Medical Policy

BlueCross BlueShield of Kansas
An Independent Licensee of the Blue Cross and Blue Shield Association

Title: COX-2 Inhibitor (Celebrex®)

- **Prime Therapeutics will review Prior Authorization requests.**

  Prior Authorization Form:
  http://www.bcbsks.com/CustomerService/Forms/pdf/COX2_Mobic_PAform.pdf

  For information concerning Prior Authorization Prescription Drugs:
  http://www.bcbsks.com/CustomerService/PrescriptionDrugs/prior_authorization.htm

  Link to Drug List (Formulary):
  http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.htm

Professional
Original Effective Date: November 2004
Revision Date(s): April 2005; May 2006; July 2006; August 2006; May 20, 2011; July 1, 2012; October 1, 2013; October 17, 2014
Current Effective Date: October 17, 2014

Institutional
Original Effective Date: October 1, 2007
Revision Date(s): May 20, 2011; July 1, 2012; October 1, 2013; October 17, 2014
Current Effective Date: October 17, 2014

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

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DESCRIPTION

The intent of the Celebrex prior authorization program is to accommodate the use of Celebrex in patients who are at high risk of developing an adverse gastrointestinal (GI) event when using a nonselective nonsteroidal anti-inflammatory drug (NSAID) based on Food and Drug Administration (FDA) approved prescribing information and/or clinical studies and/or treatment guidelines.

FDA Approved Indications and Dosage[1]

Drug	Signs/Symptoms of OA* & RA in adults	Signs/Symptoms of JRA in patients > 2 yrs	Signs/Symptoms of Ankylosing Spondylitis (AS)	Acute pain (AP) in adults	Treatment of primary dysmenorrhea (PD)	Dosage and Administration
Celebrex (celecoxib) capsules (50 mg, 100 mg, 200 mg, 400 mg)	✓	✓	✓	✓	✓	**Children >2 yrs:** **JRA:** 50 mg to 100 mg twice daily **Adults:** **OA, RA:** 100 mg to 200 mg once or twice daily **AS:** 200 mg once daily or 100 mg twice daily; if no effect after 6 weeks, 400 mg once daily or 200 mg twice daily may be tried **AP, PD:** 400 mg initially, then 200 mg twice daily as needed

*OA=osteoarthritis; RA=rheumatoid arthritis; AP=acute pain; JRA=juvenile rheumatoid arthritis; AS=ankylosing spondylitis; PD=primary dysmenorrhea

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POLICY

Prior Authorization Criteria for Approval

Celebrex will be approved when ANY ONE of the following is met:

1. The patient is 65 years of age or older
   OR
2. The patient has a history or current diagnosis of peptic ulcer (gastric or duodenal), GI bleed, GI obstruction, GI perforation
   OR
3. The patient has a history or current diagnosis that may put the patient at increased risk for developing an adverse GI event
   OR
4. The patient is currently receiving a medication* indicating risk for an adverse GI event
   (evidence of a paid claim within the past 120 days, or patient is new to the claim system within the past 120 days AND a statement by the prescriber that the patient has taken an oral anticoagulant or systemic corticosteroid in the past 120 days)
   *systemic corticosteroid OR oral anticoagulants: warfarin, dabigatran (Pradaxa) or rivaroxaban (Xarelto), or apixaban (Eliquis)

Length of approval: 12 months

RATIONALE

The key clinical issue in prescribing celecoxib, a COX-2 inhibiting agent, is whether the reduction in ulcer complications is great enough to warrant choosing celecoxib over a nonselective anti-inflammatory agent (NSAID) [i.e., diclofenac, diflunisal, fenoprofen, ibuprofen, flurbiprofen, indomethacin, ketoprofen, naproxen, piroxicam, salsalate].[10]

Celecoxib differs from the nonselective NSAIDs by primarily inhibiting COX-2 instead of both COX-1 and COX-2.The explanation that sparing COX-1 can eliminate ulcer risk, was challenged by animal studies that indicated that both COX-1 and COX-2 must be inhibited for gastric ulceration to occur. Thus, the explanation for the reduced gastrointestinal (GI) toxicity of COX-2–specific inhibitors appears to be their lack of dual COX inhibition, rather than COX-1 sparing effects. This explains why in patients taking both cardioprotective aspirin (primarily a COX-1 inhibitor) and a COX-2 inhibitor, the ulcer risk of a dual COX inhibitor would be predicted.[2-3] The large outcome studies support these predictions.[4-5]

