# Non-opioid alternatives for selected pain indications in adults

This table was created to provide examples of the role non-opioid alternatives can play in select pain conditions in adults. Management of pain indications often requires a multi-modal approach, inclusive of both pharmacologic and non-pharmacologic interventions. Medication examples provided carry a medically accepted indication* for use. Examples of non-opioid alternatives are listed alphabetically and are not intended to reflect preference for one option over another. Where individual drugs within a class are specified, these agents are most appropriate for the indication listed. **Always review for potential contraindications prior to selecting a medication for a patient.**

| Indication | Examples of Non-Opioids with Evidence of Efficacy | Clinical Considerations | Indication-Specific References |
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| **Dental Pain, Post-Extraction** | Acetaminophen<br>Oral NSAIDs (selective and non-selective) | *Some pain following dental extraction is expected. This is often related to inflammation. As such, non-opioid analgesics that target pain of this nature are first-line therapy for post-extraction dental pain. NSAIDs alone or in combination with acetaminophen may be considered for initial management.* | Carrasco-Labra A, Polk DE, Urquhart O, et al. Evidence-based clinical practice guideline for the pharmacologic management of acute dental pain in adolescents, adults, and older adults: A report from the American Dental Association Science and Research Institute, the University of Pittsburgh, and the University of Pennsylvania. J Am Dent Assoc. 2024;155(2):102-117.e9. doi:10.1016/j.adaj.2023.10.009 |
| **Dental Pain, Toothache** | Acetaminophen<br>Oral NSAIDs (selective and non-selective)<br>Topical agent: benzocaine | *Pain relief for a toothache should be utilized as a bridge between the initial appointment to address the initial complaint of pain and future appointments for definitive dental treatment to resolve the source of the pain. NSAIDs alone or in combination with acetaminophen may be considered for initial management.* | Carrasco-Labra A, Polk DE, Urquhart O, et al. Evidence-based clinical practice guideline for the pharmacologic management of acute dental pain in adolescents, adults, and older adults: A report from the American Dental Association Science and Research Institute, the University of Pittsburgh, and the University of Pennsylvania. J Am Dent Assoc. 2024;155(2):102-117.e9. doi:10.1016/j.adaj.2023.10.009 |
| **Dysmenorrhea** | Oral NSAIDs (selective and non-selective) | *Oral NSAIDs are recommended for empiric treatment at the time of symptom onset. Selection of the oral NSAID agent depends on cost, convenience of dosing and patient preference.* | The American College of Obstetricians and Gynecologists' Committee on Adolescent Health Care. ACOG Committee Opinion 760: Dysmenorrhea and endometriosis in the adolescent. Obstet Gynecol. 2018;132(6):e249–e258. |
| **Fibromyalgia** | GABA analogs: pregabalin, gabapentin<br>Skeletal muscle relaxant: cyclobenzaprine<br>SNRIs: duloxetine, milnacipran<br>TCA: amitriptyline | *Non-pharmacologic modalities are recommended for initial management of fibromyalgia, including interventions such as patient education, exercise, and/or psychological treatment. Selection of pharmacotherapy should be based on patient-specific symptoms.* | Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017;76(2):318-328. doi:10.1136/annrheumdis-2016-209724 Kundakci B, Hall M, Atzeni F, et al. International, multidisciplinary Delphi consensus recommendations on non-pharmacological interventions for fibromyalgia. Semin Arthritis Rheum. 2022;57:152101. doi:10.1016/j.semarthrit.2022.152101<br><br>Kundakci B, Hall M, Atzeni F, et al. International, multidisciplinary Delphi consensus recommendations on non-pharmacological interventions for fibromyalgia. Semin Arthritis Rheum. 2022;57:152101. doi:10.1016/j.semarthrit.2022.152101 |
