MASSACHUSETTS

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Pharmacy Medical Policy
COX II Inhibitor Drugs

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Policy Number: 002

BCBSA Reference Number: N/A

Related Policies

- Quality Care Dosing guidelines may apply to the following medications and can be found in Medical Policy #621A.
- Anti-Migraine Policy #021

Prior Authorization Information

Policy	☒ Prior Authorization ☐ Step Therapy ☒ Quantity Limit ☐ Administrative	Reviewing Department	**Pharmacy Operations:** Tel: 1-800-366-7778 Fax: 1-800-583-6289
		Policy Effective Date	**12/2023**
Pharmacy (Rx) or Medical (MED) benefit coverage	☒ Rx ☐ MED	**To request for coverage:** Providers may call, fax, or mail the attached form (Formulary Exception/Prior Authorization form) to the address below. **Blue Cross Blue Shield of Massachusetts** **Pharmacy Operations Department** 25 Technology Place Hingham, MA 02043 Tel: 1-800-366-7778 Fax: 1-800-583-6289 **Individual Consideration for the atypical patient:** Policy for requests that do not meet clinical criteria of this policy, see section labeled Individual Consideration	
Policy applies to Commercial Members: • Managed Care (HMO and POS), • PPO and Indemnity • MEDEX with Rx plan • Managed Major Medical with Custom BCBSMA Formulary • Comprehensive Managed Major Medical with Custom BCBSMA Formulary • Managed Blue for Seniors with Custom BCBSMA Formulary **Policy does NOT apply to**: • Medicare Advantage			

Summary

This is a comprehensive policy covering prior authorization and quantity limit requirements for cyclooxygenase-II (COX II) inhibitors for the treatment of various pain and inflammatory conditions.

Nonsteroidal anti-inflammatory drugs (NSAIDs) work by inhibiting cyclooxygenase (COX), also known as prostaglandin synthase (PGHS) enzyme, blocking the transformation of arachidonic acid to its metabolites (prostaglandins, prostacyclin, and thromboxane). There are two related isoforms of the COX enzyme that have been described: COX-I expressed in most tissues, which regulates normal cellular processes and COX-II, expressed only in a few organs and whose expression in other areas is increased during states of

inflammation. NSAIDs that selectively inhibit COX-- rather than both COX enzymes were developed to reduce the risk of duodenal ulcers from COX-I inhibition while preserving the anti-inflammatory effects.

The overall efficacy of COX-II selective and nonselective NSAIDs are similar when used as analgesic, anti-inflammatory, and antipyretic agents at standard doses, although response my vary in different individuals. Therefore, the choice to use a selective COX-II or nonselective NSAID is sometimes based on reducing the risk of unwanted nonselective blocking like gastrointestinal bleeding, aspirin-exacerbated respiratory disease or inhibition of platelets in patients on anticoagulation therapy.

Formulary status/requirements of the medications affected by this policy:

Drug	Formulary Status (BCBSMA Commercial Plan)	Requirement
Step 1 – Traditional NSAIDS		
Diclofenac	Covered, *QCD may apply for some formulations	Covered without any requirements
Etodolac	Covered	
Ibuprofen	Covered	
Indomethacin	Covered, *QCD may apply for some dosages	
Ketoprofen	Covered	
Meloxicam	Covered, *QCD may apply for some dosages	
Nabumetone	Covered	
Naproxen	Covered	
Step 2 - Cox-II inhibitors		
Celebrex ® (celecoxib)	Covered, PA, QCD	PA required AND prior use of TWO traditional NSAIDS
celecoxib capsules	Covered, PA, QCD	
Elyxyb ™ (celecoxib)	Covered, PA	PA required and prior use of TWO traditional NSAIDS and/or Triptans – see above for related policy (anti-migraine)
Seglentis ™ (celecoxib/tramadol)	NFNC, PA	PA required and prior use of TWO formulary alternatives

PA – Prior Authorization; QCD – Quality Care Dosing (refer to policy #621b); NFNC – Non-formulary / non-covered

Policy

No Requirements

BCBSMA formulary coverage options for traditional non-COX-II prescription strength nonsteroidal anti-inflammatory drugs (NSAIDs), include, but may not be limited to:

- † Diclofenac Potassium
- † Diclofenac Sodium DR
- † Diclofenac Sodium EC
- † Etodolac ER
- † Etodolac
- Ibuprofen
- Indomethacin
- Indomethacin ER
- Ketoprofen 75mg
- Ketoprofen 50mg
- † Meloxicam
- † Nabumetone
- Naproxen
- Naproxen EC

† **Note:** Some of these older NSAIDS traditionally viewed as nonselective have been found to be relatively selective for COX-II at lower/recommended doses, compared to other nonselective NSAIDS.

Prior Authorization Criteria

Length of Approval	24 months

Formulary Status	All requests must meet the Prior Authorizations requirement. For non-covered medications, the member **must** also have had a previous treatment failure with, or contraindication to, **at least two** covered formulary alternatives when available. See section on individual consideration for more information if you require an exception to any of these criteria requirements for an atypical patient.
Member cost share consideration	A higher non-preferred cost share may be applied if an exception request is approved for coverage of a non-preferred or a non-formulary/non-covered drug.

