?**
4. **What are the adverse effects of the NSAIDs?**
5. **What does the recommended monitoring include?**
6. **Describe the toxicity of NSAID.**

**Make a summary of this text.**