| **Gout, Acute Flare** | Colchicine<br>Glucocorticoids<br>Oral NSAIDs (selective and non-selective) | *NSAIDs, colchicine, or glucocorticoids may all be considered for acute gout flares. For patients who are able to quickly identify signs of a flare, a "medication in pocket" strategy is preferred to allow patients to quickly initiate a medication intervention. If colchicine is considered, low-dose is preferred over high-dose due to similiar efficacy and less risk of adverse events.* | FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology guideline for the management of gout. Arthritis Care Res (Hoboken). 2020;72(6):744-760. doi: 10.1002/acr.24180. Erratum in: Arthritis Care Res (Hoboken). 2020;72(8):1187. Erratum in: Arthritis Care Res (Hoboken). 2021;73(3):458. PMID: 32391934; PMCID: PMC10563586. |
| **Headache, Acute** | Acetaminophen<br>Oral NSAIDs (selective and non-selective) | *Acetaminophen or oral NSAIDs are considered first line therapy for acute headache. Non-pharmacological modalities should also be considered.* | Ford B, Dore M, Harris E. Outpatient primary care management of headaches: guidelines from the VA/DoD. Am Fam Physician. 2021;104(3):316-320. PMID: 34523900.<br><br>American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Acute Headache; Godwin SA, Cherkas DS, Panagos PD, et al. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache. Ann Emerg Med. 2019;74(4):e41-e74. doi: 10.1016/j.annemergmed.2019.07.009. |
| **Intersitial Cystitis / Bladder Pain Syndrome** | Acetaminophen<br>Anti-histamine: hydroxyzine<br>$H_2$ antagonist: cimetidine<br>Oral NSAIDs (selective and non-selective)<br>TCA: amitriptyline<br>Urinary analgesics: pentosan polysulfate, phenazopyridine | *A trial and error approach to identify the medication or combination of medications that provide effective pain control is often needed. Most patients have baseline symptoms with occasional symptom flares. Amitriptyline, cimetidine, hydroxyzine, or pentosan polysulfate may be administered as oral medications for chronic symptom management. For symptom flares, acetaminophen, oral NSAIDs, or phenazopyridine may be utilized. In situations where pentosan polysulfate sodium is being considered, the patient should be counseled on the potential risk of macular damage and vision-related injuries.* | Clemens JQ, Erickson DR, Varela NP, Lai HH. Diagnosis and treatment of interstitial cystitis/bladder pain syndrome. J Urol. 2022;208(1):34-42. |
| **Kidney Stone** | Acetaminophen<br>Oral NSAIDs (selective and non-selective) | *For acute pain related to kidney stones, non-opioid analgesics have been found to be at least as effective as opioids. If selected analgesic does not provide sufficient pain relief, referral to a specialist should be considered.* | Fontenelle LF, Sarti TD. Kidney stones: treatment and prevention. Am Fam Physician. 2019;99(8):490-496. PMID: 30990297. (NSAIDs first line) Ketoralac is only NSAID explicitly mentioned<br><br>Pearle MS, Goldfarb DS, Assimos DG et al. Medical management of kidney stones: AUA Guideline. J Urol 2014; 192: 316. (No analgesia recommendations from AUA) |
| **Low Back Pain** | Acetaminophen<br>Duloxetine<br>Oral NSAIDs (selective and non-selective)<br>Skeletal muscle relaxants | *For treatment of acute low back pain, noninvasive nonpharmacologic approaches such as superficial heat should be used as appropriate. If medication is needed, NSAIDs are considered first-line and should be used unless contraindicated. Skeletal muscle relaxants may also be used on a short-term basis. Evidence suggests acetaminophen has limited benefit, but it may be considered if NSAIDs and/or skeletal muscle relaxants are contraindicated. For subacute and chronic low back pain, if nonpharmacologic approaches such as exercise are insufficient, NSAIDs or duloxetine may be considered if not contraindicated.* | Qaseem A, Wilt TJ, McLean RM, et al. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2017;166(7):514-530. doi:10.7326/M16-2367 |
