



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

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

This is a FlexRx Standard and GenRx Standard program.

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

POLICY REVIEW CYCLE

Effective Date
06-01-2024

Date of Origin
01-01-2018

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Anaprox DS® (naproxen) Tablet*	Relief of the signs and symptoms of: <ul style="list-style-type: none"> • Rheumatoid arthritis • Osteoarthritis • Ankylosing spondylitis • Polyarticular juvenile idiopathic arthritis • Tendonitis • Bursitis • Acute gout Management of: <ul style="list-style-type: none"> • Pain • Primary dysmenorrhea 	*Generic available	1
Arthrotec® (diclofenac/misoprostol) Delayed-release tablet*	Treatment of signs and symptoms of osteoarthritis (OA) or rheumatoid arthritis (RA) in adult patients at high risk of developing NSAID-induced gastric and duodenal ulcers and their complications	*Generic available	2
Cambia® (diclofenac) Oral powder packet for solution*	Acute treatment of migraine attacks with or without aura in adults 18 years of age or older	*Generic available	3
Celebrex® (celecoxib) Capsule*	Osteoarthritis (OA) Rheumatoid Arthritis (RA)	*Generic available	27

Agent(s)	FDA Indication(s)	Notes	Ref#
	Juvenile Rheumatoid Arthritis (JRA) in patients 2 years and older Ankylosing Spondylitis (AS) Acute Pain (AP) Primary Dysmenorrhea (PD)		
Coxanto™ (oxaprozin) capsule	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)		16
Daypro® (oxaprozin) 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)	*Generic available	4
EC-Naprosyn® (naproxen) Tablet*	Relief of the signs and symptoms of: <ul style="list-style-type: none"> • Rheumatoid arthritis • Osteoarthritis • Ankylosing spondylitis • Polyarticular juvenile idiopathic arthritis 	*Generic available	5
Feldene® (piroxicam) Capsule*	Relief of the signs and symptoms of osteoarthritis (OA) Relief of the signs and symptoms of rheumatoid arthritis (RA)	*Generic available	6
Fenortho™ (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		7
Flurbiprofen Tablet*	Relief of the signs and symptoms of rheumatoid arthritis Relief of the signs and symptoms of osteoarthritis	*Generic available	30
Indocin® (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	*Generic available	8
Ketoprofen Capsule	Management of the signs and symptoms of rheumatoid arthritis and osteoarthritis		9

Agent(s)	FDA Indication(s)	Notes	Ref#
	Management of pain Treatment of primary dysmenorrhea		
Ketoprofen ER Capsule	Management of the signs and symptoms of rheumatoid arthritis and osteoarthritis		29
Lodine® (etodolac) Tablet*	For acute and long-term use in the management of signs and symptoms of the following: <ul style="list-style-type: none"> Osteoarthritis Rheumatoid arthritis For the management of acute pain	*Generic available	10
Meclofenamate 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"> Ankylosing spondylitis Acute painful shoulder (Acute subacromial bursitis/supraspinatus tendinitis) Acute gouty arthritis Meclofenamate sodium capsules are also indicated for the treatment of idiopathic heavy menstrual blood loss		11
Meloxicam Oral suspension	Osteoarthritis (OA) Rheumatoid Arthritis (RA) Juvenile Rheumatoid Arthritis (JRA) in patients 2 years of age and older		31
Mobic® (meloxicam) Tablet*	Osteoarthritis (OA) Rheumatoid Arthritis (RA) Juvenile Rheumatoid Arthritis (JRA) in patients who weigh greater than or equal to 60 kg	*Generic available	12
Nalfon® (fenoprofen) Capsule* Tablet*	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	*Generic available	13

