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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	September 8, 2011
Subject:	Celebrex	**Page:**	1 of 7

Last Review Date: June 16, 2022

Celebrex

Description

Celebrex (celecoxib)

Background
Celebrex (celecoxib) is commonly referred to as a COX-2 selective inhibitor. The mechanism of action of Celebrex is believed to be inhibition of prostaglandin synthesis, primarily via inhibition of cyclooxygenase-2 (COX-2). It is classified as a NSAID, which have become synonymous with the management of acute musculoskeletal injuries. NSAIDs reduce pain through their inhibition of the enzyme cyclooxygenase (COX), leading to a significant decrease in prostaglandin production. COX exists as two isoenzymes, COX-1 and COX-2. COX-1 enzyme exists in many body tissues, including the stomach. Most frequent side effects on the gastrointestinal tract are a result of the COX-1 inhibition, the most common being gastritis and upper gastrointestinal ulcer and bleeding. COX-2 enzyme is associated with inflammation in the joints. Selective inhibition of COX-2 should lead to decreased inflammation in musculoskeletal tissues and, by sparing COX-1, to a decrease in the incidence of GI mucosal injury (1-3).

Regulatory Status
FDA-approved indications: Celebrex is a nonsteroidal anti-inflammatory drug FDA indicated for Osteoarthritis (OA), Rheumatoid Arthritis (RA), Juvenile Rheumatoid Arthritis (JRA) in patients 2 years and older, Ankylosing Spondylitis (AS), Acute Pain (AP), and Primary Dysmenorrhea (PD) (1).

Off-Label Use: (4)
Celebrex has been shown to be safe and effective as adjunctive therapy in treating chronic synovitis and joint pain in patients with hemophilia.

Celebrex has a boxed warning regarding the gastrointestinal, cardiovascular, bleeding and renal risk. Celebrex can cause peptic ulcers, GI bleeding, and/or perforation of the stomach or intestines, which can be fatal. NSAIDS may cause an increased risk of serious CV thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with CV disease or risk factors for CV disease may be at greater risk. Celebrex is contraindicated for treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery. Celebrex is contraindicated in patients with peptic ulcer disease or history of GI bleeding. Celebrex is contraindicated in patients with advanced renal impairment and in patients at risk for renal failure due to volume depletion (1).

Principal risk factors for serious GI events and hospitalization were age, smoking, use of alcohol, a history of prior NSAID-related ulceration and its complications, corticosteroid or anticoagulant use, and debilitating disorders such as cardiovascular disease. The use of low-dose aspirin alone, in the absence of other risk factors is associated with an increased risk for both GI bleeding and death from GI complications (3).

NSAIDs should be prescribed with extreme caution in patients with a prior history of ulcer disease or gastrointestinal bleeding. To minimize the potential risk for an adverse GI event, the lowest effective dose should be used for the shortest duration consistent with individual patient treatment goals. Physicians and patients should remain alert for signs and symptoms of GI ulceration and bleeding during Celebrex therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. For high-risk patients, alternate therapies that do not involve NSAIDs should be considered. Celebrex is contraindicated in patients with active GI bleeding (1).

The safety and effectiveness of Celebrex have not been established in pediatric patients under the age of 2 years, in patients with body weight less than 10kg (22 lbs), and in patients with active systemic features (1).

Related policies
Anti-Inflammatory Pain Powders

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Celebrex may be considered **medically necessary** in patients 2 years of age or older for the treatment of acute pain, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, primary

dysmenorrhea or chronic synovitis or joint pain in patients with hemophilia; and if the conditions indicated below are met.

Celebrex may be considered **investigational** for patients below 2 years of age and for all other indications.

Prior-Approval Requirements

Prior authorization is not required if the patient has filled a prescription of at least one pharmacologic indicator of a risk factor for developing gastrointestinal (GI) adverse events (e.g., anticoagulant therapy, antiplatelet therapy or oral corticosteroid therapy) OR at least one non-steroidal anti-inflammatory drug (NSAID) prescription (e.g., NSAID or NSAID/GI combination product) OR at least one gastrointestinal medication prescription (e.g., proton pump inhibitor [PPI], histamine type 2 receptor antagonist [H2 antagonist], misoprostol, or sucralfate) within the past 365 days.

