



## Oral NSAID (Nonsteroidal Anti-Inflammatory Drugs) Step Therapy Program Summary

This program applies to Flex Closed, FlexRx Open, GenRx Open, Gen Closed, and Health Insurance Marketplace formularies.

This is a FlexRx and GenRx standard step therapy program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

### FDA APPROVED INDICATIONS<sup>1-21,25-29</sup>

Agent	Indication
<b>Anaprox DS<sup>®</sup></b> (naproxen) <sup>a</sup>  tablet	Relief of the signs and symptoms of: <ul style="list-style-type: none"> <li>• rheumatoid arthritis</li> <li>• osteoarthritis</li> <li>• ankylosing spondylitis</li> <li>• polyarticular juvenile idiopathic arthritis</li> <li>• tendonitis</li> <li>• bursitis</li> <li>• acute gout</li> </ul> Management of: <ul style="list-style-type: none"> <li>• pain</li> <li>• primary dysmenorrhea</li> </ul>
<b>Arthrotec<sup>®</sup></b> (diclofenac/ misoprostol) <sup>a</sup>  tablet	Treatment of signs and symptoms of osteoarthritis (OA) or rheumatoid arthritis (RA) in patients at high risk of developing NSAID-induced gastric and duodenal ulcers and their complications
<b>Cambia<sup>®</sup></b> (diclofenac)  oral packet for solution	Acute treatment of migraine attacks with or without aura in adults 18 years of age or older
<b>Celebrex<sup>®</sup></b> (celecoxib) <sup>a</sup>  capsule	Osteoarthritis (OA)  Rheumatoid Arthritis (RA)  Juvenile Rheumatoid Arthritis (JRA) in patients 2 years and older  Ankylosing Spondylitis (AS)  Acute Pain (AP)  Primary Dysmenorrhea (PD)
<b>Daypro<sup>®</sup></b> (oxaprozin) <sup>a</sup>  tablet	Relief of signs and symptoms of Osteoarthritis (OA)  Relief of signs and symptoms of Rheumatoid Arthritis (RA)  Relief of signs and symptoms of Juvenile Rheumatoid Arthritis (JRA)

<b>Agent</b>	<b>Indication</b>
<b>EC-Naprosyn®</b> (naproxen) <sup>a</sup>  tablet	Relief of the signs and symptoms of: <ul style="list-style-type: none"> <li>• rheumatoid arthritis</li> <li>• osteoarthritis</li> <li>• ankylosing spondylitis</li> <li>• polyarticular juvenile idiopathic arthritis</li> </ul>
<b>Feldene®</b> (piroxicam) <sup>a</sup>  capsule	Relief of the signs and symptoms of osteoarthritis (OA)  Relief of the signs and symptoms of rheumatoid arthritis (RA)
<b>Fenoprofen<sup>b</sup></b>  capsule	Relief of mild to moderate pain in adults  Relief of the signs and symptoms of rheumatoid arthritis  Relief of the signs and symptoms of osteoarthritis
<b>Fenortho™</b> (fenoprofen)  capsule	Relief of mild to moderate pain in adults  Relief of the signs and symptoms of rheumatoid arthritis  Relief of the signs and symptoms of osteoarthritis
<b>Indocin®</b> (indomethacin)  suspension	Moderate to severe rheumatoid arthritis including acute flares of chronic disease  Moderate to severe ankylosing spondylitis  Moderate to severe osteoarthritis  Acute painful shoulder (bursitis and/or tendinitis)  Acute gouty arthritis
<b>Ketoprofen<sup>ab</sup></b>  capsule	Management of the signs and symptoms of rheumatoid arthritis and osteoarthritis  Management of pain  Treatment of primary dysmenorrhea
<b>Ketoprofen ER<sup>b</sup></b>  capsule	Management of the signs and symptoms of rheumatoid arthritis and osteoarthritis
<b>Lodine®</b> (etodolac) <sup>a</sup>  tablet	For acute and long-term use in the management of signs and symptoms of the following: <ul style="list-style-type: none"> <li>• Osteoarthritis</li> <li>• Rheumatoid arthritis</li> </ul> For the management of acute pain