Celebrex ®, and Generic Celecoxib

Celebrex and Generic Celecoxib may be considered **MEDICALLY NECESSARY** and covered for the following indications when the corresponding criteria are met:

Acute Pain

1. Treatment failure with two (2) traditional non-COX-II prescription NSAIDs or a contraindication to NSAID use.
2. For a **non-formulary / non-covered COX-II drug**, a previous treatment failure with, or contraindication to, **at least two** covered formulary alternatives when available.

Arthritis

May be covered for arthritis when one or more of the following conditions are present:

1. Age 60 years or older; **OR**
2. Age 2 years or older WITH a confirmed diagnosis of Juvenile Rheumatoid Arthritis (JRA); **OR**
3. The patient has one (1) or more of the following risk factors:
    a. History of gastrointestinal ulcer or bleeding[3]
    b. Thrombocytopenia
    c. Inflammatory Bowel Disease
4. Concurrent treatment with oral or injectable corticosteroids; **OR**
5. Concurrent treatment with anticoagulants such as warfarin, heparin, Lovenox® , Fragmin®, Innohep®, Arixtra® or high-dose aspirin; **OR**
6. Concurrent treatment with oral or injectable DMARDs such as methotrexate, gold, Enbrel®, Remicade®, Humira™, Kineret®, sulfasalazine, azathioprine, cyclosporine, hydroxychloroquine, Arava®, Cuprimine®, misoprostol, Supartz™, Synvisc® or Hyalgan® in the last 130 days; **OR**
7. Current treatment with Antiplatelet therapy drugs such as Plavix®, clopidogrel cilostazol, dipyridamole, Aggrenox®, or Agrylin®; **OR**
8. Current treatment with 5-Aminosalicylates drugs such as mesalamine, olsalazine, 6-mercaptopurine and balsalazide; **OR**
9. Treatment failure with two (2) traditional non-COX-II prescription NSAIDs in last 130 days.

Polyposis

1. Documented diagnosis of familial adenomatous polyposis[4]; **AND**
2. For pediatric conditions, submission of the patient's clinical information.

Primary Dysmenorrhea

1. Treatment failure with two (2) traditional non-COX-II prescription NSAIDs or a contraindication to NSAID use; **AND**
2. For a **non-formulary / non-covered COX-II drug**, a previous treatment failure with, or contraindication to, **at least two** covered formulary alternatives when available.

Other Indications not Listed

Other, indications that are not listed can be submitted for review and may be approved for coverage under our Individual Consideration review process. Please see section on Individual Consideration for more information

Elyxyb ®

Elyxyb may be considered **MEDICALLY NECESSARY** and covered for the following indications when the corresponding criteria are met:

1. Diagnosis of migraine with moderate to severe pain intensity
2. Age 18 years or older
3. Contraindication to or treatment failure with TWO or more of the following alternatives:
    a. NSAIDs e.g., diclofenac, ibuprofen, naproxen; **OR**
    b. Triptans e.g., naratriptan, rizatriptan, sumatriptan

Seglentis ®

Seglentis may be considered **MEDICALLY NECESSARY** and when the following criteria are met:

1. Diagnosis of severe acute pain that requires use of an opioid analgesic; **AND**
2. Pain has not been adequately managed by:
    a. At least TWO formulary alternative treatment options (i.e., non-opioid analgesics – see table above for formulary options); **OR**
    b. Formulary alternative treatments have not been tolerated or not expected to be tolerated; **OR**
    c. Formulary alternative treatments have not provided or not expected to provide adequate analgesia;

Other Coverage Conditions

We do NOT cover Cox II Inhibitor drugs for patients who are on low dose aspirin therapy, unless therapy is warranted as outlined above.

For patient safety, we do NOT cover Cox II Inhibitor drugs for patients with any of the following conditions:

- Active peptic ulcer disease or bleeding[2]
- Sulfa allergy (applies to celecoxib)
- Allergy to aspirin or NSAIDs
- Severe kidney[2,6] or liver dysfunction
- Age less than 18[1] unless FDA approved for a specific condition.
- cardiovascular disease[1,2,3]
- Congestive heart failure.[1,2]

Prior Use Criteria

The plan uses prescription claim records to support criteria for prior use within previous 130 days or the trial and failure of formulary alternatives when available. Additional documentation will be required from the provider when historic prescription claim data is either not available or the medication fill history fails to establish criteria for prior use or trial and failure of formulary alternatives. Documentation will also be required to support any clinical reasons preventing the trial and failure of formulary alternatives. Please see the section on documentation requirements for more information.

Provider Documentation Requirements

Documentation from the provider to support a reason preventing trial of formulary alternative(s) must include the name and strength of alternatives tried and failed (if alternatives were tried, including dates if available) and specifics regarding the treatment failure. Documentation to support clinical basis preventing switch to formulary alternative should also provide specifics around clinical reason.

