



STEP THERAPY POLICY

POLICY: Nonsteroidal Anti-Inflammatory Drugs Step Therapy Policy

REVIEW DATE: 01/14/2026; selected revision 02/11/2026 and 04/01/2026

Note: This list is not all-inclusive.

NSAID	Product	Manufacturer
Diclofenac	diclofenac potassium tablets	Generic only
	diclofenac sodium delayed-release tablets	Generic only
	diclofenac sodium extended-release tablets	Generic only
	Lofena™ (diclofenac potassium 25 mg tablets)	Carwin, generic
	Zorvolex® (diclofenac submicronized capsules)	Iroko, AG (35 mg only)
	Zipsor® (diclofenac potassium 25 mg capsules)	Assertio, generic
	Cambia® (diclofenac powder for oral solution)	Assertio, generic
	Arthrotec® (diclofenac and misoprostol tablets)	Pfizer, generic
	diclofenac 1.5% topical solution	Generic only
	Flector® (diclofenac epolamine 1.3% topical patch)	Institut Biochimique, generic
	Licart™ (diclofenac epolamine 1.3% topical system)	Institut Biochimique
	Pennsaid® (diclofenac sodium 2% topical solution)	Horizon, generic
diclofenac sodium 1% topical gel [OTC Voltaren topical gel available]	Generic only	
Etodolac	Lodine® (etodolac tablets)	Sallus, generic
	etodolac capsules	Generic only
	etodolac extended-release tablets	Generic only
Fenoprofen	Nalfon® (fenoprofen calcium capsules and tablets)	Xspire, generic (tablets only)
	Fenoprofen capsules (brand)	Various
	Fenopron™ (fenoprofen 300 mg capsules)	Galt
Flurbiprofen	flurbiprofen tablets	Generic only
Ibuprofen	ibuprofen capsules, tablets, and oral suspension [OTC capsules, tablets, chewable tablets, oral suspension available]	Generic only
	Duexis® (ibuprofen and famotidine tablets)	Horizon, generic
Indomethacin	indomethacin capsules and extended-release capsules	Generic only
	Indocin® suspension (indomethacin oral suspension)	Iroko, generic
	Tivorbex® (indomethacin submicronized 20 mg capsules) <small>[obsolete 2/14/2024]</small>	Iroko, generic
Ketoprofen	ketoprofen capsules and extended-release capsules	Generic only
	Orudis® (ketoprofen capsules)	Allegis
Ketorolac	ketorolac tablets	Generic only
	Sprix® (ketorolac nasal spray)	Egalet, generic
Meclofenamate	meclofenamate capsules	Generic only
Mefenamic acid	mefenamic acid capsules	Generic only
Meloxicam	meloxicam tablets and capsules	Generic only
	Vivlodex™ (meloxicam submicronized capsules)	Iroko, generic
	meloxicam oral suspension	Generic only
	Zybic™ (meloxicam oral suspension)	Redmont
Nabumetone	Relafen® DS (nabumetone 1000 mg tablets)	Carwin
Naproxen	Naprosyn® (naproxen tablets and oral suspension)	Canton, generic

	[OTC tablets available]	
	EC-Naprosyn® (naproxen enteric coated tablets)	Canton, generic
	Anaprox® DS (naproxen 550 mg tablets)	Canton, generic
	Naprelan® CR (naproxen controlled-release tablets)	Almatica, generic
	Vimovo® (naproxen and esomeprazole delayed-release tablets)	Horizon, generic
Oxaprozin	Daypro® (oxaprozin tablets/caplets)	Pfizer, generic
	Coxanto® (oxaprozin capsules)	Solubiomix
Piroxicam	Feldene® (piroxicam capsules)	Pfizer, generic
Sulindac	sulindac tablets	Generic only
Tolmetin	tolmetin capsules	Generic only

AG – Authorized generic; NSAID – Nonsteroidal anti-inflammatory drug; OTC – Over-the-counter.

