STEP THERAPY POLICY

POLICY: Nonsteroidal Anti-Inflammatory Drug Step Therapy Policy

REVIEW DATE: 04/13/2022; selected revision 05/04/2022, 06/29/2022, 08/10/2022, and 01/11/2023

NSAID	Product	Manufacturer
Diclofenac	Cataflam® tablets, generic	Novartis, generic
	diclofenac sodium delayed-release tablets (generic only)	Generic only
	Lofena™ tablets, generic	Carwin, generic
	Volatren® XR extended-release tablets (obsolete 03/01/2021), generic	Novartis, generic
	Zorvolex® capsules, authorized generic for 35 mg strength	Iroko Pharmaceuticals
	Zipsor® capsules	Assertio Therapeutics
	Cambia® oral solution, generic	Assertio Therapeutics, generic
	Arthrotec® (diclofenac and misoprostol tablets), generic	Pfizer, generic
	diclofenac 1.5% solution (generic only)	Generic only
	Flector® (diclofenac epolamine 1.3% topical patch), authorized generic	Institut Biochimique SA, generic
	Licart™ (diclofenac epolamine 1.3% topical system)	Institut Biochimique SA
	Pennsaid® (diclofenac sodium 2% topical solution, generic)	Horizon Pharma, generic
	Voltaren® Gel (diclofenac sodium 1% topical gel), generic	Endo Pharmaceuticals, generic
Etodolac	Lodine® tablets, generic	Sallus, generic
	etodolac capsules (generic only)	Generic only
	etodolac extended-release tablets (generic only)	Generic only
Fenoprofen	Nalfon® capsules and tablets (generic to tablets only)	Xspire, generic
	Fenortho® capsules	Sterling Knight Pharma
	Fenoprofen capsules (brand)	Various
Flurbiprofen	flurbiprofen tablets (generic only)	Generic only
Ibuprofen	ibuprofen capsules, tablets, and oral suspension	Generic only
	Duexis® (ibuprofen and famotidine tablets, generic)	Horizon Pharma, generic
Indomethacin	indomethacin capsules and extended-release capsules (generic only)	Generic only
	Indocin® oral suspension	Iroko Pharmaceuticals
	Tivorbex® capsules, authorized generic	Iroko Pharmaceuticals
Ketoprofen	ketoprofen capsules and extended-release capsules (generic only)	Generic only
Ketorolac	ketorolac tablets (generic only)	Generic only
	Sprix® (ketorolac nasal spray, authorized generic)	Egalet
Meclofenamate	meclofenamate capsules (generic only)	Generic only
Mefenamic acid	mefenamic acid capsules (generic only)	Generic only
Meloxicam	Mobic® tablets, generic	Boehringer Ingelheim, generic
	Qmiiz™ ODT (obsolete 04/01/2020)	TerSera Therapeutics
	Vivlodex™ capsules, generic	Iroko Pharmaceuticals, generic
	meloxicam oral suspension (generic)	Generic only
Nabumetone	Relafen® tablets, generic	Blucrest, generic
	Relafen® DS tablets	Carwin Associates
Naproxen	Naprosyn® tablets and oral suspension, generic	Canton Laboratories, generic
	EC-Naprosyn® delayed-release tablets, generic	Canton Laboratories, generic
	Anaprox DS® controlled-release tablets, generic	Canton Laboratories, generic
	Naprelan® controlled-release tablets, generic	Almatica Pharma, generic
	Vimovo® (naproxen and esomeprazole delayed-release tablets, generic)	Horizon Pharma, generic
Oxaprozin	Daypro® tablets, generic	Pfizer, generic
Piroxicam	Feldene® capsules, generic	Pfizer, generic
Sulindac	sulindac tablets (generic only)	Generic only
Tolmetin	tolmetin capsules and tablets (generic only)	Generic only

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 age[2]; however, other NSAIDs are also supported 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 one product can be distinguished from another on a consistent basis. All of the products have Boxed Warnings outlining cardiovascular (CV) and gastrointestinal (GI) risks.

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 in hand, hip, and knee OA and are recommended over all other oral therapies. Unlike the prior 2012 ACR guidelines[5], the 2019 guidelines do not specifically comment on agent selection in at-risk populations (e.g., ≥ 75 years of age, history of upper GI ulcers, concomitant aspirin use, chronic kidney disease); a general statement is provided that oral NSAID doses should be as low as possible and used for the shortest possible duration. The relative merits of different oral NSAIDs were considered outside the scope of the guideline review.

The European League Against Rheumatism 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 systemic 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 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, systemic pharmacological treatment may be preferred.

