

RESEARCH MONOGRAPH . COMPOUND PROFILE

Riluzole

A benzothiazole glutamate release inhibitor with sodium channel block; the first FDA-approved drug for amyotrophic lateral sclerosis.

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COMPOUND CLASS	Glutamate release inhibitor / sodium channel blocker

ABSTRACT

Riluzole (6-(trifluoromethoxy)-1,3-benzothiazol-2-amine; CAS 1744-22-5; molecular formula C₈H₅F₃N₂OS; molecular weight 234.20) is a benzothiazole compound developed at Rhone-Poulenc and approved by the FDA in 1995 (Rilutek) for amyotrophic lateral sclerosis. The compound was the first ALS-approved drug and remained the only one until edaravone in 2017. Mechanism is multifactorial: state-dependent voltage-gated sodium channel inhibition (reducing glutamate release from presynaptic terminals), AMPA and kainate receptor antagonism (postsynaptic glutamate effect), and modest GABA-A potentiation. The combined glutamate-reducing activity addresses the excitotoxicity hypothesis of ALS pathogenesis. Plasma half-life is approximately 12 hours; metabolism is via CYP1A2. The clinical effect in ALS is modest (median survival extension approximately 2 to 3 months) but consistent across trials. Off-label use in major depressive disorder (where ketamine's NMDA mechanism inspired interest in glutamate modulators), generalized anxiety disorder, and OCD has been investigated. Used as the canonical glutamate release inhibitor in research.

1. Compound Identification

Riluzole is described as glutamate release inhibitor / sodium channel blocker. A benzothiazole glutamate release inhibitor with sodium channel block; the first FDA-approved drug for amyotrophic lateral sclerosis.

1.1 Class summary

Glutamate release inhibitor / sodium channel blocker

1.2 Subtitle

A benzothiazole glutamate release inhibitor with sodium channel block; the first FDA-approved drug for amyotrophic lateral sclerosis.

2. Abstract

Riluzole (6-(trifluoromethoxy)-1,3-benzothiazol-2-amine; CAS 1744-22-5; molecular formula C₈H₅F₃N₂OS; molecular weight 234.20) is a benzothiazole compound developed at Rhone-Poulenc and approved by the FDA in 1995 (Rilutek) for amyotrophic lateral sclerosis. The compound was the first ALS-approved drug and remained the only one until edaravone in 2017. Mechanism is multifactorial: state-dependent voltage-gated sodium channel inhibition (reducing glutamate release from presynaptic terminals), AMPA and kainate receptor antagonism (postsynaptic glutamate effect), and modest GABA-A potentiation. The combined glutamate-reducing activity addresses the excitotoxicity hypothesis of ALS pathogenesis. Plasma half-life is approximately 12 hours; metabolism is via CYP1A2. The clinical effect in ALS is modest (median survival extension approximately 2 to 3 months) but consistent across trials. Off-label use in major depressive disorder (where ketamine's NMDA mechanism inspired interest in glutamate modulators), generalized anxiety disorder, and OCD has been investigated. Used as the canonical glutamate release inhibitor in research.

3. Mechanism of Action

State-dependent sodium channel block (reducing presynaptic glutamate release); AMPA/kainate antagonism; modest GABA-A potentiation. Multi-target glutamate modulator.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Clinical 50 mg per oral administration twice daily.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Bensimon G, et al. A controlled trial of riluzole in amyotrophic lateral sclerosis. N Engl J Med 1994.
2. Lacomblez L, et al. Dose-ranging study of riluzole in amyotrophic lateral sclerosis. Lancet 1996.
3. Pittenger C, et al. Riluzole in the treatment of mood and anxiety disorders. CNS Drugs 2008.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.