

TIGLUTIK- riluzole liquid
EDW PHARMA, INC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TIGLUTIK® safely and effectively. See full prescribing information for TIGLUTIK.

TIGLUTIK (riluzole) oral suspension

Initial U.S. Approval: 1995

-----**RECENT MAJOR CHANGES**-----

Dosage and Administration (2.1, 2.3)

12/2019

-----**INDICATIONS AND USAGE**-----

TIGLUTIK is indicated for the treatment of amyotrophic lateral sclerosis (ALS) (1)

-----**DOSAGE AND ADMINISTRATION**-----

- Recommended dosage: 50 mg (10 mL), twice daily, taken orally or via percutaneous endoscopic gastrostomy tubes (PEG-tubes), every 12 hours (2.1)
- Measure serum aminotransferases before and during treatment (2.2, 5.1)
- Take at least 1 hour before or 2 hours after a meal (2.3)

-----**DOSAGE FORMS AND STRENGTHS**-----

Oral suspension: 50 mg/10 mL (5 mg/mL) in 300 mL multiple-dose bottle (3)

-----**CONTRAINDICATIONS**-----

Patients with a history of severe hypersensitivity reactions to riluzole or to any of its components (4)

-----**WARNINGS AND PRECAUTIONS**-----

- Hepatic injury: Use of TIGLUTIK is not recommended in patients with baseline elevations of serum aminotransferases greater than 5 times the upper limit of normal; discontinue TIGLUTIK if there is evidence of liver dysfunction (5.1)
- Neutropenia: Advise patients to report any febrile illness (5.2)
- Interstitial lung disease: Discontinue TIGLUTIK if interstitial lung disease develops (5.3)

-----**ADVERSE REACTIONS**-----

Most common adverse reactions (incidence greater than or equal to 5% and greater than placebo) were oral hypoesthesia, asthenia, nausea, decreased lung function, hypertension, and abdominal pain (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact ITF Pharma Inc. at 1-800-664-1490 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----**DRUG INTERACTIONS**-----

- Strong to moderate CYP1A2 inhibitors: Co-administration may increase TIGLUTIK-associated adverse reactions (7.1)
- Strong to moderate CYP1A2 inducers: Co-administration may result in decreased efficacy (7.2)
- Hepatotoxic drugs: TIGLUTIK-treated patients that take other hepatotoxic drugs may be at increased risk for hepatotoxicity (7.3)

-----**USE IN SPECIFIC POPULATIONS**-----

- Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2020

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1 INDICATIONS AND USAGE

TIGLUTIK is indicated for the treatment of amyotrophic lateral sclerosis (ALS).

2 DOSAGE AND ADMINISTRATION

2.1 Dosage Information

The recommended dosage for TIGLUTIK is 50 mg (10 mL) taken orally or via Percutaneous Endoscopic Gastrostomy tubes (PEG-tubes) twice daily, every 12 hours. TIGLUTIK should be taken at least 1 hour before or 2 hours after a meal [see *Clinical Pharmacology (12.3)*].

2.2 Monitoring to Assess Safety

Measure serum aminotransferases before and during treatment with TIGLUTIK [see *Warnings and Precautions (5.1)*].

2.3 Important Administration Instructions

Gently shake the TIGLUTIK bottle for at least 30 seconds before administration. Gently shake the TIGLUTIK bottle for at least 30 seconds before administration.

TIGLUTIK can be administered by mouth or via percutaneous endoscopic gastrostomy tubes (PEG-tubes). Both silicone and polyurethane PEG tubes can be used.

See the Instructions for Use for further administration details. See the Instructions for Use for further administration details.

3 DOSAGE FORMS AND STRENGTHS

Oral suspension: 50 mg/10 mL (5 mg/mL) slightly brown, opaque, homogeneous suspension in a 300-mL multiple-dose amber bottle.

4 CONTRAINDICATIONS

TIGLUTIK is contraindicated in patients with a history of severe hypersensitivity reactions to riluzole or to any of its components (anaphylaxis has occurred) [see *Adverse Reactions (6.1)*].

