BlueCross BlueShield Federal Employee Program

CELEBREX (celecoxib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Celebrex 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 (1). 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 (2-3).

Regulatory Status

FDA-approved indication: 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), 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).

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.; May 2019.
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.