Clinical Policy Title:	celecoxib
Policy Number:	RxA.60
Drug(s) Applied:	Celebrex®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Celebrex® is a nonsteroidal anti-inflammatory drug (NSAID). It is indicated for the treatment of:

- Osteoarthritis (OA)
- Rheumatoid arthritis (RA)
- Juvenile rheumatoid arthritis (JRA) in patients 2 years and older
- Ankylosing spondylitis (AS)
- Acute pain (AP)
- Primary dysmenorrhea (PD)

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
celecoxib (Celebrex®)	Osteoarthritis (OA)	200 mg PO once daily or 100 mg PO BID	200mg/day
celecoxib (Celebrex®)	Rheumatoid arthritis (RA)	100 to 200 mg PO BID	400mg/day
celecoxib (Celebrex®)	Juvenile rheumatoid Arthritis (JRA)	10-25 kg: 50 mg PO BID > 25 kg: 100 mg PO BID	200 mg/day
celecoxib (Celebrex®)	Ankylosing spondylitis (AS)	200 mg PO once daily or 100 mg PO BID. If no effect is observed after 6 weeks, a trial of 400 mg (single or divided doses) may be of benefit.	400mg/day
celecoxib (Celebrex®)	Acute pain (AP) or Primary dysmenorrhea (PD)	400 mg PO initially, followed by a 200 mg dose if needed on the first day. On subsequent days, 200 mg PO BID as needed	400 mg/day (600mg for one day)

- Hepatic Impairment: Reduce daily dose by 50% in patients with moderate hepatic impairment (Child-Pugh Class B).

- Poor Metabolizers of CYP2C9 Substrates: Consider a dose reduction by 50% (or alternative management for JRA) in patients who are known or suspected to be CYP2C9 poor metabolizers

Dosage Forms

- Capsules: 50 mg, 100 mg, 200 mg, and 400 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. All Indications (must meet all):

1. Age ≥ 2 years;
2. Member meets one of the following (a, b, c, d, or e):
   a. Age > 65 years;
   b. Current use of a corticosteroid;
   c. Current use of an anticoagulant (e.g., aspirin, warfarin, low molecular weight heparin, direct thrombin inhibitors, factor Xa inhibitors, clopidogrel);
   d. Prior gastrointestinal bleed or active peptic ulcer disease (not gastroesophageal reflux disease [GERD]);
   e. Both of the following (i and ii):
      i. Failure of a ≥ 4 week trial of meloxicam at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
      ii. Failure of a ≥ 4 week trial of one additional generic NSAID at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 400 mg/day (1 capsule/day).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications (must meet all)**:**

1. Currently receiving medication that has been authorized by Rxadvance or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 800 mg/day (2 capsules/day).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GERD: Gastroesophageal Reflux Disease

NSAID: Nonsteroidal Anti-Inflammatory Drug

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
naproxen sodium (Anaprox DS®)	275 - 550 mg PO BID	1650 mg/day
sulindac	150 mg - 200 mg PO BID	400 mg/day
salsalate (Disalcid®)	500 - 750 mg PO TID, titrated up to 3000 mg/day	3000 mg/day
piroxicam (Feldene®)	10 - 20 mg PO once daily	20 mg/day
indomethacin	25 - 50 mg PO BID -TID	200 mg/day
indomethacin SR	75 mg PO once daily - BID	150 mg/day
meclofenamate	50 - 100 mg PO Q4-6hr	400 mg/day
meloxicam (Mobic®)	7.5 – 15 mg PO once daily	15 mg/day
ibuprofen (Motrin®)	400 - 800 mg PO every 6-8hr	3200 mg/day
fenoprofen (Nalfon®)	200 mg PO Q4-6hr	3200 mg/day
naproxen (Naprosyn®)	250 – 500 mg PO BID	1500 mg/day
ketoprofen	25 - 75 mg PO Q6-8hr	300 mg/day
nabumetone (Relafen®)	1000 mg PO once daily or 500 mg PO BID	2000 mg/day
tolmetin (Tolmetin® DS)	400 mg PO TID, titrated up to 1800 mg/day	1800 mg/day
diclofenac sodium (Voltaren®)	50 mg PO TID	150 mg/day
oxaprozin (Daypro®)	600 - 1200 mg PO BID	1800 mg/day
etodolac (Lodine®)	400 - 500 mg PO BID	1200 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to celecoxib or any components of the drug product or sulfonamides;
  - History of asthma, urticaria, or other allergic-type reactions to aspirin or other NSAIDs;
  - In the setting of coronary artery bypass graft (CABG) surgery;

- Boxed Warning(s):
  - 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 the treatment and may increase with duration of use.
  - CELEBREX is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.
  - 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.