Age 2 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Acute Pain
2. Rheumatoid Arthritis
3. Osteoarthritis
4. Juvenile rheumatoid arthritis (JRA)
5. Ankylosing Spondylitis
6. Primary Dysmenorrhea
7. Chronic synovitis or joint pain associated with hemophilia

Prior – Approval *Renewal* Requirements

Age 2 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Acute Pain

2. Rheumatoid Arthritis
3. Osteoarthritis
4. Juvenile rheumatoid arthritis (JRA)
5. Ankylosing Spondylitis
6. Primary Dysmenorrhea
7. Chronic synovitis or joint pain associated with hemophilia

Policy Guidelines

Pre - PA Allowance

Age 2 years of age or older

Quantity

Strength	Quantity
50 mg	360 capsules per 365 days **OR**
100 mg	360 capsules per 365 days **OR**
200 mg	180 capsules per 365 days **OR**
400 mg	180 capsules per 365 days

Duration 365 days

Prior - Approval Limits

Quantity

Strength	Quantity
50 mg	Up to 400 mg per day in any combination
100 mg	
200 mg	
400 mg	

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary
NSAIDs have become synonymous with the management of acute musculoskeletal injuries. They are some of the most widely used medications, and are reliable and effective when used appropriately for pain relief and to reduce inflammation. NSAIDs reduce pain through their inhibition of the enzyme cyclooxygenase (COX), leading to a significant decrease in prostaglandin production. COX exists as two isoenzymes, COX-1 and COX-2. COX-2 inhibitors are associated with a significantly lower incidence of gastric and duodenal ulcers when compared to traditional NSAIDs. Celebrex is contraindicated in patients with active GI bleeding. The mechanism of action of Celebrex is believed to be inhibition of prostaglandin synthesis, primarily via inhibition of cyclooxygenase-2 (COX-2). It does not inhibit the cyclooxygenase-1 (COX-1). Celebrex is commonly referred to as a COX-2 selective inhibitor (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Celebrex while maintaining optimal therapeutic outcomes.

References

1. Celebrex [package insert]. New York, NY: Searle & Co and Pfizer Inc.; April 2021.
2. Farkouh ME, Greenberg BP. An Evidence-Based Review of the Cardiovascular Risks of Nonsteroidal Anti-inflammatory Drugs. *Am J Cardiol* 2009; 103:1227-1237.
3. Lanza FL, Chan FKL, Quigley EMM, et al. Guidelines for Prevention of NSAID-Related Ulcer Complications. *Am J Gasteoenterol 2009; 104:728-738.*
4. Rattray B, Nugent DJ, Young G. Celecoxib in the treatment of haemophilic synovitis, target joints, and pain in adults and children with haemophilia. Haemophilia. 2006 Sep;12(5):514-7. doi: 10.1111/j.1365-2516.2006.01311.x. PMID: 16919082.

Policy History

Date	Action	Reason
May 2007	In order to be consistent with current benefit design, we recommend that Celebrex 50mg capsules be included in the overall current upfront COX-2 standard allowance of 90 days' supply per year.	
September 2008	The Prior Approval Limits were increased by a 30 day supply (1/3 increase) to allow for members to fill up to 90-day supply at mail order after a starter quantity is filled at retail.	

May 2012	Comprehensive criteria review and update. FAP deleted (no longer FDA-approved)
March 2013	Annual editorial review and reference update. Minimum age 2 years.
June 2014	Annual review and addition of contraindication: active GI bleeding
June 2015	Annual review
March 2016	Annual review and reference update Policy number changed from 5.02.06 to 5.70.06
March 2017	Annual editorial review and reference update Addition requirements for acute pain and location of pain and no continuous use for same location in renewal
June 2017	Removal of at risk for adverse GI events, at risk for bleeding, at risk for cardiovascular events, at risk for renal impairment
September 2017	Annual review
March 2018	Annual editorial review
November 2018	Annual review. Changed Pre-PA allowance to double the quantities allowed per 365 days and Pre-PA age requirement from 55 years to 2 years of age
March 2019	Annual review
March 2020	Annual review and reference update
March 2021	Annual review
April 2021	Addition of off-label indication of chronic synovitis or joint pain associated with hemophilia. Removed location of acute pain and the renewal requirement prohibiting continuous therapy for same location as previously treated. Changed acute pain PA duration from 3 months to 12 months per FEP
May 2021	Addition of step out statement: “Prior authorization is not required if the patient has filled a prescription of at least one pharmacologic indicator of a risk factor for developing gastrointestinal (GI) adverse events (e.g., anticoagulant therapy, antiplatelet therapy or oral corticosteroid therapy) OR at least one non-steroidal anti-inflammatory drug (NSAID) prescription (e.g., NSAID or NSAID/GI combination product) OR at least one gastrointestinal medication prescription (e.g., proton pump inhibitor [PPI], histamine type 2 receptor antagonist [H2 antagonist], misoprostol, or sucralfate) within the past 365 days.”
June 2021	Annual review and reference update
September 2021	Annual review
December 2021	Annual review. Changed PA Qty Limits from #tabs/90 days to MDDL of 400mg.
March 2022	Annual review

June 2022	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.