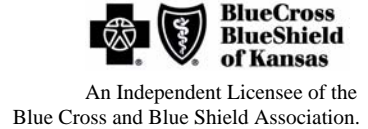


Medical Policy



Title: COX-2 Inhibitors Prior Authorization Criteria

Professional

Original Effective Date: November 2004
 Revision Date(s): April 2005; May 2006;
 July 2006, August 2006
 Current Effective Date: October 1, 2007

Institutional

Original Effective Date: October 1, 2007
 Revision Date(s):
 Current Effective Date: October 1, 2007

Prior Authorization Form:

http://www.bcbsks.com/CustomerService/Forms/pdf/COX2_Mobic_PAform.pdf

DESCRIPTION

Brand	generic	Dosage Form
Celebrex [®]	celecoxib	oral capsule

FDA APPROVED INDICATIONS¹

Celebrex^{®1}

Carefully consider the potential benefits and risks of Celebrex and other treatment options before deciding to use Celebrex. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Celebrex[®] is indicated

- For relief of the signs and symptoms of osteoarthritis
- For relief of the signs and symptoms of rheumatoid arthritis in adults
- For relief of the signs and symptoms of juvenile rheumatoid arthritis in patients 2 years and older
- For the relief of signs and symptoms of ankylosing spondylitis
- For the management of acute pain in adults
- For the treatment of primary dysmenorrhea, and
- To reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis (FAP), as an adjunct to usual care (e.g., endoscopic surveillance, surgery). It is not known whether there is a clinical benefit from a reduction in the number of colorectal polyps in FAP patients. It is also not known whether the effects of Celebrex treatment will persist after Celebrex is discontinued. The efficacy and safety of Celebrex treatment in patients with FAP beyond six months have not been studied.

POLICY**CLINICAL RATIONALE FOR SELECTING COX-2 INHIBITORS FOR PRIOR AUTHORIZATION***Prior Authorization Criteria and Plan Design*

The intent of the Prior Authorization (PA) criteria for COX-2 inhibitors is to accommodate their use for the treatment of labeled indications while encouraging use of cost-effective generic nonsteroidal anti-inflammatory drugs (NSAIDs) as first-line agents when possible. The cyclooxygenase-2 inhibitors (COX-2) medications were selected for the PA edit because there is evidence that they are overused as first-line agents when equally effective, less expensive generic agents are available within the NSAID class.²⁻⁹

The key clinical issue is whether the reduction in ulcer complications is great enough to warrant prescribing COX-1 sparing (COX-2) agents instead of nonselective agents.¹⁰ This decision depends primarily on the individual patient's risk for developing an NSAID-induced ulcer complication.^{6,7,10,11} The risk of cardiovascular events has also become a factor in consideration for use of COX-2 inhibitors.¹²⁻¹⁷ In April 2005 the Food and Drug Administration (FDA) issued a public health advisory announcing the withdrawal of Bextra[®] (valdecoxib) from the market and the addition of "black box" warnings to the Celebrex product labeling, indicating potential cardiovascular risk and encouraging avoidance in high risk individuals.^{12,13} Product labeling for nonselective NSAIDs also were to be revised to indicate potential cardiovascular risk.^{12,13} Studies and data analysis are on-going to further define how this risk varies with agent, dose, or duration of therapy.¹²⁻¹⁷

COX-2 inhibitors have not demonstrated greater efficacy than traditional NSAID comparators in relieving the signs and symptoms of osteoarthritis or rheumatoid arthritis. Published evaluations and reviews have found no clear difference in efficacy between COX-2 inhibitors and nonselective NSAIDs.^{2-9,18}

Nonselective NSAID agents are well documented to increase the risk for upper gastrointestinal (GI) events such as ulcers, bleeding, perforation, and obstruction.^{1,6,11,19} Studies also suggest that NSAIDs may increase the risk of developing similar lower GI adverse events.²⁰⁻²² In addition, studies have shown that patients with a prior history of peptic ulcer disease and/or gastrointestinal bleeding and who use NSAIDs, have a greater than 10-fold higher risk for developing a GI bleed than patients with neither of these risk factors.^{1,6,7,11,19} Previous upper GI bleed and/or peptic ulcer disease has been determined to be the single most important predictor of another upper GI bleed or another incidence of peptic ulcer disease.^{23,24}