OA Research Society International 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 or frailty. 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 2019, the American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults.[7] The Beers Criteria acknowledge that many non-selective NSAIDs increase the risk of GI bleeding or peptic ulcer disease in high-risk groups, which include patients > 75 years of age or taking parenteral corticosteroids, anticoagulants, or antiplatelet agents. It is noted that use of a proton pump inhibitor (PPI) or misoprostol reduces but does not eliminate the risks. The Beers Criteria also note that in patients with a history of gastric or duodenal ulcers, non-cyclooxygenase-2 selective NSAIDs should be avoided because they may exacerbate existing ulcers or cause new or additional ulcers.

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 histamine$_2$ receptor antagonist (H_2RA) [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.

Automation: For single-entity NSAIDs (Step 2a), a patient with a history of two Step 1a Products within the 130-day look-back period is excluded from Step Therapy. (Note: naproxen/esomeprazole delayed-release tablets [Vimovo, generic] and ibuprofen/famotidine tablets [Duexis, generic] are not included in Step 2a.) For naproxen/esomeprazole delayed-release tablets (Vimovo, generic) [Step 2b], a patient with a history of one prescription PPI and one naproxen product within the 130-day look-back period is excluded from Step Therapy. For ibuprofen/famotidine tablets (Duexis, generic) [Step 2c], a patient with a history of one prescription H_2RA and one prescription oral ibuprofen product within the 130-day look-back period is excluded from Step Therapy.

Step 1a/2a

Step 1a NSAIDs:

- Cataflam
- diclofenac potassium 50 mg
- diclofenac potassium 25 mg capsules
- diclofenac sodium (IR and ER)
- diclofenac sodium and misoprostol
- diclofenac sodium topical solution 1.5%*
- etodolac (IR and ER)
- flurbiprofen
- ibuprofen
- indomethacin (IR and ER)
- ketoprofen IR 50 mg and 75 mg
- ketorolac (tablets)
- meclofenamate
- mefenamic acid
- meloxicam tablets
- nabumetone
- naproxen**
- oxaprozin
- piroxicam
- sulindac
- tolmetin 200 mg

Step 2a NSAIDs:

- Anaprox DS
- Arthrotec
- Cambia, diclofenac potassium powder packet
- Daypro
- diclofenac potassium 25 mg tablets
- diclofenac sodium 1% topical gel*
- diclofenac sodium 2% topical solution*
- Feldene
- Fenoprofen (brand), fenoprofen 600 mg
- Fenortho
- Flector patch, diclofenac epolamine 1.3% patch*
- Indocin
- ketoprofen ER 200 mg
- ketoprofen IR 25 mg
- Licart*
- Lodine
- Lofena
- meloxicam capsules
- meloxicam suspension
- Mobic
- Nalfon
- Naprelan and generics
- Naprosyn, EC-Naprosyn, and generic suspension
- Pennsaid 2%*
- Qmiiz
- Relafen
- Relafen DS
- Sprix, ketorolac nasal spray
- Tivorbex, indomethacin 20 mg capsule
- tolmetin 400 mg, 600 mg
- Vivlodex
- Voltaren Gel 1%*
- Voltaren XR
- Zipsor
- Zorvolex, diclofenac 35 mg capsule

IR – Immediate-release; ER – Extended-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

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 suspension, approve naproxen suspension, meloxicam suspension, or Indocin suspension.
Note: OTC ibuprofen suspension would count as an alternative.

3. If the patient has tried generic diclofenac sodium topical solution 1.5% 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, Licart topical system, diclofenac sodium 1% topical gel, or Voltaren Gel.

4. If the patient has tried generic diclofenac sodium topical solution 1.5% and the patient has a chronic musculoskeletal pain condition (e.g., osteoarthritis) and is at risk of NSAID-associated toxicity, approve Pennsaid 2%, diclofenac sodium 2% topical solution, diclofenac sodium 1% topical gel, or Voltaren Gel.
Note: Examples of risk factors of NSAID-associated toxicity include patients with a previous gastrointestinal bleed, 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% and the patient has hand or knee osteoarthritis, approve Pennsaid 2%, diclofenac sodium 2% topical solution, diclofenac sodium 1% topical gel, or Voltaren Gel.

6. No other exceptions are recommended.

Vimovo and generic naproxen/esomeprazole delayed-release tablets

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.

2. No other exceptions are recommended.

Duexis and generic ibuprofen/famotidine tablets

1. If the patient has tried one prescription histamine$_2$ receptor antagonist (H_2RA) [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 H_2RAs.
Note: Separate trials of a prescription H_2RA and a prescription ibuprofen product are required; a previous trial of Duexis or generic ibuprofen/famotidine does not count.

No other exceptions are recommended.

REFERENCES

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