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Nonsteroidal Anti-inflammatory Drugs

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INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see “Coding Information” below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following nonsteroidal anti-inflammatory products for employer group plans:

- **Coxanto** 300 mg capsule
- **diclofenac potassium** 25 mg capsule (Zipsor generic)
- **diclofenac potassium** 25 mg tablet (Lofena generic)
- **Fenoprofen** 200 mg or 400 mg capsule
- **Fenortho®** (fenoprofen 200 mg capsule)
- **Indocin®** (indomethacin) 25 mg/ 5 mL oral suspension
- **Indocin®** (indomethacin) 50 mg suppository
- **indomethacin** 20 mg capsule
- **ketoprofen** 25 mg capsule
- **Kiprofen™** (ketoprofen) 25 mg capsule
- **Lofena™** (diclofenac potassium) 25 mg tablet
- **mefenamic acid** 250 mg capsule
- **meloxicam** 5 mg and 10 mg capsule
- **meloxicam** 7.5 mg/5 mL oral suspension
- **Nalfon** (fenoprofen calcium) 200 mg and 400 mg capsules
- **Naprelan®** (naproxen) 375 mg, 500 mg, and 750 mg extended release tablet
- **Naproxen CR** (naproxen) 375 mg and 500 mg controlled release tablet
- **Naproxen ER** (naproxen) 375 mg, 500 mg, and 750 mg extended release tablet
- **Naprosyn** (naproxen) 125 mg /5 mL oral suspension
- **naproxen** 125 mg /5 mL oral suspension
- **oxaprozen** 300 mg capsule
- **Relafen** (nabumetone) 500 mg and 750 mg tablet
- **Relafen DS** (nabumetone) 1000 mg tablet
- **Sprix®** (ketorolac) nasal solution; 15.75 mg / spray
- **Tivorbex®** (indomethacin) 20 mg and 40 mg capsule
- **Tolectin®** (tolmetin) 600 mg tablet
- **Vivlodex™** (meloxicam) 5 mg and 10 mg capsule
- **Zipsor®** (diclofenac potassium) 25 mg capsule
- **Zorvolex®** (diclofenac) 18 mg and 35 mg capsule

Medical Necessity Criteria

The product(s) in the table below are considered medically necessary when the following are met:

Employer Plans:

Product	Criteria
Coxanto (oxaprozin) 300 mg capsule	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to FIVE prescription-strength nonsteroidal anti-inflammatory drugs
diclofenac potassium 25 mg capsule or tablet	There is documentation of the following: A. Individual has had an inadequate response, contraindication, or is intolerant to FIVE prescription-strength oral nonsteroidal anti-inflammatory drugs (excluding diclofenac) Examples include: etodolac, flurbiprofen, ibuprofen, ketoprofen, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, indomethacin

Product	Criteria
fenoprofen 200 mg capsule	There is documentation of BOTH the following (A <u>and</u> B): A. Individual has intolerance to fenoprofen 600 mg tablets B. Individual has had an inadequate response or contraindication to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding fenoprofen)
Fenorthis (fenoprofen 200 mg capsule)	There is documentation of BOTH the following (A <u>and</u> B): A. Individual has intolerance to fenoprofen 600 mg tablets B. Individual has had an inadequate response or contraindication to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding fenoprofen)
fenoprofen 400 mg capsule	There is documentation of BOTH the following (A <u>and</u> B): A. Individual has intolerance to fenoprofen 600 mg tablets B. Individual has had an inadequate response or contraindication to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding fenoprofen)
Indocin (indomethacin) 25 mg/ 5 mL oral suspension	There is documentation of BOTH of the following (A <u>and</u> B): A. Individual has an inability to swallow indomethacin 25 mg or 50 mg capsules B. Inadequate response, contraindication or intolerance ibuprofen 100 mg / 5 mL oral suspension
Indocin (indomethacin) 50 mg suppository	There is documentation of BOTH the following (A <u>and</u> B): A. Individual has an inability to use indomethacin 25 mg or 50 mg capsules B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding indomethacin)
indomethacin 20 mg capsule	There is documentation of BOTH the following (A <u>and</u> B): A. Individual is intolerant to indomethacin 25 mg or 50 mg capsules B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding indomethacin)
ketoprofen 25 mg capsule	There is documentation of BOTH the following (A <u>and</u> B): A. Individual is intolerant to ketoprofen 50 mg capsules B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding ketoprofen)
Kiprofen (ketoprofen) 25 mg capsule	Failure or intolerance to FIVE unique prescription-strength oral nonsteroidal anti-inflammatory drugs Examples include: diclofenac, etodolac, flurbiprofen, ibuprofen, ketoprofen, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, indomethacin
Lofena (diclofenac potassium) 25 mg tablet	There is documentation of the following: A. Individual has had an inadequate response, contraindication, or is intolerant to FIVE prescription-strength oral nonsteroidal anti-inflammatory drugs (excluding diclofenac)

