

Scottish Paediatric and Adolescent Rheumatology Network - SPARN

Guide to Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

**NOTE**

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient’s case notes at the time the relevant decision is taken.

***Mechanism of Action:***

* NSAIDS inhibit cyclo-oxygenase and thus reduce prostaglandins causing anti-inflammatory and analgesic effect.
* Single dose: has analgesic activity
* Regular full doses: lasting analgesic and anti-inflammatory effect.

***Choice:***

* The choice of NSAID is based on formulation, frequency of dosing regimen, side effect profile and contra-indications. (Table 1).
* There is a variation in individual response and tolerance
* Full analgesic effect can take up to 1 week and anti-inflammatory effect may not be achieved for up to 3 weeks.
* In Juvenile Idiopathic Arthritis (JIA) it may take 4-12 weeks to be effective.
* Slow-release preparations given in the evening may be helpful for early morning stiffness.
* Consider concomitant gastro-protective cover when using long-term or alongside corticosteroids
* Use lowest effective dose for shortest time period
* The role of cyclooxygenase-2 (Cox-2) inhibitors, a type of NSAID which reduces the risk of peptic ulceration, is undetermined in children.
* Check for ***drug interactions*** before use:

 ACE inhibitors: risk of hyperkalaemia and renal damage;

 warfarin: effect enhanced by NSAIDs;

methotrexate: elimination can be reduced by NSAIDs and may increase the risk of toxicity

bisphosphonates : NSAIDS increase the risk of renal impairment

* Check for ***contraindications*:**
* Absolute- active or previous peptic ulceration or GI bleeding, severe heart failure, moderate to severe renal impairment.
* Relative - asthma, coagulation defects, renal, cardiac, or hepatic impairment, inflammatory bowel disease
* ***Side effects*** are rare but include:
* Central nervous system : headache, hyperactivity, dizziness, vertigo, anxiety depression, tinnitus, aseptic meningitis in SLE (rare).
* Cardiovascular : risk of events undetermined in children. In adults, increase in

 thrombotic events.

* Haematological : blood disorders are rare albeit bleeding times may be prolonged.
* GI : All NSAIDS are associated with GI toxicity. Ibuprofen has the lowest risk.

 Children tolerate NSAIDS better. Common side effects are nausea, abdominal pain,

bleeding, ulceration, hepatic damage, pancreatitis. Ibuprofen has the lowest GI risk. Apparent intolerance of NSAIDs should raise concern of GI pathology

(e.g. *Helicobacter pylori* disease, inflammatory bowel disease).

* Renal : may provoke renal failure in pre-existing renal impairment. Rarely papillary necrosis or tubulointerstitial nephritis (later interstitial fibrosis) leading to renal impairment.
* Skin : NSAIDs may cause pseudoporphyria (photosensitive blistering rash leaving scars)—most common with Naproxen and in fair-skinned individuals.
* Respiratory : worsen asthma, alveolitis, pulmonary eosinophilia
* Other rare side effects : visual disturbances, Stevens–Johnson syndrome, Toxic Epidermal Necrolysis.

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| **Table 1 Dosage/administration/formulations** |
| **Drug** | **Age** | **Dose** | **Formulations** | **Comments** |
| **Ibuprofen** | >3 months | 10mg/kg3–4 times a day | 200mg and 400mg Tablets100mg in 5ml Suspension | Weakest NSAID, but least side effects.Avoid high doses in uncontrolled hypertensionWeaker anti-inflammatory properties |
| **Naproxen** | >2yr | 5-7.5mg/kgTwice a day | 250mg and 500mg Tablets125mg in 5ml and 250mg in 5ml Suspension more cost effective | Good efficacy.Generally low incidence of side effects but associated with pseudoporphyria in JIA |
| **Diclofenac sodium** | >6 months | 1.5–2.5mg/kgTwice a day. Max 150mg daily | 25mg and 50mg TabletsDispersible tablets unlicensed special25mg, 50mg, 100mg modified release tablets100mg Suppositories | Similar actions and side effects to Naproxen |
| **Piroxicam** | >6 yrs | Up to 15kg: 5mg16–25kg: 10mg26–45kg: 15mg46kg and over: 20mgOnce a day | 20mg capsules10mg and 20mg Dispersible tablets / “Melts” | More GI side effects, more serious skin reactionsNot 1st line As effective as NaproxenLong duration of actionInitiate by physicians experienced in treating rheumatic diseaseReview use after 2 weeks and periodically thereafter |
| **Indomethacin** | >1 month | 0.5– 1mg/kg/dose Twice a day | 25mg and 50mg Capsules100mg Suppositories | Mostly used to treat enthesitis-related arthritis and sJIAHigh incidence of side effectsSimilar action to NaproxenRarely used in children |
| **Meloxicam** | >12 yrs | <50kg: 7.5mg50kg and over: 15mgOnce a day | 7.5 mg and 15mg Tablets and dispersible tablets | consider in adolescents intolerant to other NSAIDSSelective COX-2 inhibitor |
| **Diclofenac potassium** | >6 months | 75-100mg daily in2-3 divided doses  | 25mg and 50mg Tablets |  |
| **Flurbiprofen** | >12 yrs | 150-200mg daily in2-4 divided doses then increase to 300mg daily | 50mg and 100mg Tablets only |  |

**References:**

1. Kelly A, Ramanan AV. The principles of pharmacological treatment of juvenile idiopathic arthritis. *Paediatrics and Child Health* 2011; 563-568

2. British National Formulary for Children. UK:BMJ publishing group; 2022

3. Oxford Handbook of Paediatric Rheumatology. Oxford University press; 2012

4. Ruperto et al. A Randomized, Double-Blind Clinical Trial of Two Doses of

Meloxicam Compared With Naproxen in Children With Juvenile Idiopathic Arthritis. *Arthritis & Rheumatism*. Vol. 52, No. 2, February 2005, pp 563–572

DOI 10.1002/art.20860

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Date: 26 July 2023