INSTRUCTIONS FOR USE

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Cigna National Formulary Coverage:

OVERVIEW

Nonsteroidal anti-inflammatory drugs (NSAIDs) are indicated primarily for the treatment of acute and chronic conditions that require an agent with analgesic and anti-inflammatory activity, although other uses exist.¹ For example, Cambia® (diclofenac potassium oral solution) is the only NSAID indicated for the acute treatment of migraine attacks with or without aura in adults ≥ 18 years of age²; however, other NSAIDs are also supported for this use in clinical practice guidelines.³

Overall, it appears that NSAID products have similar clinical efficacy when given at equipotent doses for the management of acute pain and other pain-related conditions; however, individual responses to NSAIDs may vary among patients for reasons that are not well understood. No product can be distinguished from another

on a consistent basis. All of the products have Boxed Warnings outlining cardiovascular (CV) and gastrointestinal (GI) risks.¹

Guidelines and Recommendations

The American College of Rheumatology (ACR)/Arthritis Foundation hand, hip, and knee osteoarthritis (OA) guidelines (2019) strongly recommend topical NSAIDs for knee OA and conditionally recommend topical NSAIDs for hand OA.⁴ Topical NSAIDs are not expected to be efficacious in hip OA due to the depth of the affected joint. Oral NSAIDs are strongly recommended for patients with hand, hip, and/or knee OA and are recommended over all other oral therapies. These agents are the mainstay of pharmacological management of OA. Safe use of NSAIDs is recommended, including utilization of the lowest possible doses for the shortest period of time. The relative merits of different oral NSAIDs were considered outside the scope of the guideline review.

The European League Against Rheumatism (EULAR) hand OA guidelines (2018) state that optimal management of hand OA generally requires a multidisciplinary approach, including non-pharmacological therapies and pharmacological therapies.⁵ The guidelines specifically recommend topical treatments as preferred over oral therapies because of safety reasons. Topical NSAIDs are the first pharmacological topical treatment of choice for hand OA. The guidelines cite pooled safety data comparing topical diclofenac gel with placebo, which showed similar low rates of adverse events (AEs) in subgroups of low-risk versus high-risk patients (≥ 65 years of age with comorbid hypertension, type 2 diabetes or cerebrovascular and/or CV disease). The guidelines additionally note that when a large number of joints are affected, oral pharmacological treatment may be preferred.

OA Research Society International (OARSI) guidelines for non-surgical management of knee, hip, and polyarticular OA (2019) comment on oral and topical NSAID use in a variety of settings.⁶ For knee OA, topical NSAIDs are strongly recommended (Level 1A) for patients without comorbidities, as well as for patients with GI or CV comorbidities. For patients with GI comorbidities, selective cyclooxygenase-2 (COX-2) inhibitors and nonselective oral NSAIDs, in combination with a proton pump inhibitor (PPI), were conditionally recommended due to their benefits on pain and functional outcomes. Topical and oral NSAIDs are both conditionally recommended in the setting of widespread pain; it is noted that for topical NSAIDs, the number of joints being treated should be monitored due to potential risk of exceeding recommended doses. Oral NSAIDs, but not topical NSAIDs, are conditionally recommended in the setting of hip OA.

Beers Criteria

In 2023, the American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults.⁷ The Beers Criteria acknowledge that many nonselective NSAIDs increase the risk of GI bleeding or peptic ulcer disease in high-risk groups, which include patients > 75 years of age or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. It is noted that use of a PPI or misoprostol reduces but does not eliminate the risks. Indomethacin

and ketorolac (including the parenteral formulation) should be avoided due to the increased risk of GI bleeding/peptic ulcer disease and acute kidney injury in older adults. Indomethacin is more likely to cause central nervous system AEs and appears to have the most AEs among the NSAIDs. NSAIDs and cyclooxygenase (COX)-2 inhibitors should be avoided in patients with symptomatic heart failure due to the potential to promote fluid retention and/or exacerbate heart failure. In patients with kidney or urinary tract disease (creatinine clearance < 30 mL/min), it is noted that NSAIDs (non-COX and COX selective, oral and parenteral, nonacetylate salicylates) may increase the risk of acute kidney injury and further decline in renal function. It is recommended to avoid these agents.

