CELECOXIB

THERAPEUTICS

Brands
- Celebrex

Generic?
Yes

Class
- Nonsteroidal anti-inflammatory (NSAID) – COX-2 selective inhibitor

Commonly Prescribed For
(FDA approved in bold)
- Rheumatoid arthritis
- Osteoarthritis
- Acute pain or primary dysmenorrhea
- Ankylosing spondylitis
- Headaches, arthritis, painful inflammatory disorders
- Musculoskeletal pain

How the Drug Works
- Inhibits cyclo-oxygenase-2 (COX-2) thus inhibiting synthesis of prostaglandins, mediators of inflammation

How Long until It Works
- Less than 2 hours

If It Works
- Continue to use

If It Doesn’t Work
- Some patients only have a partial response where some symptoms are improved but others persist or continue to wax and wane without stabilization of pain
- Other patients may be nonresponders, sometimes called treatment-resistant or treatment-refractory
- Consider increasing dose, switching to another agent or route or adding an appropriate augmenting agent or utilizing an entirely different nonpharmacologic approach (e.g. neuromodulation)
- Consider biofeedback or hypnosis for pain
- Consider physical medicine approaches to pain relief
- Consider the presence of noncompliance and counsel patient
- Switch to another agent with fewer adverse effects

Best Augmenting Combos for Partial Response or Treatment Resistance
- Consider adding an opioid

Tests
- None for healthy individuals
- Blood urea nitrogen (BUN)/creatinine – if suspected renal issues
- Consider checking liver function tests for long-term use

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
- Effects on prostaglandins likely cause most GI and renal AEs

Notable AEs
- Inhibition of platelet aggregation is usually mild
- Elevation in hepatic transaminases (usually borderline)
- Peripheral edema
- Dizziness, fever, headache, insomnia
- Rash
- Abdominal pain, diarrhea, dyspepsia, flatulence, nausea, vomiting
- Arthralgia, back pain
- Cough, nasopharyngitis, pharyngitis, rhinitis, sinusitis, upper respiratory tract infection

Life-Threatening or Dangerous AEs
- GI ulcers and bleeding, increasing with duration of therapy
- May worsen congestive heart failure
- May increase risk of fluid retention and edema, cardiovascular events, including MI and stroke
- Renal insufficiency, proteinuria, and hyperkalemia
- Thrombocytopenia
- Hypersensitivity reactions – most common in patients with asthma, anaphylactoid reaction, Stevens–Johnson syndrome, toxic epidermal necrolysis
Weight Gain
- Unusual

Sedation
- Not unusual

What to Do about AEs
- For significant GI or intracranial bleeding, stop drug. Some AEs respond to lowering dose
- Administer tablet with food or milk to decrease GI distress
- For GI irritation: consider sucralfate, H₂-receptor antagonist, proton pump inhibitors, or prostaglandin analog

Best Augmenting Agents for AEs
- Proton pump inhibitors may reduce risk of GI ulcers
- Many AEs cannot be improved with an augmenting agent

DOSING AND USE

Usual Dosage Range
- 100–400 mg/day

Dosage Forms
- Capsule, oral: 50 mg, 100 mg, 200 mg, 400 mg

How to Dose
- Use the lowest effective dose for the shortest duration of time, consistent with individual patient treatment goals
- Osteoarthritis: oral: 200 mg/day as a single dose or in divided doses twice daily
- Ankylosing spondylitis: oral: 200 mg/day as a single dose or in divided doses twice daily; if no effect after 6 weeks, may increase to 400 mg/day. If no response following 6 weeks of treatment with 400 mg/day, consider discontinuation and alternative treatment
- Rheumatoid arthritis: oral: 100–200 mg twice daily
- Acute pain or primary dysmenorrhea: oral: initial dose: 400 mg, followed by an additional 200 mg if needed on day 1; maintenance dose: 200 mg twice daily as needed

Dosing Tips
- Taking with food decreases absorption and reduces GI AEs

Overdose
- GI distress or bleed, drowsiness, paresthesias, and numbness are most common. Severe overdose may cause hypertension, metabolic acidosis, hepatic or renal failure, and cardiac arrest. Consider multiple doses of activated charcoal or hemodialysis for severe cases

Long-Term Use
- Safe for long-term use

Habit Forming
- No

How to Stop
- No need to taper

Pharmacokinetics
- Half-life is 11 hours (fasted), dose peak at ~3 hours. Hepatic metabolism via CYP2C9; forms inactive metabolites. Excretion: feces (~57% as metabolites; <3% as unchanged drug), urine (27% as metabolites; <3% as unchanged drug). 97% protein bound
- Substrate of CYP2C9 (major), CYP3A4 (minor); inhibits CYP2C8 (moderate), CYP2D6 (weak)

Drug Interactions
- Use with alcohol, bisphosphonates, corticosteroids, anticoagulants, and other NSAIDs increases GI bleeding risk
- Cyclosporin and NSAIDs increase risk of nephrotoxicity
- Cholestyramine may decrease absorption
- Aspirin use may decrease NSAID serum levels and increases risk of GI AEs
- May blunt effectiveness of beta-blockers and angiotensin-converting enzyme (ACE) inhibitors
- May decrease effect of loop diuretics and spironolactone
May increase drug levels and effects of digoxin, aminoglycosides, methotrexate, lithium, and phenytoin

Other Warnings/ Precautions

- Risk factors for GI bleeding include smoking, alcoholism, older age, poor health status, and treatment with anticoagulants or corticosteroids
- May cause photosensitivity

Do Not Use

- Hypersensitivity to celecoxib or any other NSAIDs, aspirin, sulfonamides, renal or hepatic disease, pain in the setting of coronary artery bypass graft (CABG) surgery

Breast-Feeding

- Most NSAIDs are excreted in breast milk. Do not breast-feed due to effects on infant cardiovascular system

THE ART OF PAIN PHARMACOLOGY

Potential Advantages

- Can be used in perioperative period without increased bleeding
- Less insult to GI mucosa than traditional nonselective NSAIDs

Potential Disadvantages

- Usual NSAID drawbacks

Primary Target Symptoms

- Pain
- Inflammation

Pearls

- Celecoxib is the only COX-2 selective inhibitor approved/available in the United States
- No significant effect on platelet function, since platelets do not contain COX-2
- Less GI insult than traditional or nonselective NSAIDs
- In a pooled analysis of 21 randomized clinical trials with celecoxib and nonselective NSAIDs, among older adults, the incidence of GI intolerability was lower with celecoxib than with naproxen, ibuprofen, or diclofenac. Fewer older patients discontinued due to GI intolerability AEs with celecoxib than with either naproxen or ibuprofen

SPECIAL POPULATIONS

Renal Impairment

- Use with caution in chronic renal insufficiency as may worsen renal function. Use low dose and monitor frequently

Hepatic Impairment

- Use with caution in patients with significant disease. May have increased risk of GI bleeding and toxicity

Cardiac Impairment

- May cause fluid retention and decompensation in patients with cardiac failure. May cause hypertension or lower effectiveness of antihypertensives

Elderly

- More likely to experience GI bleeding or CNS AEs

Pregnancy

- Category C, except category D in 3rd trimester. May prolong pregnancy and increase risk of septal heart defects, incidence of dystocias, and delivery time. May cause premature closure of ductus arteriosus and pulmonary hypertension. Do not use, especially in 3rd trimester

(continued) CELECOXIB
Suggested Reading


