Duzallo (lesinurad, allopurinol)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Duzallo
- **Generic name:** Lesinurad, allopurinol
- **Pharmacological class:** URAT1 inhibitor + xanthine oxidase inhibitor
- **Strength and Formulation:** 200mg/200mg, 200mg/300mg; tabs
- **Manufacturer:** Ironwood Pharmaceuticals
- **How supplied:** Bottle—5, 30, 90
- **Legal Classification:** Rx

Duzallo


NDC 70785-022-30
30 Tablets
DUZALLO®
lesinurad/allopurinol
tablets
200 mg/300 mg
Dispense the accompanying
Medication Guide to each patient.
Rx only
Ironwood

Indications

- **Hyperuricemia associated with gout** in patients who have not achieved target serum uric acid levels with an appropriate daily dose of allopurinol alone

Limitation of use

- Not for treatment of **asymptomatic hyperuricemia**

Dosage & Administration

- Take in the AM with food and water
- ≥18yrs: 1 tab daily
- Patients on daily allopurinol dose
  - **200mg:** initially one 200mg/200mg tab daily
  - **300mg:** initially one 200mg/300mg tab daily
  - **>300mg**: initially one tab in place of an equal portion of the total daily allopurinol dose
  - **<300mg** (or <200mg with eCLCr <60mL/min): not recommended

Considerations for Special Populations

- **Pregnancy:** Limited data to inform drug-associated risk
- **Nursing mothers:** Consider benefits with potential adverse effects
- **Pediatric:** <18yrs: not established
- **Elderly:** No overall differences in safety or efficacy observed
- **Renal impairment:** See Contraindications
- **Hepatic impairment:** Severe impairment: not recommended

Contraindications

- Severe renal impairment (eCLCr <30mL/min)
- End-stage renal disease (ESRD)
- Kidney transplant recipients or dialysis patients
- Tumor lysis syndrome or Lesch-Nyhan syndrome

Warnings/Precautions

- Risk of acute renal failure
- Assess renal function prior to initiation and periodically thereafter
- Renal impairment (eCLCr<45mL/min): **do not initiate**
- If eCLCr <60mL/min or with SCr elevations 1.5–2X pre-treatment value: monitor more frequently; if SCr >2X pre-treatment value: interrupt treatment

Warnings/Precautions

- **Discontinue** therapy if eCLCr is persistently <45mL/min
- Maintain adequate hydration (2L of liquid per day)
- Give **gout flare prophylaxis** if patient not currently taking lesinurad
- Discontinue immediately if rash occurs

Warnings/Precautions

- Elevate liver function if anorexia, weight loss, or pruritus develops
- Pre-existing **liver disease**: perform LFTs periodically
- Females should use additional non-hormonal methods of contraception

Interactions

- Caution with concomitant moderate CYP2C9 inhibitors (eg, fluconazole, amiodarone) and in CYP2C9 poor metabolizers
- Antagonized by moderate CYP2C9 inducers (eg, rifampin, carbamazepine), aspirin >325mg/day
- Antagonizes CYP3A substrates (eg, sildenafil, amlodipine)

Interactions

- May affect sensitive CYP3A substrate (eg, HMG-CoA reductase inhibitors); monitor
- Concomitant epoxide hydrolase inhibitors (eg, valproic acid): not recommended
- May reduce efficacy of hormonal contraceptives
- Potentiates azathioprine and mercaptopurine toxicity; reduce dose of these by ⅓ to ¼ of usual dose and monitor

Interactions

- Assess PT periodically with concomitant coumarin anticoagulants (eg, dicumarol, warfarin)
- May potentiate chlorpropamide, cyclosporine
- Increased rash with ampicillin, amoxicillin
- Monitor renal function with thiazides

Adverse Reactions

- Headache
- Influenza
- Blood creatinine increased
- GERD
- Skin rash
- Renal events
- Gout flares
- Hepatotoxicity
- Cardiovascular events
- Drowsiness
- Bone marrow depression
- Severe hypersensitivity reactions (eg, eosinophilia, SJS, TEN)

Mechanism of Action

- **Lesinurad** reduces serum uric acid levels by inhibiting the function of transporter proteins involved in uric acid reabsorption in the kidney
- **Allopurinol** reduces production of uric acid by inhibiting the biochemical reactions immediately preceding its formation

Clinical Studies

- The efficacy of allopurinol + lesinurad has been demonstrated in 2 multicenter, randomized, double-blind, placebo-controlled, 12-month studies in adults with hyperuricemia and gout **(Study 1 and 2)**

Clinical Studies

- Patients were randomized to receive lesinurad 200mg, lesinurad 400mg, or placebo once daily in addition to their stable allopurinol dose (average 310mg dose)
- Efficacy was determined by:
  - Proportion of patients achieving target serum uric acid levels (<6mg/dL)
  - Rate of gout flare

Clinical Studies

- Lesinurad 200mg in combination with allopurinol was superior to allopurinol alone in lowering serum uric acid to <6mg/dL at Month 6
  - **Study 1** (N=603): 54% vs. 28% (difference 0.26, 95% CI: 0.17, 0.36)
  - **Study 2** (N=610): 55% vs. 23% (difference 0.32, 95% CI: 0.23, 0.41)
- Effects were maintained throughout the 12-month studies

Clinical Studies

- In Study 1 and 2, the rates of gout flare requiring treatment from Month 6 to 12 were not statistically different between lesinurad 200mg in combination with allopurinol vs. allopurinol alone

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

http://www.empr.com/duzallo/drug/34749/