Agent(s)	FDA Indication(s)	Notes	Ref#
Naprelan CR® (naproxen ER) Tablet*	rheumatoid arthritis (RA) Osteoarthritis (OA) Ankylosing spondylitis (AS) Tendinitis, bursitis Acute gout Primary dysmenorrhea (PD) The relief of mild to moderate pain	*Generic available	14
Naprosyn® (naproxen) Tablet* Suspension*	The relief of the signs and symptoms of: <ul style="list-style-type: none"> • Rheumatoid arthritis • Osteoarthritis • Ankylosing spondylitis • Polyarticular juvenile idiopathic arthritis <ul style="list-style-type: none"> • Tendonitis • Bursitis • Acute gout Management of: <ul style="list-style-type: none"> • Pain • Primary dysmenorrhea 	*Generic available	15
Relafen DS™ (nabumetone) Tablet	Relief of signs and symptoms of osteoarthritis and rheumatoid arthritis		26
Tivorbex® , Indomethacin Capsule*	Treatment of mild to moderate acute pain in adults	*Generic available	17
Tolmetin Capsule Tablet	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. The safety and effectiveness of tolmetin sodium capsules have not been established in pediatric patients under 2 years of age.		18
Zipsor® (diclofenac) Capsule*	Relief of mild to moderate acute pain in adult and pediatric patients 12 years of age and older	*Generic available	20

Agent(s)	FDA Indication(s)	Notes	Ref#
Zorvolex®, Diclofenac Capsule	Management of mild to moderate acute pain Management of osteoarthritis pain		21

See package insert for FDA prescribing information: <https://dailymed.nlm.nih.gov/dailymed/index.cfm>

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 osteoarthritis (OA) or rheumatoid arthritis (RA).(24) Additionally, there is interpatient variability in response to individual NSAIDs. This phenomenon is not well understood.(23) 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.(24) 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.(22-24)
Safety	All NSAIDs carry the following box warnings:(1-19,20-21,26-27, 29-31) <ul style="list-style-type: none"> • 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

Number	Reference
1	Anaprox DS prescribing information. Canton Laboratories. April 2021.
2	Arthrotec prescribing information. Pfizer Labs. December 2022.
3	Cambia prescribing information. Assertio Therapeutics. April 2021.
4	Daypro prescribing information. Pfizer Labs. November 2022.
5	EC-Naprosyn prescribing information. Canton Laboratories. April 2021.
6	Feldene prescribing information. Pfizer Labs Inc. November 2022.
7	Fenortho prescribing information. Sterling Knight Pharmaceuticals. March 2021.
8	Indocin prescribing information. Zyla Life Sciences US LLC. April 2021.
9	Ketoprofen prescribing information. Misemer Pharmaceutical, Inc. September 2022.
10	Lodine prescribing information. Sallus Laboratories, LLC. October 2016.
11	Meclofenamate prescribing information. Mylan Pharmaceuticals Inc. May 2021.
12	Mobic prescribing information. Boehringer Ingelheim. April 2021.
13	Nalfon prescribing information. Xspire Pharma. April 2021.
14	Naprelan CR prescribing information. Almatica Pharma, Inc. April 2023.
15	Naprosyn prescribing information. Athena Bioscience, LLC. April 2021.
16	Coxanto prescribing information. Solubiomix, LLC. October 2023.

Number	Reference
17	Tivorbex prescribing information. Iroko Pharmaceuticals, LLC. January 2018.
18	Tolmetin prescribing information. Rising Pharma Holdings, Inc. June 2023.
19	Reference no longer used.
20	Zipsor prescribing information. Assertio. May 2021.
21	Zorvolex prescribing information. Iroko Pharmaceuticals, LLC. April 2021.
22	Schuchen RH, Mucke M, Conrad R. Systematic review and meta-analysis on non-opioid analgesics in palliative medicine. <i>J Cachexia Sarcopenia Muscle</i> . 2018;9(7):1235-1254. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6351677/#_ffn_sectitle .
23	Solomon DH, et al. NSAIDs: Therapeutic Use and Variability of Response in Adults. UpToDate. Last updated September 2021. Literature review current through November 2023.
24	Agency for Healthcare Research and Quality (AHRQ). Comparative Effectiveness and Safety of Analgesics for Osteoarthritis. February 2012. Available at: Analgesics for Osteoarthritis - NCBI Bookshelf (nih.gov).
25	Reference no longer used.
26	Relafen DS prescribing information. Carwin Pharmaceutical Associates, LLC. May 2022.
27	Celebrex prescribing information. Pfizer / GD Searle, LLC. April 2021.
28	Reference no longer used.
29	Ketoprofen ER prescribing information. Mylan Pharmaceuticals Inc. March 2021.
30	Flurbiprofen prescribing information. Teva Pharmaceuticals, USA, Inc. November 2021.
31	Meloxicam suspension prescribing information. Avondale Pharmaceuticals LLC. June 2022.

