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. 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(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).

Celebrex product labeling carries a boxed warning regarding cardiovascular and gastrointestinal risks. Celebrex may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. Celebrex causes an increased risk of serious gastrointestinal 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 (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
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). Celebrex product labeling carries a boxed warning regarding cardiovascular and gastrointestinal risks.

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

References