ETODOLAC

THERAPEUTICS

Brands
- Lodine

Generic?
Yes

Class
- Nonsteroidal anti-inflammatory (NSAID)

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

How the Drug Works
- Like other NSAIDs, inhibits cyclo-oxygenase thus inhibiting synthesis of prostaglandins, a mediator of inflammation

How Long until It Works
- Less than 4 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 side effects

- Consider evaluation for another diagnosis or for a comorbid condition (e.g. medical illness, substance abuse, etc.)

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)
- Dizziness, chills/fever, depression, nervousness
- Rash, pruritus
- Dyspepsia, abdominal cramps, diarrhea, flatulence, nausea, vomiting, constipation, melena, gastritis
- Dysuria
- Weakness
- Blurred vision
- Tinnitus
- Polyuria

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 myocardial infarction 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.

### DOSSING AND USE

**Usual Dosage Range**
- 400–1200 mg/day

**Dosage Forms**
- Capsule, oral: 200 mg, 300 mg
- Tablet, oral: 400 mg, 500 mg
- Tablet, extended release, oral: 500 mg, 600 mg

**How to Dose**
- Pain management/rheumatoid arthritis/osteoarthritis: immediate release 400 mg twice daily or 300 mg 2 or 3 times daily as appropriate or 500 mg twice daily (maximum daily dose 1000 mg); extended release 400–1000 mg/day
- Acute pain: immediate release 200–400 mg orally every 6–8 hours, maximum daily dose 1000 mg

**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 5–8 hours (terminal, adults), extended release; children 6–16 years 12 hours, dose peak at 1–3 hours (immediate release), 5–6 hours (extended release), increased 1.4–3.8 hours with food.
- Bioavailability 100%, absorption greater than 80% onset of analgesic action 2–4 hours.
- Hepatic metabolism to active metabolite (6MNA) and inactive metabolites.
- Excretion: urine 73% (1% unchanged) and fecal 16%.
- 99% protein bound.

**Drug Interactions**
- Use with alcohol, bisphosphonates, corticosteroids, anticoagulants, and other NSAIDs increases GI bleeding risk.
- Cyclosporin and other 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 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.

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(continued) ETODOLAC
Do Not Use

- Hypersensitivity to any NSAID, treatment with anticoagulants, renal or hepatic disease, age under 12, rectal bleeding or proctitis (suppositories), pain in the setting of coronary artery bypass graft (CABG) surgery

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

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

- Once-daily dosing (extended-release formulation)

Potential Disadvantages

- Usual NSAID drawbacks

Primary Target Symptoms

- Pain
- Inflammation

Pearls

- May have somewhat reduced GI toxicity, perhaps due to preferential COX-2 inhibition over COX-1
- S- (+)-Etodolac, the S-isomer of the racemate etodolac, may be more potent (2.6 times more potent) and better tolerated than the racemate etodolac

Suggested Reading