| **Migraine, Acute** | 5-$HT_1$ agonists<br>5-$HT_{1F}$ agonist<br>Acetaminophen<br>CGRP antagonists: rimegepant, ubrogepant, zavegepant<br>Ergot derivatives: dihydroergotamine<br>Oral NSAIDs (selective and non-selective) | *For mild-moderate acute migraines, an NSAID or acetaminophen is considered a first-line options. For moderate-severe acute migraines, 5-$HT_1$ agonists, commonly referred to as "triptans" are considered first-line. Consider CGRP receptor antagonists for moderate-severe migraines when 5-$HT_1$ agonists are ineffective or contraindicated. The 5-$HT_{1F}$ agonist, lasmiditan, is considered second-line for moderate-severe migraines when 5-$HT_1$ agonists are ineffective or contraindicated. Do not administer 5-$HT_{1F}$ agonists unless patient can wait 8 hours between dosing and operating heavy machinery/driving. Do not use dihydroergotamine within 24 hours of triptans or another ergotamine preparation. 5-$HT_1$ agonists should not be used within 24 hours of a different 5-$HT_1$ agonists.* | Ailani J, Burch RC, Robbins MS; the Board of Directors of the American Headache Society. The American Headache Society consensus statement: update on integrating new migraine treatments into clinical practice. Headache. 2021;61(7):1021-1039. doi: 10.1111/head.14153<br><br>Aukerman G, Knutson D, Miser WF; Department of Family Medicine, Ohio State University College of Medicine and Public Health, Columbus, Ohio. Management of the acute migraine headache. Am Fam Physician. 2002;66(11):2123-2130.<br><br>Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: the american headache society evidence assessment of migraine pharmacotherapies. *Headache* . 2015;55(1):3-20. doi:10.1111/head.12499 |
| **Musculoskeletal Pain, Acute (Not otherwise specified)** | Acetaminophen<br>Oral NSAIDs (selective and non-selective)<br>Skeletal muscle relaxants<br>Topical agent: capsaicin<br>Topical NSAID: diclofenac | *For acute pain (duration <1 month) related to musculoskeletal injuries such as sprains, muscle strains, whiplash, etc., topical NSAIDs are recommended as first-line treatment, followed by oral NSAIDs or acetaminophen.* | Qaseem A, McLean RM, O'Gurek D, et al. Nonpharmacologic and pharmacologic management of acute pain from non-low back, musculoskeletal injuries in adults: a clinical guideline from the American College of Physicians and American Academy of Family Physicians. Ann Intern Med. 2020;173(9):739-748. doi:10.7326/M19-3602 |
| **Neuropathic Pain, General** | GABA analogs: gabapentin, pregabalin<br>TCAs: amitriptyline, desipramine, nortriptyline<br>Topical agents: capsaicin cream or patch, lidocaine patch | *Neuropathic pain can be secondary to a number of conditions (chemotherapy, amputation, etc). Regardless of etiology, pharmacologic approaches to neuropathy are similar. GABA analogs and the SNRI duloxetine may be considered as an initial therapy option. Tricyclic antidepressants may also be effective but the analgesic benefit must be weighed against the side effect profile of this drug class. Topical agents may also be considered in patients for whom systemic therapy may not be optimal but evidence to support their use is limited.* | Chou R, Wagner J, Ahmed AY, Blazina I, et. al. Treatments for acute pain: a systematic review [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020 Dec. Report No.: 20(21)-EHC006. PMID: 33411426. |
| **Neuropathic Pain, Diabetic Peripheral Neuropathy** | Anticonvulsants: lamotrigine, valproic acid<br>GABA analogs: gabapentin, pregabalin<br>SNRIs: desvenlafaxine, duloxetine, venlafaxine<br>TCAs: amitriptyline, desipramine, impramine, nortriptyline<br>Topical agents: capsaicin cream or patch, lidocaine patch | *Gabapentin, pregabalin, or duloxetine may all be considered as an initial treatment option for symptomatic neuropathic pain in diabetes. Tricyclic antidepressants may also be effective but the analgesic benefit must be weighed against the side effect profile of this drug class. Topical agents may also be considered in patients for whom systemic therapy may not be optimal but evidence to support their use is limited. Select anticonvulsants such as lamotrigine and valproic acid have shown benefit but carry additional risk.* | Pop-Busui R, Boulton AJ, Feldman EL, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes Care. 2017;40(1):136-154. |
| **Neuropathic Pain, Postherpetic neuralgia** | GABA analogs: gabapentin, pregabalin<br>TCAs: amitriptyline, desipramine, imipramine, nortriptyline<br>Topical agents: capsaicin cream or patch, lidocaine patch | *Choice of initial therapy should be based on the clinical characteristics of the patient, such as the severity of their symptoms and concomitant conditions. Additionally, consider medication side effects, patient preference, and treatment costs.* | Saguil A, Kane S, Mercado M, Lauters R. Herpes zoster and postherpetic neuralgia: prevention and management. Am Fam Physician. 2017;96(10):656-663. |