Agent	Indication
<b>Meclofenamate<sup>b</sup></b>  capsule	For reduction of fever in adults  For relief of mild to moderate pain in adults  For relief of signs and symptoms of juvenile arthritis  For relief of the signs and symptoms of rheumatoid arthritis  For relief of the signs and symptoms of osteoarthritis  For treatment of primary dysmenorrhea  For acute or long-term use in the relief of signs and symptoms of the following: <ul style="list-style-type: none"> <li>• Ankylosing spondylitis</li> <li>• Acute painful shoulder (Acute subacromial bursitis/supraspinatus tendinitis)</li> <li>• Acute gouty arthritis</li> </ul> Meclofenamate sodium capsules are also indicated for the treatment of idiopathic heavy menstrual blood loss
<b>Mobic<sup>®</sup></b> (meloxicam) <sup>a</sup>  tablet	Osteoarthritis (OA)  Rheumatoid Arthritis (RA)  Juvenile Rheumatoid Arthritis (JRA) in patients who weigh $\geq 60$ kg
<b>Nalfon<sup>®</sup></b> (fenoprofen)  capsule tablet <sup>a</sup>	Relief of mild to moderate pain in adults  Relief of the signs and symptoms of rheumatoid arthritis  Relief of the signs and symptoms of osteoarthritis
<b>Naprelan CR<sup>®</sup></b> (naproxen ER) <sup>a</sup>  tablet	rheumatoid arthritis (RA)  Osteoarthritis (OA)  Ankylosing spondylitis (AS)  Tendinitis, bursitis  Acute gout  Primary dysmenorrhea (PD)  The relief of mild to moderate pain

<b>Agent</b>	<b>Indication</b>
<b>Naprosyn®</b> (naproxen)  tablet <sup>a</sup> suspension <sup>a</sup>	The relief of the signs and symptoms of: <ul style="list-style-type: none"> <li>• rheumatoid arthritis</li> <li>• osteoarthritis</li> <li>• ankylosing spondylitis</li> <li>• polyarticular juvenile idiopathic arthritis</li> <li>• tendonitis</li> <li>• bursitis</li> <li>• acute gout</li> </ul> Management of: <ul style="list-style-type: none"> <li>• pain</li> <li>• primary dysmenorrhea</li> </ul>
<b>Onstel®</b> (mefenamic acid) <sup>a</sup>  capsule	For relief of mild to moderate pain in patients ≥ 14 years of age, when therapy will not exceed one week (7 days)  For treatment of primary dysmenorrhea.
<b>Qmiiz ODT™</b> (meloxicam)  orally disintegrating tablet	Osteoarthritis in adults (OA)  Rheumatoid Arthritis in adults (RA)  Juvenile Rheumatoid Arthritis (JRA) Pauciarticular and Polyarticular Course, in pediatric patients who weigh greater than or equal to 60 kg
<b>Relafen DS™</b> (nabumetone)  tablet	Relief of signs and symptoms of osteoarthritis and rheumatoid arthritis
<b>Tivorbex®, Indomethacin<sup>b</sup></b>  capsule	Treatment of mild to moderate acute pain in adults
<b>Tolmetin</b>  capsule <sup>b</sup> tablet <sup>b</sup>	Relief of signs and symptoms of rheumatoid arthritis and osteoarthritis  Treatment of acute flares and the long-term management of the chronic disease  Treatment of juvenile rheumatoid arthritis
<b>Vivlodex™</b> (meloxicam)  capsule	Management of osteoarthritis (OA) pain
<b>Zipsor®</b> (diclofenac)  capsule	Relief of mild to moderate acute pain
<b>Zorvolex®</b> (diclofenac)  capsule	Management of mild to moderate acute pain  Management of osteoarthritis pain

a - Available as a generic; used as prerequisite, not target, in step therapy program

b - Authorized generic or single source generic; targeted in step therapy program