POLICY AGENT SUMMARY STEP THERAPY

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
			M ; N ; O			
	diclofenac sodium tab er	100 MG	M ; N ; O	Y		
	flurbiprofen tab	100 MG ; 50 MG	M ; N ; O	N ; Y		
	ketoprofen cap er	200 MG	M ; N ; O	N		
	meclofenamate sodium cap	100 MG ; 50 MG	M ; N ; O	N		
	mefenamic acid cap	250 MG	M ; N ; O	Y		
	meloxicam cap	10 MG ; 5 MG	M ; N ; O	Y		
	sulindac tab	150 MG ; 200 MG	M ; N ; O	Y		
	tolmetin sodium cap	400 MG	M ; N ; O	N		
	tolmetin sodium tab	600 MG	M ; N ; O	N		
Aleve ; Aleve arthritis ; All day pain relief ; All day relief ; Anaprox ds ; Cvs all day pain relief ; Cvs naproxen sodium ; Eq all day pain relief ; Eq naproxen sodium ; EqI naproxen sodium ; Ft all day pain relief ; Gnp naproxen ; Goodsense naproxen sodium ; Hm naproxen sodium ; Hy-vee all day relief ; Mediprofen ; Pamprin all day maximum s ; Px	naproxen sodium tab	220 MG ; 275 MG ; 550 MG	M ; N ; O	O ; Y		

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
all day relief ; Qc naproxen sodium ; Ra naproxen sodium ; Sb naproxen sodium ; Sm naproxen sodium						
Arthrotec 50 ; Arthrotec 75	diclofenac w/ misoprostol tab delayed release	50-0.2 MG ; 75-0.2 MG	M ; N ; O	O ; Y		
Cambia	diclofenac potassium (migraine) packet	50 MG	M ; N ; O	O ; Y		
Cataflam ; Lofena	diclofenac potassium tab	25 MG ; 50 ; 50 MG	M ; N ; O	Y		
Celebrex	celecoxib cap	100 MG ; 200 MG ; 400 MG ; 50 MG	M ; N ; O	O ; Y		
Coxanto	oxaprozin cap	300 MG	M ; N ; O	M		
Daypro	oxaprozin tab	600 MG	M ; N ; O	O ; Y		
Ec-naprosyn ; Ec-naproxen	naproxen tab ec	375 MG ; 500 MG	M ; N ; O	O ; Y		
Elyxyb	celecoxib oral soln	120 MG/4.8ML	M ; N ; O	N		
Feldene	piroxicam cap	10 MG ; 20 MG	M ; N ; O	O ; Y		
Fenortho ; Nalfon	fenoprofen calcium cap	200 MG ; 400 MG	M ; N ; O	M ; O ; Y		
Indocin	indomethacin susp	25 MG/5ML	M ; N ; O	O ; Y		
Kiprofen	ketoprofen cap	25 MG ; 50 MG ; 75 MG	M ; N ; O	M ; N		
Lodine	etodolac tab	400 MG ; 500 MG	M ; N ; O	O ; Y		
Mobic	meloxicam tab	15 MG ; 7.5 MG	M ; N ; O	O ; Y		
Nalfon	fenoprofen calcium tab	600 MG	M ; N ; O	O ; Y		
Naprelan	naproxen sodium tab er	375 MG ; 500 MG ; 750 MG	M ; N ; O	O ; Y		
Naprosyn	naproxen susp	125 MG/5ML	M ; N ; O	O ; Y		
Naprosyn	naproxen tab	250 MG ; 375 MG ; 500 MG	M ; N ; O	O ; Y		
Relafen ; Relafen ds	nabumetone tab	1000 MG ; 500 MG ; 750 MG	M ; N ; O	N ; Y		
Tivorbex	indomethacin cap	20 MG ; 25 MG ; 50 MG	M ; N ; O	M ; N ; Y		
Zipsor	diclofenac potassium cap	25 MG	M ; N ; O	O ; Y		
Zorvolex	diclofenac cap	18 MG ; 35 MG	M ; N ; O	M ; N		

