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
Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to relieve pain and reduce signs of inflammation including swelling and redness. NSAIDs have a wide variety of indications including rheumatoid arthritis, osteoarthritis, mild to moderate pain, primary dysmenorrhea, tendonitis, and bursitis.1,5

CLINICAL RATIONALE
Efficacy
While there are many trials comparing the efficacy of the various NSAIDs no one agent has demonstrated a clear advantage over others in the treatment of OA or RA.1 Additionally, there is inter-patient variability in response to individual NSAIDs. This phenomenon is not well understood.2 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.3 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.3

Safety
In general, NSAIDs are fairly well tolerated. However, adverse gastrointestinal events occur in a small, but important percentage of patients. The U.S. FDA has placed a class warning on the labels of NSAIDs stating, “...symptomatic upper GI ulcers appear to occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year.” According to data from the Arthritis, Rheumatism, and Aging Medical Information System (ARAMIS), thirteen of every 1000 patients with rheumatoid arthritis who take NSAIDs for one year have a serious GI complication. For patients with osteoarthritis, the risk is somewhat lower (7.3 per 1000 patients per year).2 COX-2 inhibitors were developed in part to have superior gastrointestinal safety compared to older NSAIDs. THE AHRQ review of analgesics for osteoarthritis stated that celecoxib was associated with a lower risk of ulcer complications compared to nonselective NSAIDs.3

The U.S. Food and Drug Administration (FDA) is strengthening an existing label warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) increase the chance of a heart attack or stroke. Based on FDA’s comprehensive review of new safety information, FDA is requiring updates to the drug labels of all NSAIDs.6

• The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID. The risk may increase with longer use of the NSAIDs. The risk appears greater at higher doses.
• It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs;
however, this newer information is not sufficient for us to determine that the risk of any particular NSAID is definitely higher or lower than that of any other particular NSAID.

- NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with varying estimates of how much the risk is increased, depending on the drugs and the doses studied.
- In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.
- Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack.
- There is an increased risk of heart failure with NSAID use.

The American Heart Association (AHA) issued a recommendation for the use of NSAIDs in patients with known CV disease or at risk of ischemic heart disease. They advise starting with acetaminophen or aspirin at the lowest efficacious dose, especially for short term needs. The AHA recommends a “stepped care approach” to management of musculoskeletal symptoms in the above patient group. The statement made in this guideline is, “If symptoms are not adequately controlled by nonselective NSAIDs, subsequent steps involve prescription drugs with increasing degrees of COX-2-inhibitory activity, ultimately concluding with COX-2-selective NSAIDs.”

The Agency for Healthcare Research and Quality (AHQR) Comparative Effectiveness Review 2011: Analgesics for Osteoarthritis (OA) states that celecoxib and most nonselective, non-aspirin NSAIDs appear to be associated with an increased risk of serious cardiovascular harms.

REFERENCES
Oral NSAID Step Therapy

OBJECTIVE
The intent of the Oral NSAIDs Step Therapy (ST) program is encourage the use of cost-effective prescription strength generic oral NSAIDs before brand oral NSAID products but to accommodate for use of brand oral NSAID products when the more cost-effective generics cannot be used due to documented intolerance, FDA labeled contraindication, or hypersensitivity. The Oral NSAIDs ST program will require the use of at least two prescription strength generic oral NSAID products before approval of a brand product.

TARGET AGENTS (brands only)
- Anaprox (naproxen)a
- Anaprox DS (naproxen)a
- Arthrotec (diclofenac/misoprostol)a
- Cambia (diclofenac packets)
- Cataflam (diclofenac potassium)a
- Celebrex (celecoxib)a
- Clinoril (sulindac)a
- Daypro (oxaprozin)a
- EC-Naprosyn (naproxen)a
- Feldene (piroxicam)a
- Fenoprofenab
- Fenortho (fenoprofen)
- Indocin (indomethacin)
- Ketoprofenb
- Lodine (etodolac)a
- Meclofenamateb
- Mobic (meloxicam)a
- Nalfon (fenoprofen)b
- Naprelan (naproxen)a
- Naprelan CR (naproxen)a
- Naprosyn (naproxen)a
- Ponstel (mefenamic acid)a
- Tivorbex (indomethacin)
- Tolmetinb
- Vivlodex (meloxicam)
- Voltaren XR (diclofenac sodium)a
- Zipsor (diclofenac potassium)
- Zorvolex (diclofenac)

a – available as a generic; used as prerequisite not target in step therapy program
b – available as authorized generic or single source generic, and targeted in step therapy program

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Oral NSAIDs (brands) will be approved when ONE of the following is met:
1. The patient’s medication history includes use of at least two prescription strength generic oral NSAIDs in the past 180 days
   OR
2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least two prescription strength generic oral NSAIDs.

Length of approval: 12 months
Step Therapy Supplement

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

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE

The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL

The requested agent will be approved when ONE of the following are 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 include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

   OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) 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: As per program specific criteria