Individual Consideration (For Atypical Patients)

Our medical policies are written for most people with a given condition. Each policy is based on peer reviewed clinical evidence. We also take into consideration the needs of atypical patient populations and diagnoses.

If the coverage criteria outlined is unlikely to be clinically effective for the prescribed purpose, the health care provider may request an exception to cover the requested medication based on an individual's unique clinical circumstances. This is also referred to as "individual consideration" or an "exception request."

Some reasons why you may need us to make an exception include: therapeutic contraindications; history of adverse effects; expected to be ineffective or likely to cause harm (physical, mental, or adverse reaction).

To facilitate a thorough and prompt review of an exception request, we encourage the provider to include additional supporting clinical documentation with their request. This may include:

- Clinical notes or supporting clinical statements;
- The name and strength of formulary alternatives tried and failed (if alternatives were tried) and specifics regarding the treatment failure, if applicable;
- Clinical literature from reputable peer reviewed journals;
- References from nationally recognized and approved drug compendia such as American Hospital Formulary Service® Drug Information (AHFS-DI), Lexi-Drug, Clinical Pharmacology, Micromedex or Drugdex®; and
- References from consensus documents and/or nationally sanctioned guidelines.

Providers may call, fax or mail relevant clinical information, including clinical references for individual patient consideration, to:

Blue Cross Blue Shield of Massachusetts
Pharmacy Operations Department
25 Technology Place
Hingham, MA 02043
Phone: 1-800-366-7778
Fax: 1-800-583-6289

We may also use prescription claims records to establish prior use of formulary alternatives or to show if step therapy criteria has been met. We will require the provider to share additional information when prescription claims data is either not available or the medication fill history fails to establish use of preferred formulary medications or that step therapy criteria has been met.

Policy History

Date	Action
12/2023	Reformatted Policy and updated IC to align with 118E MGL § 51A. Added summary description for NSAIDS and Traditional NSAIDS. Added criteria for Elyxyb for Migraine. Added criteria for Seglentis.
7/2023	Reformatted Policy.
4/2023	Updated to remove CAPXIB & Elyxyb as they manufactures have removed marketing of the medications.

4/2022	Updated to add Seglentis ™ to the policy as non-covered.
2/2022	Updated to add Elyxyb ™ as Nonformulary.
6/2017	Update Address for Pharmacy Operations.
6/2016	Added Generic to policy, added JRA indication, and adjusted age language to allow for new FDA indications and added CapXib as non-covered.
2/2014	Updated ExpressPAth language and remove Blue Value.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
2/2012	Updated to include employee fax number on Outpatient Retail Pharmacy Prior Authorization Form.
7/2010	Reviewed - Medical Policy Group - Orthopedics, Rehabilitation Medicine and Rheumatology. No changes to policy statements.
9/2009	Policy updated to change 180 day look back period to 130 days, add sample language and to remove Medicare Part D criteria from Medical Policy.
7/2008	Reviewed - Medical Policy Group - Orthopedics, Rehabilitation Medicine and Rheumatology. No changes to policy statements.
7/2007	Reviewed - Medical Policy Group - Orthopedics, Rehabilitation Medicine and Rheumatology. No changes to policy statements.
7/2006	Reviewed - Medical Policy Group - Orthopedics, Rehabilitation Medicine and Rheumatology. No changes to policy statements.
11/2001	New Policy, effective 11/2001, describing covered and non-covered indications.

Forms

To request prior authorization using the Massachusetts Standard Form for Medication Prior Authorization Requests (eForm), click the link below:

Massachusetts Standard Form for Medication Prior Authorization Requests #434

References

1. Abramson SB, Weissmann G. The mechanisms of action of nonsteroidal anti-inflammatory drugs. Arthritis Rheum 1989; 32:1
2. DeWitt DL, Meade EA, Smith WL. PGH synthase isoenzyme selectivity: the potential for safer nonsteroidal anti-inflammatory drugs. Am J Med 1993; 95:40S
3. Brooks PM, Day RO. Nonsteroidal anti-inflammatory drugs--differences and similarities. N Engl J Med 1991; 324:1716
4. US Physicians' Health Study, the UK Doctors Study, the Thrombosis Prevention Trial, and the Hypertension Optimal Treatment Trial. Comparatively http://www.arthritis.org/resources/news/cox2_statement.asp for more details.
5. The Coxibs, Selective Inhibitors of Cyclooxygenase-2, by G. Fitzgerald and C. Patrono, NEJM Vol. 345, No. 6, August 9, 2001, 433-442.
6. Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis. C. Bombardier et al, NEJM 2000;343:1520-8.
7. The Effect of Celecoxib, a Cyclooxygenase-2 Inhibitor, in Familial Adenomatous Polyposis. G. Steinbach et al. NEJM 2000;342:1946-52.
8. Cyclooxygenase-2 Inhibitor Celecoxib: A Possible Cause of Gastropathy and Hypoprothrombinemia. Linder JD et al, in the Southern Medical Journal Sep 2000; 93(9):930-932.
9. Cyclooxygenase-2: A Major Therapeutic Advance? by Emery in Am J Med 2001, Jan 8;110(1A):42S-45S.