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| **Osteoarthritis** | Acetaminophen | *Treatment recommendations include both lifestyle changes and/or medications. The choice of treatments depends on the location of the osteoarthritis, patient characteristics and preferences. Oral NSAIDs are recommended for osteoarthritis of the knee, hip, and/or hand. Topical agents are recommended based on osteoarthritis location. Duloxetine may also be considered.* | Kolasinski SL, Neogi T, Hochberg MC, et. al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2020;72(2):149-162. doi: 10.1002/acr.24131. |
| | Oral NSAIDs (selective and non-selective) | | |
| | Topical agent: capsaicin cream | | |
| | Topical NSAID: diclofenac | | |
| **Postoperative Pain, Outpatient** | Acetaminophen | *For post-operative pain, treatment plans should use a multimodal analgesic approach. Non-opioid analgesics, potentially on an around-the-clock schedule, may be used to reduce or avoid the need for opioids in post-operative pain management. Specific pharmacotherapy recommendations depend on the procedure and patient-specific factors.* | Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain 2016;17:131–57. Erratum in: J Pain 2016;17:508–10. |
| | Oral NSAIDs (selective and non-selective) | | Overton HN, Hanna MN, Bruhn WE, et al. Opioid-prescribing guidelines for common surgical procedures: an expert panel consensus. J Am Coll Surg. 2018;227(4):411-418. |
| | Selective sodium channel blocker (suzetrigine) | | |
| **Postpartum Pain, Outpatient** | Acetaminophen | *The postpartum pain experience is variable (e.g., mode of delivery). Individualized, stepwise multimodal approaches to pain management should be utilized. Non-opioid analgesics are effective components in the management of postpartum pain, but the stepwise approach allows for the addition of low-dose, low-potency, and short-acting opioids when needed. Selection of analgesics should consider safety and implications on breastfeeding.* | Pharmacologic stepwise multimodal approach for postpartum pain management: ACOG Clinical Consensus No. 1. Obstet Gynecol 2021;138:507–17. |
| | NSAID: ibuprofen | | |
| **Restless Leg Syndrome** | Dipyridamole | *Routine serum iron assessments and, if indicated, iron supplementation is an essental component of RLS patient care (Note: In patients with RLS, iron supplementation indices are different than the general adult population.) Nonpharmacologic measures, such as the avoidance of exacerbating factors, should be considered prior to medication therapy. The use of non-ergot dopamine agonists (pramipexole, ropinirole, and rotigotine) are discouraged as standard care.* | Winkelman JW, Berkowski JA, DelRosso LM, et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2025;21(1):137-152. doi:10.5664/jcsm.11390 |
| | GABA analogs: gabapentin, gabapentin enacarbil, pregabalin | | Silber MH, Buchfuhrer MJ, Earley CJ, et al. The management of restless legs syndrome: an updated algorithm. *Mayo Clin Proc* . 2021;96(7):1921-1937. doi:10.1016/j.mayocp.2020.12.026 |
| **Rheumatoid Arthritis;<br>Psoriatic Arthritis;<br>Axial Spondyloarthritis**;<br>Inflammatory Arthritis Conditions** | Oral NSAIDs (selective and non-selective) | *Management of inflammatory arthritis conditions should focus on DMARDs which can reduce disease activity, slow progression, and decrease symptoms, including pain. Short-term use of glucocorticoids or NSAIDs can help to reduce symptoms before DMARDs achieve full effectiveness.*<br><br>***Includes radiographic axial spondyloarthritis and nonradiographic axial spondyloarthritis* | Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken). 2021;73(7):924-939. doi:10.1002/acr.24596 |
| | | | Ward MM, Deodhar A, Gensler LS, et al. 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. Arthritis Rheumatol. 2019;71(10):1599-1613. doi:10.1002/art.41042 |
| | | | Gossec L, Kerschbaumer A, Ferreira RJO, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update. Ann Rheum Dis. 2024;0(1):1-14. doi:10.1136/ard-2024-225531 |
| **Tendinopathy; Tendonitis; Bursitis** | Acetaminophen | *Resting the affected area, stretching, and ice are very effective strategies for most patients. May take up to six months for symptoms to improve. For acute bursitis, ice, elevation, and rest. For chronic bursitis, ice, elevation, appropriate padding, and compression wraps.* | Wilson J, Best T. Common overuse tendon problems: a review and recommendations for treatment. Am Fam Physician. 2005;72(5):811-818. |
| | Topical or oral NSAIDs (selective and non-selective) | | Khodaee M. Common superficial bursitis. Am Fam Physician. 2017;95(4):224-231. |
| **Trigeminal Neuralgia** | Anticonvulsants: carbamazepine, oxcarbazepine, lamotrigine | *Treatment of trigeminal neuralgia can be challenging. Initial therapy with carbamazepine may be considered followed by oxcarbazepine if non-responsive. Lamotrigine or GABA analogs may be considered if no response to other agents.* | Gronseth G, Cruccu G, Alksne J, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. Neurology. 2008;71(15):1183-1190. |
| | GABA analogs: gabapentin | | Chong MS, Bahra A, Zakrzewska JM. Guidelines for the management of trigeminal neuralgia. Cleve Clin J Med. 2023;90(6):355–362. doi: 10.3949/ccjm.90a.22052. |

