

Non-Opioid & Adjunct Analgesics Guide

MOA • Indications • Contraindications • Dosing • Pearls

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Christine Collins, MD, Joseph D'Orazio, MD



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Acetaminophen (APAP)

Mechanism	<ul style="list-style-type: none">• Central analgesic/antipyretic• Works via its metabolite AM404 activating TRPV1 and cannabinoid receptors, inhibits central prostaglandin synthesis
Indications	<ul style="list-style-type: none">• Analgesia• Fever
Contraindications / precautions	<ul style="list-style-type: none">• Severe hepatic impairment or active liver disease; chronic heavy alcohol use• Avoid unintentional duplicate APAP from combination products.
Adult dosing	<ul style="list-style-type: none">• 1,000 mg q6h.• Max (typical adult): 4,000 mg/day• IV: no significant improvement in analgesia. Give IV in patient's who can not tolerate PO or are NPO.• Consider lower maximum daily dose (<2,000 mg a day) in frail, malnourished, chronic alcohol use, liver disease.
Pearls	<ul style="list-style-type: none">• Schedule• Ask specifically about OTC cold/flu products or use of oxycodone-acetaminophen products to prevent overdose.• Pair with NSAIDs when able for pain

NSAIDs (General)

Mechanism	<ul style="list-style-type: none">• COX-1/COX-2 inhibition → reduced prostaglandin synthesis• Analgesic, antipyretic, anti-inflammatory
Indications	<ul style="list-style-type: none">• Inflammatory pain (sprains/strains, arthritis, renal colic, dysmenorrhea).
Contraindications / precautions	<ul style="list-style-type: none">• Active GI bleed or high-risk peptic ulcer disease.• CKD/AKI• Heart failure or significant cardiovascular disease; recent MI• Pregnancy• Concurrent anticoagulation/antiplatelets increases bleeding risk.
Adult dosing (examples)	<ul style="list-style-type: none">• Ibuprofen: 400 mg PO q6h• Naproxen: 500 mg PO q12h• Ketorolac: 10 mg q6h• Celecoxib: 100-200 mg daily• Meloxicam: 7.5-15 mg daily
Pearls	<ul style="list-style-type: none">• Use the lowest effective dose for the shortest duration.• Avoid stacking multiple NSAIDs• Consider GI protection (PPI) for higher-risk patients if NSAID necessary• Consider NSAIDs more selective to COX-2 (celecoxib, meloxicam in patient's with GI, kidney disease or higher risk for bleeding)

Diclofenac

Mechanism	<ul style="list-style-type: none">• NSAID (COX inhibition) with anti-inflammatory and analgesic effects• Available as topical (lower systemic exposure) and oral formulations
Indications	<ul style="list-style-type: none">• Topical: osteoarthritis pain in superficial joints (hands, knees), localized soft-tissue pain.• Oral: inflammatory and musculoskeletal pain when benefits outweigh risks.
Contraindications / precautions	<ul style="list-style-type: none">• Oral has same class warnings as other NSAIDs.• Topical: apply to intact skin only; avoid occlusive dressings; wash hands after application.
Adult dosing	<ul style="list-style-type: none">• Topical 1% gel: upper extremity 2 g QID (max 8 g/day per joint); lower extremity 4 g QID (max 16 g/day per joint); max 32 g/day total.• Oral immediate-release (typical): 50 mg PO BID-TID; max commonly 150 mg/day (formulation-dependent).
Pearls	<ul style="list-style-type: none">• Topical diclofenac is useful when you want NSAID benefit with less systemic exposure.• Avoid applying heat over topical NSAIDs (may increase absorption)

Capsaicin

Mechanism	<ul style="list-style-type: none">• TRPV1 agonist → initial burning, then 'defunctionalization' of nociceptor fibers and reduced substance P signaling• Analgesia often improves after repeated use.
Indications	<ul style="list-style-type: none">• Localized neuropathic pain (e.g., postherpetic neuralgia).• Musculoskeletal pain/arthritis (topical creams).
Contraindications / precautions	<ul style="list-style-type: none">• Avoid broken/irritated skin, mucous membranes, or near eyes.• Significant local burning is common; counsel patients up front.• 8% patch application requires trained clinician and protective equipment.
Adult dosing	<ul style="list-style-type: none">• Low concentration cream (0.025-0.1%): apply thin layer 3-4 times daily; benefit may take days to weeks.• Capsaicin 8% patch: single 60-minute application (PHN) or 30-minute application on feet (DPN); may repeat no more often than every 3 months.
Pearls	<ul style="list-style-type: none">• Gloves for application; wash hands well after use.• Expect burning early—this is the main reason people stop; encourage brief trial period.• For 8% patch, pretreat area with topical anesthetic to improve tolerability.