5 WARNINGS AND PRECAUTIONS

5.1 Hepatic Injury

TIGLUTIK can cause liver injury. Cases of drug-induced liver injury, some of which were fatal, have been reported in patients taking riluzole. Asymptomatic elevations of hepatic transaminases have also been reported, and in some patients have recurred upon re-challenge with riluzole.

In clinical studies, the incidence of elevations in hepatic transaminases was greater in riluzole-treated patients than placebo-treated patients. The incidence of elevations of ALT

above 5 times the upper limit of normal (ULN) was 2% in riluzole-treated patients. Maximum increases in ALT occurred within 3 months after starting riluzole. About 50% and 8% of riluzole-treated patients in pooled controlled efficacy studies (Studies 1 and 2) had at least one elevated ALT level above ULN and above 3 times ULN, respectively [see *Clinical Studies (14)*].

Monitor patients for signs and symptoms of hepatic injury, every month for the first 3 months of treatment, and periodically thereafter. The use of TIGLUTIK is not recommended if patients develop hepatic transaminases levels greater than 5 times the ULN. Discontinue TIGLUTIK if there is evidence of liver dysfunction (e.g., elevated bilirubin). Concomitant use with other hepatotoxic drugs may increase the risk for hepatotoxicity [see *Drug Interactions (7.3)*].

5.2 Neutropenia

TIGLUTIK can cause neutropenia. Cases of severe neutropenia (absolute neutrophil count less than 500 per mm³) within the first 2 months of riluzole treatment have been reported. Advise patients to report febrile illnesses.

5.3 Interstitial Lung Disease

TIGLUTIK can cause interstitial lung disease, including hypersensitivity pneumonitis. Discontinue TIGLUTIK immediately if interstitial lung disease develops.

6 ADVERSE REACTIONS

The following adverse reactions are described below and elsewhere in the labeling:

- Hepatic Injury [see *Warnings and Precautions (5.1)*]
- Neutropenia [see *Warnings and Precautions (5.2)*]
- Interstitial Lung Disease [see *Warnings and Precautions (5.3)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse Reactions in Controlled Clinical Trials of Riluzole Tablets

In the placebo-controlled clinical trials in patients with ALS (Study 1 and 2), a total of 313 patients received riluzole 50 mg twice daily [see *Clinical Studies (14)*]. The most common adverse reactions in riluzole-treated patients (in at least 5% of patients and more frequently than on placebo) were asthenia, nausea, decreased lung function, hypertension, and abdominal pain. The most common adverse reactions leading to discontinuation in the riluzole group were nausea, abdominal pain, constipation, and elevated ALT.

There was no difference in the rate of adverse reactions leading to discontinuation between females and males. However, the incidence of dizziness was higher in females (11%) than in males (4%). The adverse reaction profile was similar in older and younger patients. There are insufficient data to assess racial differences in the adverse reaction profile.

Table 1 lists adverse reactions that occurred in at least 2% of riluzole-treated patients (50 mg twice daily) in pooled Study 1 and 2, and at a higher rate than on placebo.

Table 1. Adverse Reactions in Pooled Placebo-Controlled Trials (Studies 1 and 2) in Patients with ALS

Adverse Reaction	Riluzole Tablets 50 mg twice daily (N=313) %	Placebo (N=320) %
Asthenia	19	12
Nausea	16	11
Decreased lung function	10	9
Hypertension	5	4
Abdominal pain	5	4
Vomiting	4	2
Arthralgia	4	3
Dizziness	4	3
Dry mouth	4	3
Insomnia	4	3
Pruritus	4	3
Tachycardia	3	1
Flatulence	3	2
Increased cough	3	2
Peripheral edema	3	2
Urinary Tract Infection	3	2
Circumoral paresthesia	2	0
Somnolence	2	1
Vertigo	2	1
Eczema	2	1