Product	Criteria
	Examples include: etodolac, flurbiprofen, ibuprofen, ketoprofen, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, indomethacin
mefenamic acid 250 mg capsule	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to FIVE prescription-strength nonsteroidal anti-inflammatory drugs (excluding mefenamic) Examples include: diclofenac, etodolac, flurbiprofen, ibuprofen, ketoprofen, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, indomethacin
meloxicam 5 mg and 10 mg capsule	There is documentation of BOTH the following (A <u>and</u> B): A. Individual is intolerant to meloxicam 7.5 mg or 15 mg tablets B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription-strength nonsteroidal anti-inflammatory drugs (excluding meloxicam)
meloxicam 7.5 mg/5 mL oral suspension	There is documentation of BOTH of the following (A <u>and</u> B): A. Individual has an inability to swallow meloxicam 7.5 mg or 15 mg tablets B. Inadequate response, contraindication, or intolerance to ibuprofen 100 mg / 5 mL oral suspension
Nalfon (fenoprofen calcium) 200 mg and 400 mg capsules	There is documentation of BOTH the following (A <u>and</u> B): A. Individual is intolerant to fenoprofen 600 mg tablets B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription-strength nonsteroidal anti-inflammatory drugs (excluding fenoprofen)
Naprelan (naproxen) 375 mg, 500 mg, and 750 mg extended release tablet	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to BOTH the following (A <u>and</u> B): A. naproxen 250 mg, 375 mg, or 500 mg immediate release tablets B. FOUR prescription-strength nonsteroidal anti-inflammatory drugs (excluding naproxen)
naproxen CR (naproxen) 375 mg and 500 mg controlled release tablet	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to BOTH the following (A <u>and</u> B): A. naproxen 250 mg, 375 mg, or 500 mg immediate release tablets B. FOUR prescription-strength nonsteroidal anti-inflammatory drugs (excluding naproxen)
naproxen ER (naproxen) 375 mg, 500 mg, and 750 mg extended release tablet	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to BOTH the following (A <u>and</u> B): A. naproxen 250 mg, 375 mg, or 500 mg immediate release tablets B. FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding naproxen)
Naprosyn (naproxen) 125 mg /5 mL oral suspension	There is documentation of BOTH of the following (A <u>and</u> B): A. Individual has an inability to swallow naproxen 250 mg, 375 mg, or 500 mg immediate release tablets B. Inadequate response, contraindication, or intolerance to ibuprofen 100 mg / 5 mL oral suspension
naproxen 125 mg /5 mL oral suspension	There is documentation of BOTH of the following (A <u>and</u> B): A. Individual has an inability to swallow naproxen 250 mg, 375 mg, or 500 mg immediate release tablets