**Abbreviation Key**: DMARD=disease-modifying antirheumatic drug; FDA=U.S. Food and Drug Administration; GABA=gamma-aminobutyric acid; NSAID=non-steroidal anti-inflammatory drug; SNRI=serotonin and norepinephrine reuptake inhibitor; TCA: tricyclic antidepressant

**Methodology**: The list of indications included in this table was adapted from topics addressed in the CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. The intended audience for this table are general practitioners who may encounter patients with pain conditions in their practice. Non-opioid examples and clinical considerations were based on review of this guideline and its cited references; FDA labeling; the Micromedex drug information database; and additional clinical guidelines and resources.

***Medically accepted indications** include FDA-approved, labeled indications and off-label uses supported in a recognized compendium. Micromedex DrugDex® is accepted as one of these compendia.

**The following general references were reviewed for all indications (indication-specific references are available in the designated row):**


Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. MMWR Recomm Rep. 2022;71(3):1-95. doi: 10.15585/mmwr.rr7103a1

U.S Food and Drug Administration. FDA Online Label Repository. Available at http://labels.fda.gov

U.S Food and Drug Administration. Drug@FDA. FDA Approved Drug Products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm

Micromedex™ (electronic version). Merative, Ann Arbor, Michigan, USA. Available at https://www.micromedexsolutions.com/

UpToDate® (online database). Wolters Kluwer, Waltham, Massachusetts, USA. Available at: https://www.uptodate.com/