Lidocaine Patches / Topical Systems

Mechanism	<ul style="list-style-type: none">• Local anesthetic - voltage-gated sodium channel blockade• Minimal systemic absorption when used as directed.
Indications	<ul style="list-style-type: none">• Neuropathic pain, especially postherpetic neuralgia.• Off-label: focal neuropathic or myofascial pain when skin is intact.
Contraindications / precautions	<ul style="list-style-type: none">• Hypersensitivity to amide local anesthetics.• Apply to intact skin only; avoid open wounds or active rash.• Avoid external heat sources over patches (heating pads, hot packs).
Adult dosing	<ul style="list-style-type: none">• Lidocaine 5% patch: up to 3 patches at once, applied once daily for up to 12 hours in a 24-hour period (12 on/12 off).
Pearls	<ul style="list-style-type: none">• You can cut patches to fit the painful area (keep within max number).• If skin irritation occurs, shorten wear time or rotate sites.• Great add-on for focal neuropathic pain without systemic sedation.

Gabapentin

Mechanism	<ul style="list-style-type: none">• Binds alpha-2-delta subunit of voltage-gated calcium channels → decreased excitatory neurotransmitter release• Not a GABA agonist despite the name
Indications	<ul style="list-style-type: none">• Neuropathic pain (PHN, diabetic neuropathy) and neuropathic components of mixed pain.• Adjunct when pain is burning, shooting, allodynia, or hyperalgesia.
Contraindications / precautions	<ul style="list-style-type: none">• Renal impairment: requires dose adjustment• Sedation, dizziness, gait instability—higher risk in older adults and with other CNS depressants.
Adult dosing	<ul style="list-style-type: none">• Start: 100-300 mg PO at bedtime (or TID if inpatient monitoring).• Titrate: increase by 100-300 mg per dose every 1-3 days as tolerated.• Typical effective range: 900-3,600 mg/day divided TID (lower in CKD).
Pearls	<ul style="list-style-type: none">• Start low and titrate—fast titration increases dizziness/somnolence.• Set expectations: may take several days to weeks for meaningful benefit.• If stopping after prolonged use, taper to avoid withdrawal symptoms.

Skeletal Muscle Relaxants

Mechanism	<ul style="list-style-type: none">• Most skeletal muscle relaxants work centrally (sedation and reduced polysynaptic reflex activity), not directly on muscle.• Different agents have different receptor profiles (anticholinergic, alpha-2 agonism, etc.).
Indications	<ul style="list-style-type: none">• Acute painful muscle spasm (most evidence acute low back pain)• Upper Motor Neuron conditions: Multiple sclerosis, spinal cord injury, stroke
Contraindications / precautions	<ul style="list-style-type: none">• Sedation, dizziness, and falls—use caution in older adults and with other CNS depressants.• Avoid driving/operating machinery; avoid alcohol.• Cyclobenzaprine: anticholinergic effects; avoid with MAOIs; caution with serotonergic meds.• Tizanidine: hypotension/bradycardia; avoid with strong CYP1A2 inhibitors (e.g., ciprofloxacin, fluvoxamine).
Adult dosing (common options)	<ul style="list-style-type: none">• Cyclobenzaprine: 5 mg PO TID; may increase to 10 mg TID; use short-term (up to 2-3 weeks).• Methocarbamol: 1,500 mg PO QID for 48-72h, then reduce (e.g., 750-1,000 mg QID).• Tizanidine: start 2 mg PO; may repeat q6-8h; max 36 mg/day.
Pearls	<ul style="list-style-type: none">• Not first line for all MSK pain, consider risk vs. benefit• Cyclobenzaprine has the most clinical trial data and has consistently shown efficacy for muscle spasm pain• Benefit is modest for many patients; choose the least sedating option and reassess quickly• Prefer nighttime dosing when possible to reduce daytime impairment.• Avoid polypharmacy

Ketamine (Sub-dissociative Analgesia)

Mechanism	<ul style="list-style-type: none">• NMDA receptor antagonism; also interacts with opioid, monoaminergic, and cholinergic systems• At sub-dissociative doses provides analgesia with less respiratory depression than opioids
Indications	<ul style="list-style-type: none">• Moderate to severe acute pain when opioids are undesirable or inadequate (e.g., opioid-tolerant, OUD, hemodynamic instability).• Adjunct for hyperalgesia, severe neuropathic pain flares, and certain procedural contexts.
Contraindications / precautions	<ul style="list-style-type: none">• Relative: uncontrolled hypertension, tachyarrhythmia, active psychosis, severe agitation without ability to monitor.• Monitor for nausea, dysphoria, dizziness; provide calm environment.
Adult dosing	<ul style="list-style-type: none">• IV sub-dissociative (SDK): 0.1-0.3 mg/kg (max 30 mg) IV over 10-15 minutes.• Infusion: 0.1-0.2 mg/kg/hour• Consider antiemetic; avoid rapid IV push to reduce adverse effects.
Pearls	<ul style="list-style-type: none">• Slow administration decreases unpleasant perceptual effects.• Document indication and dose clearly; counsel patient about 'weird feeling' possibility.• Pairs well with multimodal regimen (APAP/NSAID, regional anesthesia, topical agents).

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