## CLINICAL RATIONALE

### Efficacy

While there are many trials comparing the efficacy of the various non-steroidal anti-inflammatory drugs (NSAIDs) no one agent has demonstrated a clear advantage over others in the treatment of OA or RA.<sup>22</sup> Additionally, there is interpatient variability in response to individual NSAIDs. This phenomenon is not well understood.<sup>23</sup> The Agency for Healthcare Research and Quality (AHRQ) 2011 comparative effectiveness and safety review of analgesics for osteoarthritis (reviewing the current evidence) states that COX-2 selective NSAIDs and nonselective NSAIDs do not differ in efficacy for pain relief, based on many good quality, published trials.<sup>24</sup> The agency also concludes that when compared to each other, none of the analgesics appear to offer greater benefits relative to adverse effects at this time.<sup>22-24</sup>

### Safety

All NSAIDs carry the following black box warnings:<sup>1-21,25-29</sup>

- Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.
- NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

## REFERENCES

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25. Qmiiz ODT prescribing information. TerSera Therapeutics, LLC. October 2018.
26. Relafen DS prescribing information. Carwin Pharmaceutical Associates, LLC. September 2019.
27. Celebrex prescribing information. Pfizer / GD Searle, LLC. May 2019.
28. Fenoprofen prescribing information. Xspire Pharma. May 2016.
29. Ketoprofen ER prescribing information. Mylan Pharmaceuticals Inc. September 2018

## Oral NSAID Step Therapy

### TARGET AGENTS (brands only)

**Anaprox DS**<sup>®</sup> (naproxen)<sup>a</sup>  
**Arthrotec**<sup>®</sup> (diclofenac/misoprostol)<sup>a</sup>  
**Cambia**<sup>®</sup> (diclofenac)  
**Celebrex**<sup>®</sup> (celecoxib)<sup>a</sup>  
**Daypro**<sup>®</sup> (oxaprozin)<sup>a</sup>  
**EC-Naprosyn**<sup>®</sup> (naproxen)<sup>a</sup>  
**Feldene**<sup>®</sup> (piroxicam)<sup>a</sup>  
**Fenoprofen**<sup>b</sup>  
**Fenorho**<sup>™</sup> (fenoprofen)  
**Indocin**<sup>®</sup> (indomethacin)  
**Indomethacin**<sup>b</sup>  
**Ketoprofen**<sup>ab</sup>  
**Ketoprofen ER**<sup>b</sup>  
**Lodine**<sup>®</sup> (etodolac)<sup>a</sup>  
**Meclofenamate**<sup>b</sup>  
**Mobic**<sup>®</sup> (meloxicam)<sup>a</sup>  
**Nalfon**<sup>®</sup> (fenoprofen)<sup>a</sup>  
**Naprelan CR**<sup>®</sup> (naproxen ER)<sup>a</sup>  
**Naprosyn**<sup>®</sup> (naproxen)<sup>a</sup>  
**Ponstel**<sup>®</sup> (mefenamic acid)<sup>a</sup>  
**Qmiiz ODT**<sup>™</sup> (meloxicam)  
**Relafen DS**<sup>™</sup> (nabumetone)  
**Tivorbex**<sup>®</sup> (indomethacin)  
**Tolmetin**<sup>b</sup>  
**Vivlodex**<sup>™</sup> (meloxicam)  
**Zipsor**<sup>®</sup> (diclofenac)  
**Zorvolex**<sup>®</sup> (diclofenac)

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### PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

**Target Agent (oral NSAID brands)** will be approved when ONE of the following is met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
  - a. A statement by the prescriber that the patient is currently taking the requested agent  
**AND**
  - b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent  
**AND**
  - c. The prescriber states that a change in therapy is expected to be ineffective or cause harm**OR**
2. The patient's medication history includes use of at least two prescription strength generic oral NSAIDs within the past 999 days  
**OR**
3. BOTH of the following:
  - a. The prescriber has stated that the patient has tried at least two prescription strength generic oral NSAID agents  
**AND**
  - b. Prescription strength generic oral NSAID agents were discontinued due to lack of effectiveness or an adverse event**OR**
4. The patient has an intolerance to at least two prescription strength generic oral NSAIDs  
**OR**

5. The patient has an FDA labeled contraindication, or hypersensitivity to ALL prescription strength generic oral NSAIDs
- OR**
6. The prescriber has provided documentation that ALL prescription strength generic oral NSAID agents cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

**Length of approval:** 12 months