APPENDIX D: General Information

- The risk vs. benefit of COX-II therapy should be individualized based on patient's previous GI history, other co-morbid conditions (e.g., angina, ischemic heart disease, myocardial infarction (MI), coronary artery disease, stroke), age, concurrent medications (e.g., warfarin, oral corticosteroids), duration and dose.
- Celebrex has been associated with an increased risk of serious adverse cardiovascular (CV) events in a long-term placebo controlled trial. Based on the currently available data, FDA has concluded that an increased risk of serious adverse CV events appears to be a class effect of NSAIDs. FDA has requested that the package insert for all NSAIDs, including Celebrex, be revised to include a boxed warning to highlight the potential increased risk of CV events and the well described risk of serious, and potentially life- threatening, gastrointestinal bleeding.

References

1. Celebrex Prescribing Information. New York, NY: G.D. Searle, LLC; May 2019. Available at: http://www.celebrex.com/. Accessed February 3, 2021.
2. Lanza FL, Chan FK, Quigley EM et al. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol. 2009 Mar;104(3):728-38. doi: 10.1038/ajg.2009.115. Epub 2009 Feb 24.
3. Kolasinski SL, Neogi T et al. American College of Rheumatology 2019 Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip and Knee. Arthritis Rheum. 2020 Feb;2(71): 220-233. doi: 10.1002/art.41142.
4. Ringold S, Angeles-Han, ST, Beukelman T et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approahces for Non-Systemic Polyarthritis, Sacroilitis, and Enthesitis Arthritis Rheum. 2019Jun;6(71):717-734. doi: 10.1002/art.23870.
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6. Yeomans ND. A comparison of omeprazole with ranitidine for ulcers associated with nonsteroidal anti-inflammatory drugs. N Engl J Med 1998;338:727-734.
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osteoarthritis and rheumatoid arthritis (CLASS Study). JAMA 2000;284:1247- 1255.

8. Mukherjee, et al. Risk of cardiovascular events associated with selective COX-2 inhibitors. JAMA 2001;286:954-959.
9. Juni, et al. Are selective COX 2 inhibitors superior to traditional non steroidal anti- inflammatory drugs. BMJ 2002;324:1287-1288.
10. Solomon DH, et al. Relationship between selective cyclooxygenase-2 inhibitors and acute myocardial infarction in older adults. Circulation 2004;109(17):2068-2073.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Updated max doses:	4/29/2020	05/20/2020

Indication	Dosing Regimen	Maximum Dose
Osteoarthritis	200 mg PO once daily or 100 mg PO BID	200mg/day
Rheumatoid arthritis	100 to 200 mg PO BID	400mg/day
Juvenile rheumatoid arthritis	10-25 kg: 50 mg PO BID > 25 kg: 100 mg PO BID	200 mg/day
Ankylosing spondylitis	200 mg PO once daily or 100 mg PO BID. If no effect is observed after 6 weeks, a trial of 400 mg daily may be of worthwhile	400mg/day
Acute pain or Primary dysmenorrhea	400 mg PO initially, followed by a 200 mg	400 mg/day (600mg for one day)

	dose if needed on the first day. On subsequent days, 200 mg PO BID as needed	
Updated Criteria II, A, i to: Currently receiving medication that has been authorized by Rxadvance, or documentation supports that member is currently receiving Cabometyx® or Cometriq® for a covered indication and has received this medication for at least 30 days;	05/08/2020	05/20/2020
Policy was reviewed: 1. Clinical Policy Title Table was updated. 2. Drug(s) Applied was updated. 3. Last Review Date was updated. 4. Line of Business Policy Applies to was update to all lines of business. 5. APPENDIX B: Therapeutic Alternatives verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance...." 6. APPENDIX C: Contraindications/Boxed Warnings were updated. 7. Initial Approval criteria: Medicaid approval duration were updated from length of benefit to 12 months. 8. Continued Approval criteria: Medicaid approval duration were updated from length of benefit to 12 months. 9. Anaprox®, Indocin®, Indocin SR®, Meclomen®, Orudis®, Clinoril® were removed from therapeutic alternatives table due to off market. 10. References were updated.	02/03/2021	03/09/2021

11. Updated indication and dosing information to include abbreviations: Osteoarthritis (OA), Rheumatoid arthritis (RA), Juvenile rheumatoid arthritis (JRA) in patients 2 years and older, Ankylosing spondylitis (AS), Acute pain (AP), Primary dysmenorrhea (PD) 12. Updated dosing information for Ankylosing Spondylitis: If no effect is observed after 6 weeks, a trial of 400 mg (single or divided doses) may be of benefit. 13. Dosing information updated to include: Hepatic Impairment: Reduce daily dose by 50% in patients with moderate hepatic impairment (Child-Pugh Class B). Poor Metabolizers of CYP2C9 Substrates: Consider a dose reduction by 50% (or alternative management for JRA) in patients who are known or suspected to be CYP2C9 poor metabolizers.		