Acetaminophen and Non-Steroidal Anti-Inflammatory Drugs Quick Reference Sheet

Recommend:  **ACETAMINOPHEN** **+**  **NSAID**

Key points:

- Kidney: acute kidney injury is mostly present in those with other risk factors, including older age. Use with caution in those with chronic kidney disease.
- Bleeding: anti-platelet effect is due to COX-1 inhibition, but NSAIDs block COX in a reversible fashion. Normal platelet function

ACETAMINOPHEN SAFETY AND SIDE EFFECTS

Drug	Usual Dose	Max Daily Dose (mg)	Relative COX Selectivity	
			COX-1	COX-2
Acetaminophen	1000 mg three to four times per day	4000	-	-

Consider:

- Caution should be observed in patients with liver disease, active alcohol use, and G6PD deficiency
- Consider all sources of acetaminophen including combination products and OTC cough/cold products when recommending acetaminophen
- Acetaminophen overdose may occur with 5-6 grams daily for prolonged use (6-8+weeks) or acute ingestion of at least 7.5 grams

NON-STEROIDAL ANTI-INFLAMMATORY SAFETY AND SIDE EFFECTS

Drug	Usual Dose	Max Daily Dose (mg)	Relative COX Selectivity	
			COX-1	COX-2
Ibuprofen	400-800 mg three to four times per day	3200	++	
Naproxen	200-400 mg two or three times per day	1375-1500	++	
Ketorolac	10 mg four times per day	40	+++	
Diclofenac	35-50 mg two to three times per day	200		++
Meloxicam	15 mg daily	15		+++
Celecoxib	100-200mg two times per day	400		+++

Consider:

- Caution should be observed in patients with a history of cardiovascular, gastrointestinal, and kidney disease
- Cardiovascular: avoid use in patients with heart failure. Coronary, vascular, and death are risks associated with long term use. Out of hospital cardiac arrest is associated with short term use.
- Gastrointestinal: Risk is low (<2%) but present in long term use and those at risk. Risk may be mitigated with the use of concomitant proton pump inhibitor (PPI, e.g. over the counter omeprazole) during treatment course.
    - Increased risk of gastrointestinal complications (all NSAIDs), which remains constant over time
        - Caution in those over 60 years of age, history of peptic ulcers, gastrointestinal bleeds, and Helicobacter pylori infections

- Kidney: acute kidney injury is mostly present in those with other risk factors, including older age. Use with caution in those with chronic kidney disease.
- Bleeding: anti-platelet effect is due to COX-1 inhibition, but NSAIDs block COX in a reversible fashion. Normal platelet function returns within 1-3 days depending on the drug (e.g. 1 day for ibuprofen, 2 days for naproxen, diclofenac, and 3 days for piroxicam).

DENTAL SPECIFIC HIGHLIGHTS

- **If ibuprofen 400 mg is not adequately treating the patient's pain, this is not a failure. Try increasing the dose as tolerated for an adequate duration before determining treatment failure.**
    - Most studies in patients with dental pain use lower doses of NSAIDs in combination with acetaminophen (i.e. 400 mg of ibuprofen plus 1000 mg of acetaminophen)
        - Single dose studies show ibuprofen 400 mg provided about half of patients with at least 50% pain relief
            - ❖ Ibuprofen 600 mg provided 79% of patients with at least 50% pain relief
            - ❖ Ibuprofen 800 mg provided 100% of patients with at least 50% pain relief
- **If ibuprofen does not work (after trying 800 mg doses) or the patient cannot use it, consider prescribing celecoxib 200 mg two times per day**
    - Compared to ibuprofen 400 mg and tramadol 100 mg, celecoxib showed improved pain control
- **Ibuprofen 400, 600, and 800 mg have lower numbers needed to treat (better pain relief) than oxycodone 10mg/ acetaminophen 1000mg**
    - Although not based on head-to-head studies, it takes treating 2.7 patients with 10 mg of oxycodone and 1000mg of acetaminophen for 1 to benefit.
    - It takes treating 2.4 and 1.6 patients with ibuprofen 400 or 600mg, and 800mg, respectively for 1 to benefit.
- **When using acetaminophen for pain, use 1000 mg up to four times per day scheduled**
    - Compared to lower doses of acetaminophen, 1000 mg outperformed the rest in studies.
    - Review all sources of acetaminophen and ensure patient does not use more than recommended
    - Per the U.S. FDA, the maximum total daily dose of acetaminophen is 4000mg (4mg/day)[1]

References:

[1]https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-prescription-acetaminophen-products-be-limited-325-mg-dosage-unit

https://www.knowyourdose.org/wp-content/uploads/2015/05/Acetaminophen-Report.pdf