POLICY STATEMENT

This program has been developed to encourage the use of two Step 1a Products prior to the use of a Step 2a Product. Of note, naproxen/esomeprazole delayed-release tablets (Vimovo, generic) and ibuprofen/famotidine tablets (Duexis, generic) are not included in Step 2a. A trial of one prescription naproxen product (Step 1b) and one prescription proton pump inhibitor (PPI) [Step 1b] is required prior to the use of naproxen/esomeprazole delayed-release tablets (Vimovo, generic) [Step 2b]. A trial of one prescription oral ibuprofen product (Step 1c) and one prescription oral histamine₂-receptor antagonist (H₂RA) [Step 1c] is required prior to the use of ibuprofen/famotidine tablets (Duexis, generic) [Step 2c]. If the Step Therapy rule is not met for a Step 2 Product (a, b, or c) at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Step 1a/2a

Step 1a NSAIDs:

- | | | |
|--------------------------------------|--|---------------------|
| • diclofenac potassium 50 mg tablets | • diclofenac sodium topical solution 1.5%* | • ketorolac tablets |
| • diclofenac sodium (IR and ER) | • etodolac (IR and ER) | • meclofenamate |
| • diclofenac sodium and misoprostol | • flurbiprofen | • mefenamic acid |
| • diclofenac sodium 1% topical gel* | • ibuprofen | • meloxicam tablets |
| | • indomethacin (IR and ER) | • nabumetone |
| | • ketoprofen IR 50 mg and 75 mg | • naproxen** |
| | | • oxaprozin |
| | | • piroxicam |
| | | • sulindac |
| | | • tolmetin 200 mg |

Step 2a NSAIDs:

- | | | |
|--|--|---|
| • Anaprox DS | • Daypro | • fenoprofen 600 mg tablets |
| • Arthrotec | • diclofenac sodium 2% topical solution* | • Flector patch, diclofenac epolamine 1.3% patch* |
| • Cambia, diclofenac potassium powder packet | • Feldene | |
| • Coxanto | • Fenopron | |
| | • Fenoprofen (brand) | |

- Indocin, indomethacin oral suspension
- ketoprofen ER 200 mg
- ketoprofen IR 25 mg
- Licart*
- Lodine
- Lofena, diclofenac potassium 25 mg tablets
- meloxicam capsules
- meloxicam oral suspension
- Nalfon
- Naprelan and generics
- Naprosyn (brand)
- EC-Naprosyn , naproxen DR 500 mg tablets
- naproxen oral suspension
- Orudis
- Pennsaid 2%*
- Relafen DS
- Sprix, ketorolac nasal spray
- Tivorbex, indomethacin 20 mg capsule
- tolmetin 400 mg, 600 mg
- Vivlodex
- Zipsor, diclofenac potassium 25 mg capsules
- Zorvolex, diclofenac 35 mg capsule
- Zybic suspension

IR – Immediate-release; ER – Extended-release; DR – Delayed-release.

* Denotes topical product

** Some generic naproxen products are Step 2a

Step 1b/2b

Step 1b (brand or generic):

- Prescription naproxen sodium
- Prescription naproxen

AND

- Prescription dexlansoprazole
- Prescription esomeprazole magnesium
- Prescription esomeprazole strontium
- Prescription lansoprazole
- Prescription omeprazole
- Prescription omeprazole magnesium
- Prescription omeprazole/sodium bicarbonate
- Prescription pantoprazole (oral)
- Prescription rabeprazole

Step 2b NSAID:

- Vimovo
- naproxen/esomeprazole delayed-release tablets

Step 1c/2c

Step 1c (brand or generic):

- Prescription ibuprofen (oral)

AND

- Prescription cimetidine (oral)
- Prescription famotidine (oral)
- Prescription nizatidine (oral)
- Prescription ranitidine (oral)

Step 2c NSAID:

- Duexis

- ibuprofen/famotidine tablets

Nonsteroidal Anti-Inflammatory Drugs Step Therapy Policy product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.

CRITERIA

Step 2a NSAIDs

- 1.** If the patient has tried two different Step 1a prescription-strength NSAIDs for the current condition, approve a Step 2a NSAID.

Note: Celecoxib is accepted as a generic NSAID. Also, over-the-counter (OTC) NSAIDs count as alternatives if the patient used prescription-strength doses.

- 2.** If the patient has tried ibuprofen oral suspension, approve naproxen oral suspension, meloxicam oral suspension, Indocin (indomethacin) oral suspension, or Zybic (meloxicam) oral suspension.

Note: OTC ibuprofen oral suspension would count as an alternative.

- 3.** If the patient has tried generic diclofenac sodium topical solution 1.5% OR diclofenac sodium 1% topical gel and the patient has difficulty swallowing or cannot swallow tablets or liquid dosage forms (solution/suspension), approve ketorolac nasal spray (Sprix, authorized generic), Pennsaid 2%, diclofenac sodium 2% topical solution, Flector Patch, diclofenac epolamine 1.3% patch, or Licart topical system.