Additional Adverse Reactions with TIGLUTIK

In an open-label pharmacokinetic study in healthy subjects (n=36), oral hypoesthesia was observed in 29% of subjects taking TIGLUTIK, compared to 6% in patients taking riluzole tablets, under fasting conditions.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of riluzole. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Acute hepatitis and icteric toxic hepatitis [see *Warnings and Precautions (5.1)*]
- Renal tubular impairment
- Pancreatitis

7 DRUG INTERACTIONS

7.1 Agents that may Increase Riluzole Blood Concentrations

CYP1A2 Inhibitors

Co-administration of riluzole (a CYP1A substrate) with CYP1A2 inhibitors was not evaluated in a clinical trial; however, in vitro findings suggest an increase in riluzole exposure is likely. The concomitant use of strong or moderate CYP1A2 inhibitors (e.g., ciprofloxacin, enoxacin, fluvoxamine, methoxsalen, mexiletine, oral contraceptives, thiabendazole, vemurafenib, zileuton) with TIGLUTIK may increase the risk of TIGLUTIK - associated adverse reactions [see *Clinical Pharmacology (12.3)*].

7.2 Agents that may Decrease Riluzole Plasma Concentrations

CYP1A2 Inducers

Co-administration of riluzole (a CYP1A substrate) with CYP1A2 inducers was not evaluated in a clinical trial; however, in vitro findings suggest a decrease in riluzole exposure is likely. Lower exposures may result in decreased efficacy [see *Clinical Pharmacology (12.3)*].

7.3 Hepatotoxic Drugs

Clinical trials in ALS patients excluded patients on concomitant medications which were potentially hepatotoxic (e.g., allopurinol, methyldopa, sulfasalazine). TIGLUTIK-treated patients who take other hepatotoxic drugs may be at an increased risk for hepatotoxicity [see *Warnings and Precautions (5.1)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no studies of riluzole in pregnant women, and case reports have been inadequate to inform the drug-associated risk. The background risk for major birth defects and miscarriage in patients with amyotrophic lateral sclerosis is unknown. In the U.S. general population, the background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

In studies in which riluzole was administered orally to pregnant animals, developmental toxicity (decreased embryofetal/offspring viability, growth, and functional development) was observed at clinically relevant doses [see *Data*]. Based on these results, women should be advised of a possible risk to the fetus associated with use of TIGLUTIK during pregnancy.

Data

Animal Data

Oral administration of riluzole (3, 9, or 27 mg/kg/day) to pregnant rats during the period of organogenesis resulted in decreases in fetal growth (body weight and length) at the high dose. The mid dose, a no-effect dose for embryofetal developmental toxicity, is

approximately equal to the recommended human daily dose (RHDD, 100 mg) on a mg/m² basis. When riluzole was administered orally (3, 10, or 60 mg/kg/day) to pregnant rabbits during the period of organogenesis, embryofetal mortality was increased at the high dose and fetal body weight was decreased and morphological variations increased at all but the lowest dose tested. The no-effect dose (3 mg/kg/day) for embryofetal developmental toxicity is less than the RHDD on a mg/m² basis. Maternal toxicity was observed at the highest dose tested in rat and rabbit.

When riluzole was orally administered (3, 8, or 15 mg/kg/day) to male and female rats prior to and during mating and to female rats throughout gestation and lactation, increased embryofetal mortality and decreased postnatal offspring viability, growth, and functional development were observed at the high dose. The mid dose, a no-effect dose for pre- and postnatal developmental toxicity, is approximately equal to the RHDD on a mg/m² basis.

8.2 Lactation

Risk Summary

There are no data on the presence of riluzole in human milk, the effects on the breastfed infant, or the effects on milk production. Riluzole or its metabolites have been detected in milk of lactating rat. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TIGLUTIK and any potential adverse effects on the breastfed infant from TIGLUTIK or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

In rats, oral administration of riluzole resulted in decreased fertility indices and increases in embryoletality [see *Nonclinical Toxicology (13.1)*].