The gastro-protective agent misoprostol and two of the proton pump inhibitors (PPIs)—esomeprazole (Nexium[®]) and lansoprazole (Prevacid[®])—are FDA-labeled for prophylaxis or treatment of NSAID-induced gastric ulcers.^{9,25-33} The pharmaceutical compendia (USP/DI, AHFS-DI) list prevention and/or treatment of NSAID-induced gastric ulcers as accepted uses (labeled or unlabeled) for misoprostol, esomeprazole, lansoprazole, and

omeprazole.²⁸⁻²⁹ A Cochrane review (2002) concluded that misoprostol, PPIs, and double dose H2-receptor antagonists (H2RAs) may be effective at preventing chronic NSAID-related endoscopic gastric and duodenal ulcers.³⁰ Other reviews similarly concluded that misoprostol and PPIs may be effective in reducing the risk of clinically significant upper GI adverse events associated with nonselective NSAIDs; normal doses of H2RAs have not been shown to be as effective.^{9,31-33} Patients who have adverse GI effects from using nonselective NSAIDs may add misoprostol or a PPI. The step edit uses these combinations to identify patients at risk for or with a history of adverse GI events from nonselective NSAIDs.

Therapy with COX-2 inhibitors compared to nonselective NSAIDs may be associated with a lower incidence of both upper and lower GI adverse events;^{1,2,6-8,11,20,22,34,35} For example, a comparative study of celecoxib and traditional NSAIDs determined that celecoxib, when used for 6 months in a dosage 2 to 4 times the maximum therapeutic dosage, is associated with a lower incidence of combined clinical upper GI events than the comparators, ibuprofen and diclofenac, used at standard therapeutic dosages.²

Although there appears to be a synergism between *Helicobacter pylori* and the formation of peptic ulcer and bleeding,³⁶ the diagnosis of *H. pylori* alone is not included in the criteria for approval. Guidelines for the treatment of *H. pylori* suggest discontinuation of NSAID agents during eradication therapy and ulcer healing, if possible.³⁷ There is insufficient data indicating that use of COX-1 sparing agents instead of nonselective NSAIDs decrease the risk of an adverse GI event in *H. pylori* positive patients.³⁷

In addition to a past history of ulcer disease, pharmacoepidemiological studies have identified several other co-therapies or co-morbid conditions that may increase the risk for GI bleeding such as treatment with oral corticosteroids, treatment with anticoagulants, longer duration of NSAID therapy, smoking, alcoholism, older age, and poor general health status.¹ Corticosteroid drugs do not independently cause ulcer disease. The use of these drugs in conjunction with NSAIDs however increases the risk of a GI event approximately twofold.^{11,23} Patients with the diagnosis of rheumatoid arthritis (RA) may be at an increased risk for developing a GI adverse event because RA patients are likely to be prescribed corticosteroids as part of their treatment regimen.³⁸ The patient's previous prescription claims are used to identify the patient's potential risk for an NSAID-induced ulcer complication. Concomitant oral anticoagulant use also increases the risk of peptic ulcer bleed in the setting of NSAID therapy.²³ The increase in risk ranges from two- to 12-fold, depending upon the patient population be studied.^{6,7,11,19,24,39} Clinical literature does document that smoking and alcohol may be factors in the pathogenesis of peptic ulcer disease, but the evidence for alcohol and smoking as risk factors for NSAID-related GI events has been inconsistent.^{27,40-47}

Age alone puts patients at a higher risk for developing a GI-adverse event.^{6,7,11,19,23} There does not appear to be a threshold age where the risk of a GI complication increases abruptly; rather, the risk of a complication appears to increase gradually with advancing age.^{6,7,11,19,23} Thus, the older the patient is, the greater is their risk of a GI complication.

One study defined elderly as patients who are 65 years of age or older.⁴⁸ Two analyses define elderly as 76 years of age for rofecoxib and 81 years of age for celecoxib.^{36,37}

Electronic Claims Edit

The overall process for prior authorization requires that another drug or drugs be tried for a specific quantity of drug in the previous time period before the claim drug. If the patient has met any of the requirements outlined below, the requested prior authorization medication will be paid under the patient's current prescription benefit. If the patient does not meet the electronic claims edit criteria, then the system will reject with the message indicating that prior authorization is necessary. The manual PA criteria for approval would then be applied to requests submitted by the patients' practitioner for evaluation.