- 4.** If the patient has tried generic diclofenac sodium topical solution 1.5% OR diclofenac sodium 1% topical gel and the patient has a chronic musculoskeletal pain condition (e.g., osteoarthritis) and is at risk of NSAID-associated toxicity, approve Pennsaid 2%, or diclofenac sodium 2% topical solution.

Note: Examples of risk factors of NSAID-associated toxicity include patients with a previous gastrointestinal bleed, history of peptic ulcer disease, impaired renal function, cardiovascular disease, hypertension, heart failure, elderly patients with impaired hepatic function, or taking concomitant anticoagulants.

- 5.** If the patient has tried generic diclofenac sodium topical solution 1.5% OR diclofenac sodium 1% topical gel and the patient has hand or knee osteoarthritis, approve Pennsaid 2%, or diclofenac sodium 2% topical solution.

Step 2b NSAID (Vimovo, generic)

- 1.** If the patient has tried one prescription proton pump inhibitor (PPI) [e.g., omeprazole, lansoprazole, pantoprazole] and one prescription naproxen product

(brand or generic), approve naproxen/esomeprazole delayed-release tablets (Vimovo, generic).

Note: Do not approve naproxen/esomeprazole delayed-release tablets (Vimovo, generic) if the patient has only tried over-the-counter (OTC) naproxen, NSAIDs other than naproxen, a COX-2 inhibitor (celecoxib), or OTC PPIs.

Note: Separate trials of a prescription PPI and a prescription naproxen product are required; a previous trial of Vimovo or generic naproxen/esomeprazole does not count.

Step 2c NSAID (Duexis, generic)

1. If the patient has tried one prescription histamine₂-receptor antagonist (H₂RA) [e.g., famotidine, ranitidine, nizatidine] and one prescription ibuprofen product (brand or generic), approve ibuprofen/famotidine tablets (Duexis, generic).

Note: Do not approve ibuprofen/famotidine tablets (Duexis, generic) if the patient has only tried over-the-counter (OTC) ibuprofen, NSAIDs other than ibuprofen, a COX-2 inhibitor (celecoxib), or OTC H₂RAs.

Note: Separate trials of a prescription H₂RA and a prescription ibuprofen product are required; a previous trial of Duexis or generic ibuprofen/famotidine does not count.

REFERENCES

1. Facts and Comparisons Online®. Wolters Kluwer Health, Inc.; Last updated May 28, 2025. Available at: <http://fco.factsandcomparisons.com/action/home>. Accessed on December 18, 2025. Search term: Nonsteroidal anti-inflammatory agents.
2. Cambia® oral solution [prescribing information]. Lake Forest, IL: Assertio; December 2024.
3. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019; 59:1-18.
4. Kolasinki 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 Rheumatol*. 2020; 72(2):220–233.
5. Kloppenburg M, Kroon F, Blanco FJ, et al. 2018 update of the EULAR recommendations for the management of hand osteoarthritis. *Ann Rheum Dis*. 2019; 78:16-24.
6. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage*. 2019; 27(11):1578-1589.
7. The American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023;71(7):2052-2081.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	Coxanto: Coxanto capsule was added to the Policy to Step 2a.	01/17/2024
Selected Revision	Indomethacin suspension: indomethacin oral suspension (generic Indocin suspension) was added to the Policy to Step 2a.	02/14/2024
Annual Revision	Step 1a NSAIDs: Cataflam (brand name) is obsolete and was removed throughout the Policy.	01/22/2025

	Step 2a NSAIDs: Fenortho, Mobic, Voltaren Gel, Voltaren XR, Qmiiz ODT, and Relafen (all brand names) are obsolete and were removed throughout the Policy.	
Selected Revision	Fenopron (fenoprofen calcium capsules) was added to the Policy to Step 2a. Diclofenac potassium 25 mg capsules and naproxen DR 500 mg tablets were moved from Step 1a to Step 2a. Diclofenac sodium 1% topical gel was moved from Step 2a to Step 1a. The previous requirement for trial of "generic diclofenac sodium topical solution 1.5%" was updated to include "or diclofenac sodium 1% topical gel" throughout the Policy.	03/05/2025
Annual Revision	No criteria changes.	01/14/2026
Selected Revision	Orudis was added to Step 2a.	02/11/2026
Selected Revision	Zybic was added to Step 2a. The Step 2a exception criteria for a patient who has tried ibuprofen oral suspension was updated to approve Zybic.	04/01/2026

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