RILUZOLE

THERAPEUTICS

Brands
- Rilutek

Generic?
No

Class
- Neuromuscular drug, centrally acting

Commonly Prescribed for
(FDA approved in bold)
- Amyotrophic lateral sclerosis (ALS)

How the Drug Works
- The mode of action is unknown, but the effect in ALS is felt to be from glutamate antagonism. Putative mechanisms include inhibition of glutamate release, interference with transmitter binding at excitatory amino acid receptors, and inactivation of voltage-gated sodium channels. In animal models, appears to be neuroprotective in mice with human superoxide dismutase mutations and has sedative and myorelaxant properties at large doses

How Long Until It Works
- Steady state is reached in 5 days, but it can take months to assess any clinical effect from the drug

If It Works
- ALS is a degenerative disease and deterioration is the general rule. Riluzole can increase survival or time to tracheostomy but is not a cure

If It Doesn’t Work
- It is difficult to determine if the treatment is effective, especially because ALS progression varies greatly from patient to patient. Supportive care is the mainstay of current ALS treatment. This may include monitoring and treatment of gait, swallowing and respiratory difficulties

Best Augmenting Combos
for Partial Response or Treatment-Resistance
- No other medication is indicated for the treatment of ALS progression

Tests
- Measure serum transaminases, including ALT levels, at baseline and monthly for 3 months. Then evaluate every 3 months for the first year and periodically after that. Once ALT exceeds 5 times normal, begin checking weekly, and discontinue if ALT exceeds 10 times normal or clinical symptoms, such as jaundice, occur

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
- Unknown

Notable AEs
- Nausea, weakness, dizziness, diarrhea, abdominal pain, pneumonia, tremor, anorexia, somnolence, and paresthesias. Elevation of hepatic transaminases

Life-Threatening or Dangerous AEs
- Neutropenia and hepatic effects. Neutropenia is uncommon (less than 1/1000 in clinical trials). Hepatic transaminase elevation is common (about 50% of patients will experience one elevated level) but usually clinically insignificant

Weight Gain
- Unusual

Sedation
- Unusual

What to Do About AEs
- Check blood counts on all patients with febrile illness and treat aggressively

Best Augmenting Agents for AEs
- AEs cannot be improved with use of augmenting agents
### DOSING AND USE

#### Usual Dosage Range
- ALS – 50 mg every 12 hours

#### Dosage Forms
- Tablets: 50 mg

#### How to Dose
- Start at 50 mg dose twice daily

**Dosing Tips**
- Taking with a high-fat meal will reduce absorption

#### Overdose
- Unknown

#### Long-Term Use
- Safe for long-term use

#### Habit Forming
- No

#### How to Stop
- No need to taper

#### Pharmacokinetics
- Metabolized by CYP450 1A2 isozyme. 60% bioavailability and 96% protein bound. Elimination half-life is about 12 hours. Drug excreted in urine and feces. Female patients generally metabolize more slowly and Japanese patients appear to have about 50% slower clearance of drug, even when adjusting for body weight

**Drug Interactions**
- CYP1A2 inhibitors (caffeine, amitriptyline, quinolones, theophylline) increase levels of riluzole and 1A2 inducers (rifampin, omeprazole, cigarette smoke, and charcoal-broiled food) lower levels. The effect of riluzole itself on CYP1A2 activity is unknown

#### Do Not Use
- Known hypersensitivity to the drug

### Hepatic Impairment
- Use with caution due to known hepatic risks of riluzole. Significant hepatic impairment may increase drug levels

### Cardiac Impairment
- No known effects

### Elderly
- No known effects. AEs similar to younger patients in those with normal renal and hepatic function

### Children and Adolescents
- Not studied in children (ALS is rare in pediatrics)

### Pregnancy
- Category C. Use only if benefits of medication outweigh risks

### Breast Feeding
- Unknown if excreted in breast milk. Do not use

### THE ART OF NEUROPHARMACOLOGY

#### Potential Advantages
- Only medication approved for the treatment of ALS. Relatively well-tolerated

#### Potential Disadvantages
- Lack of effectiveness and cost. Patients or caregivers expecting dramatic improvement from the drug are likely to be disappointed

#### Primary Target Symptoms
- Survival and delay of need for tracheostomy

#### Pearls
- Well-tolerated with few major AEs, but does not reverse ALS symptoms or the disease itself
- Do not expect noticeable clinical improvement
- In clinical trials, extended life 3 to 6 months on average and delayed need for tracheostomy

### SPECIAL POPULATIONS

#### Renal Impairment
- Severe renal disease may slow drug clearance. Use with caution
Suggested Reading