The intent of the initial electronic claims edit is to electronically identify patients that may have a contraindication for the non-selective NSAID (those that inhibit both cyclooxygenase-1 and cyclooxygenase-2). The system edit reviews claims that have a days supply that ends within 120 days prior to the new COX-2 claim. Contraindications to the non-selective NSAIDs are identified by detecting medications in the claims history that are indicators for a previous or future gastrointestinal (GI) adverse event.

The initial electronic claims edit will identify patients who are taking or have taken an oral anticoagulant or systemic corticosteroid in the 120 days prior to the current COX-2 inhibitor claim. The electronic edit will also identify patients who are taking or have taken a nonselective NSAID with misoprostol or a proton pump inhibitor (PPI), including the combination product Arthrotec[®] (diclofenac sodium/misoprostol), in the previous 120 days. A 120 day timeframe was selected to accommodate various treatment regimens of these medications. The claims system is designed to identify and count any oral anticoagulant or systemic corticosteroid claim with a days supply that overlaps into the 120-day look-back period.

The initial electronic claims edit will also electronically identify patients who are 65 years of age or older and will allow use of a COX-2 inhibitor based on the patient's age alone. The age of 65 and older was selected because the product labeling for Celebrex defines a geriatric patient as being 65 years of age or older.¹

Prior Authorization (PA) Criteria for Approval

The intent of the *PA Criteria for Approval* is to ensure that patients who are at a greater risk for a GI-adverse event when using non-selective NSAIDs (by diagnoses, medications or medical history) are identified and approved. The criteria for approval repeat the electronic claims edit requirements to ensure that all previous therapies that meet the criteria are taken into account. In addition, patients with a prior history of peptic ulcer, regardless of cause, are approved through the PA review process.

Patients with past or present ulcer and current *H. pylori* infection will be approved through the prior authorization process based on the ulcer history. Although a poor

health status and long term disease may increase the patients' risk for a GI bleed, patients are not automatically approved because they have a chronic disease (e.g., rheumatoid arthritis) unless their medication history increases their risk. Patient smoking and alcohol use will be evaluated in the context of persistent or permanent physiologic changes. Patients prescribed celecoxib to reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis (FAP) will also be granted a manual approval.

The length of the PA approval is indefinite. Indefinite approvals may be subject to re-evaluation if selection criteria change or safety issues become apparent.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Celebrex (celecoxib)

Initial and Renewal Evaluation

1. Is the patient 65 years of age or older?
If yes, approve indefinitely. If no, continue to 2.
2. Please indicate if the patient has a history or current diagnosis of one of the following?
 - a. Peptic ulcer (includes duodenal and stomach)
 - b. Gastrointestinal (GI) bleed
 - c. GI obstruction
 - d. GI perforation
 - e. NoneIf a, b, c, or d, approve indefinitely. If e, continue to 3.
3. Does the patient have a current diagnosis or medical history that may put the patient at increased risk for developing a GI adverse event?
If yes, approve indefinitely. If no, continue to 4.
4. Is the patient currently taking an oral anticoagulant [e.g., Coumadin (warfarin)]?
If yes, approve indefinitely. If no, continue to 5.
5. Is the patient currently taking systemic corticosteroids on a regular basis (i.e., long-term daily or pulse-therapy)?
If yes, approve indefinitely. If no, continue to 6.
6. Is the patient currently taking a nonselective NSAID and misoprostol or a PPI, including the combination product Arthrotec[®] (diclofenac sodium/misoprostol)?
If yes, approve indefinitely. If no, continue to 7.
7. Is the practitioner prescribing Celebrex (celecoxib) to reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis (FAP)?
If yes, approve indefinitely. If no, deny.

CONCLUSION

The COX-2 inhibitors electronic claims edit is designed to identify patients by their medication history and to provide automatic payment of claims when the patient's medication history indicates current or recent use of an anticoagulant or a systemic corticosteroid, or a nonselective NSAID with misoprostol or a PPI, including the

combination product Arthrotec[®] (diclofenac sodium/misoprostol). Claims will also automatically pay if the member is age 65 or older. The electronic claims edit process allows for automatic payment of these agents when a medical diagnosis for a GI condition putting the member at high risk for adverse events from nonselective NSAID therapy or a diagnosis of FAP is documented. The PA review process allows for individual review of claims for COX-2 inhibitors to identify patients who have a history for, or are at a greater risk for developing, a GI adverse event that is not apparent on electronic claims history. The electronic claims edit optimizes the use of first line generic agents before the COX-2 inhibitors.

REVISIONS

Effective 04-2005	Bextra removed.
Effective 08-2006	Mobic removed.

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