Celecoxib is the only COX-2 inhibitor remaining on the US market after the removal of rofecoxib and valdecoxib by the FDA due to the increased risks of cardiovascular (CV) and thromboembolic events. The Adenoma Prevention with Celecoxib Study, which included 2026 patients assigned to celecoxib 200 mg twice daily, celecoxib 400 mg twice daily, or placebo, was stopped early by the National Cancer Institute after a mean follow-

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up of 33 months[9]. A significantly higher number of celecoxib-treated patients experienced a myocardial infarction (MI), stroke, or CV death compared with those receiving placebo (Odds ratio [OR], 2.5 for celecoxib 400 mg daily; 95% confidence interval [CI], 1.0–7.0; P=.06, and OR, 3.4 for celecoxib 800 mg daily 95% CI, 1.4–9.3; P=009).[9]

Strategies for gastroprotection therefore include supplementation with a synthetic prostaglandin analog (misoprostol), gastric acid suppression (proton pump inhibitors), or the selective use of those NSAIDs least likely to inhibit gastric prostaglandins. This decision depends primarily on the individual patient's risk for developing an NSAID-induced ulcer and their CV risk history.[2-5] Risk factors for NSAID-related GI complications are previous GI event, especially if complicated by age, concomitant use of anticoagulants, corticosteroids, other NSAIDs including low-dose aspirin, high-dose NSAID therapy, and chronic debilitating disorders, especially cardiovascular disease.[6]

For those individuals who require NSAIDs, and have a history of gastrointestinal adverse events associated with nonselective NSAID use, or are intolerant to nonselective NSAIDs the FDA recommends COX-2 selective agents for "limited use."[7] The FDA also recommends that physicians take into consideration the safety information about the selective COX-2 inhibitors and make decisions on an individual patient basis.[7]

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."[8]

Celecoxib's prescribing information has been updated to include a boxed warning indicating potential cardiovascular and gastrointestinal risks that are consistent with warnings of other NSAIDs. Additionally, a medication guide is now required for celecoxib. The boxed warning also includes a new contraindication for celecoxib in the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.[1]

The Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review 2011: Analgesics for Osteoarthritis (OA) states that celecoxib and most nonselective, nonaspirin NSAIDs appear to be associated with an increased risk of serious cardiovascular harms.[11]

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CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

There is no specific HCPCS code for Celebrex® (celecoxib).

REVISIONS

07-01-2012	In Policy section: ▪ Removed the following medical necessity criteria: "The patient has a diagnosis of familial adenomatous polyposis (FAP)" ▪ Removed the word "gastrointestinal" in Item 2 to read, "The patient has a history or current diagnosis of peptic ulcer (gastric or duodenal), GI bleed, GI obstruction, GI perforation." ▪ Revised length of approval from: "Length of approval: Indefinite" to: "Length of approval if criteria 1 or 2 or 3 are met: Indefinite Length of approval if criteria 4 met: Up to 12 months"
	Rationale section added
	Referenced updated
10-01-2013	Title revised from "COX-2 Inhibitor (Celebrex®) Prior Authorization Criteria" to "COX-2 Inhibitor (Celebrex®)" ▪ Added under Prior Authorization Form link "Prime Therapeutics will review Prior Authorization requests."
	In Description section: ▪ Removed Target Drugs reference ▪ Added FDA Approved Indications and Dosage chart
	In Policy section: ▪ In Item #4 added list of medication indicating risk for an adverse GI event to read, "*systemic corticosteroid OR oral anticoagulants: warfarin, dabigatran (Pradaxa) or rivaroxaban (Xarelto), or apixaban (Eliquis)". This addition did not change the policy intent.
	Rationale section updated
	Coding section added to reflect "There is no specific HCPCS code for Celebrex® (celecoxib)"
	References updated
10-17-2014	Description section reviewed
	In policy section: ▪ Added look-back period ▪ Revised Length of approval from "Length of approval if criteria 1, 2 or 3 are met: Indefinite" and "Length of approval if criteria 4 is met: Up to 12 months" to "Length of approval: 12 months"
	Coding section reviewed
	Rationale section reviewed

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	In Revision section: ▪ Removed update details for 04-2005, 08-2006, 10-01-2007, 05-20-2011.
	References updated

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