Product	Criteria
	B. Inadequate response, contraindication, or intolerance to ibuprofen 100 mg / 5 mL oral suspension
oxaprozin 300 mg capsule	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to FIVE prescription-strength nonsteroidal anti-inflammatory drugs
Relafen (nabumetone) 500 mg and 750 mg tablet	There is documentation of ALL of the following (A, B, <u>and</u> C): A. Individual has had an inadequate response to nabumetone 500 mg tablets B. Individual is intolerant to nabumetone 750 mg tablets C. Individual has had an inadequate response, contraindication, or is intolerant to THREE prescription strength nonsteroidal anti-inflammatory drugs (excluding nabumetone)
Relafen DS (nabumetone) 1000 mg tablet	There is documentation of ALL of the following (A, B, <u>and</u> C): A. Individual has had an inadequate response to nabumetone 500 mg tablets B. Individual is intolerant to nabumetone 750 mg tablets C. Individual has had an inadequate response, contraindication, or is intolerant to THREE prescription-strength nonsteroidal anti-inflammatory drugs (excluding nabumetone)
Sprix (ketorolac) nasal solution; 15.75 mg / spray	There is documentation of BOTH of the following (A <u>and</u> B): A. Individual has had an intolerance or inability to swallow ketorolac 10 mg tablets B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding ketorolac)
Tivorbex (indomethacin) 20 mg and 40 mg capsule	There is documentation of BOTH of the following (A <u>and</u> B): A. Individual has had an inadequate response or intolerance to indomethacin 25 mg capsules or 50 mg capsules B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription-strength nonsteroidal anti-inflammatory drugs (excluding indomethacin)
Tolectin (tolmetin) 600 mg tablet	Trial of FIVE prescription-strength oral nonsteroidal anti-inflammatory drugs Examples include: diclofenac, etodolac, flurbiprofen, ibuprofen, ketoprofen, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, indomethacin
Vivlodex (meloxicam) 5 mg and 10 mg capsule	There is documentation of BOTH the following (A <u>and</u> B): A. Individual is intolerant to meloxicam 7.5 mg or 15 mg tablets B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription-strength nonsteroidal anti-inflammatory drugs (excluding meloxicam)
Zipsor (diclofenac potassium) 25 mg capsule	There is documentation of ALL of the following (A, B, <u>and</u> C): A. Individual has had an intolerance to diclofenac sodium 25 mg tablets B. Individual has had an intolerance to diclofenac sodium or potassium 50 mg tablets

Product	Criteria
	C. Individual has had an inadequate response, contraindication, or is intolerant to THREE prescription strength nonsteroidal anti-inflammatory drugs (excluding diclofenac)
Zorvolex (diclofenac) 18 mg and 35 mg capsule	There is documentation of BOTH the following (A <u>and</u> B): A. Individual is intolerant to diclofenac 50 mg tablets or diclofenac 25 mg delayed-release tablets B. Individual has had an inadequate response, contraindication, or is intolerant to FOUR prescription strength nonsteroidal anti-inflammatory drugs (excluding diclofenac)

Individual and Family Plans:

Product	Criteria
Coxanto (oxaprozin 300 mg capsule)	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to FIVE prescription-strength nonsteroidal anti-inflammatory drugs
oxaprozin 300 mg capsule	There is documentation the individual has had an inadequate response, contraindication, or is intolerant to FIVE prescription-strength nonsteroidal anti-inflammatory drugs
Tolectin (tolmetin) 600 mg tablet	Trial of FIVE prescription-strength oral nonsteroidal anti-inflammatory drugs Examples include: diclofenac, etodolac, flurbiprofen, ibuprofen, ketoprofen, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, indomethacin

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Nonsteroidal anti-inflammatory drugs are considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months

Reauthorization approval duration: up to 12 months

Background

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 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.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 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 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.

References

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4. 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 Rheumatol.* 2020; 72(2):220–233.
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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.

Revision Details

Summary of Changes	Review Date	Effective Date
Removed Vimovo, naproxen/esomeprazole, Duexis, and ibuprofen/famotidine from policy.	5/59/2025	7/15/2025

The policy effective date is in force until updated or retired

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