CLIENT SUMMARY – STEP THERAPY

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	flurbiprofen tab	100 MG ; 50 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
	ketoprofen cap er	200 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
	meclofenamate sodium cap	100 MG ; 50 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	tolmetin sodium cap	400 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
	tolmetin sodium tab	600 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Aleve ; Aleve arthritis ; All day pain relief ; All day relief ; Anaprox ds ; Cvs all day pain relief ; Cvs naproxen sodium ; Eq all day pain relief ; Eq naproxen sodium ; Eq naproxen sodium ; Ft all day pain relief ; Gnp naproxen ; Goodsense naproxen sodium ; Hm naproxen sodium ; Hy-vee all day relief ; Mediproxen ; Pamprin all day maximum s ; Px all day relief ; Qc naproxen sodium ; Ra naproxen sodium ; Sb naproxen sodium ; Sm naproxen sodium	naproxen sodium tab	220 MG ; 275 MG ; 550 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Arthrotec 50 ; Arthrotec 75	diclofenac w/ misoprostol tab delayed release	50-0.2 MG ; 75-0.2 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Cambia	diclofenac potassium (migraine) packet	50 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Celebrex	celecoxib cap	100 MG ; 200 MG ; 400 MG ; 50 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Coxanto	oxaprozin cap	300 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Daypro	oxaprozin tab	600 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Ec-naprosyn ; Ec-naproxen	naproxen tab ec	375 MG ; 500 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Feldene	piroxicam cap	10 MG ; 20 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Fenortho ; Nalfon	fenoprofen calcium cap	200 MG ; 400 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Indocin	indomethacin susp	25 MG/5ML	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Kiprofen	ketoprofen cap	25 MG ; 50 MG ; 75 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Lodine	etodolac tab	400 MG ; 500 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Mobic	meloxicam tab	15 MG ; 7.5 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Nalfon	fenoprofen calcium tab	600 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Naprelan	naproxen sodium tab er	375 MG ; 500 MG ; 750 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Naprosyn	naproxen susp	125 MG/5ML	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Naprosyn	naproxen tab	250 MG ; 375 MG ; 500 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Relafen ; Relafen ds	nabumetone tab	1000 MG ; 500 MG ; 750 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Tivorbex	indomethacin cap	20 MG ; 25 MG ; 50 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Zipsor	diclofenac potassium cap	25 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx
Zorvolex	diclofenac cap	18 MG ; 35 MG	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx

STEP THERAPY CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	<p>TARGET AGENT(S) (brands only)</p> <p>Anaprox DS (naproxen) -a Arthrotec (diclofenac/misoprostol) -a Cambia (diclofenac) -b Celebrex (celecoxib) -a Coxanto (oxaprozin) Daypro (oxaprozin) -a EC-Naprosyn (naproxen) -a Feldene (piroxicam) -a Fenortho (fenoprofen) Flurbiprofen tablet -ab Indocin (indomethacin) suspension -a</p>

Module	Clinical Criteria for Approval
	<p> Ketoprofen capsule -b Ketoprofen ER capsule -b Lodine (etodolac) -a Meclofenamate capsule-b Meloxicam suspension -b Mobic (meloxicam) tablet -a Nalfon (fenoprofen) capsule and tablet -a Naprelan CR (naproxen) tablet -a Naprosyn (naproxen) tablet and suspension -a Relafen DS (nabumetone) tablet Tivorbex, Indomethacin capsule -ab Tolmetin capsule and tablet -b Zipsor (diclofenac) capsule -a Zorvolex, Diclofenac capsule -b </p> <p> a – Available as a generic; included as a prerequisite in the step therapy program b – Branded generic product(s) available; targeted in the step therapy program </p> <p> Target Agent will be approved when ONE of the following is met: </p> <ol style="list-style-type: none"> 1. The patient is currently being treated with the requested agent as indicated by ALL of the following: <ol style="list-style-type: none"> 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: <ol style="list-style-type: none"> 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 or hypersensitivity to at least two prescription strength generic oral NSAIDs OR 5. The patient has an FDA labeled contraindication 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 <p> Length of Approval: 12 months </p>