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

In clinical studies of riluzole, 30% of patients were 65 years and over. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Hepatic Impairment

Patients with mild [Child-Pugh's (CP) score A] or moderate (CP score B) hepatic impairment had increases in AUC, compared to patients with normal hepatic function. Thus, patients with mild or moderate hepatic impairment may be at increased risk of adverse reactions. The impact of severe hepatic impairment on riluzole exposure is unknown.

Use of TIGLUTIK is not recommended in patients with baseline elevations of serum aminotransferases greater than 5 times upper limit of normal or evidence of liver dysfunction (e.g., elevated bilirubin) [see *Clinical Pharmacology (12.3)*].

8.7 Japanese Patients

Japanese patients are more likely to have higher riluzole concentrations. Consequently, the risk of adverse reactions may be greater in Japanese patients [see *Clinical Pharmacology* (12.3)].

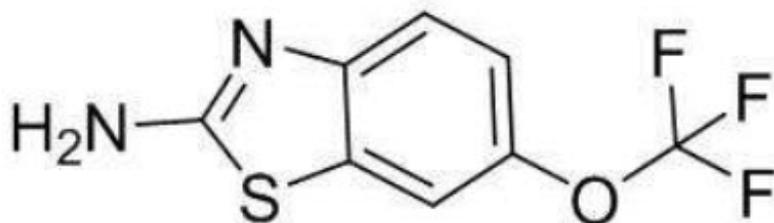
10 OVERDOSAGE

Reported symptoms of overdose following ingestion of riluzole ranging from 1.5 to 3 grams (30 to 60 times the recommended dose) included acute toxic encephalopathy, coma, drowsiness, memory loss, and methemoglobinemia.

No specific antidote for the treatment of TIGLUTIK overdose is available. For current information on the management of poisoning or overdose, contact a certified poison control center.

11 DESCRIPTION

Riluzole is a member of the benzothiazole class. The chemical designation for riluzole is 2-amino-6-(trifluoromethoxy)benzothiazole. Its molecular formula is $C_8H_5F_3N_2OS$, and its molecular weight is 234.2. The chemical structure is:



Riluzole is a white to slightly yellow powder that is very soluble in dimethylformamide, dimethylsulfoxide, and methanol; freely soluble in dichloromethane; sparingly soluble in 0.1 N HCl; and very slightly soluble in water and in 0.1 N NaOH.

TIGLUTIK (50 mg/10mL) oral suspension is a slightly brown, opaque, homogeneous suspension containing 50 mg of riluzole per 10 mL of suspension.

TIGLUTIK also contains the following inactive ingredients: magnesium aluminum silicate, noncrystallizing sorbitol solution, polyoxyl 20 cetostearyl ether, purified water, saccharin sodium, simethicone emulsion, sodium lauryl sulfate, and xanthan gum.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism by which riluzole exerts its therapeutic effects in patients with ALS is unknown.

12.2 Pharmacodynamics

The clinical pharmacodynamics of riluzole has not been determined in humans.

12.3 Pharmacokinetics

A pharmacokinetic study in healthy adult subjects who received riluzole suspension 50 mg under fasting conditions demonstrated similar pharmacokinetics following intragastric administration via feeding tubes and oral administration.

Table 2 displays the pharmacokinetic parameters of riluzole.

Table 2. Pharmacokinetics of Riluzole *

Absorption	
Bioavailability (oral)	Approximately 60%
Dose Proportionality	Linear over a dose range of 25 mg to 100 mg every 12 hours (1/2 to 2 times the recommended dosage)
Food effect †	AUC ↓ 9% and Cmax ↓ 55% (high fat meal)
Time to peak plasma concentration (median) †	0.8 hours
Distribution	
Plasma Protein Binding	96% (Mainly to albumin and lipoproteins)
Elimination	
Elimination half-life	<ul style="list-style-type: none"> • 12 hours (CV=35%) • The high individual variability in the clearance of riluzole is potentially attributable to variability of CYP1A2. The clinical implications are not known.
Accumulation	Approximately 2-fold
Metabolism	
Fraction metabolized (% dose)	At least 88% <ul style="list-style-type: none"> • Oxidation: CYP1A2 • Direct and sequential glucuronidation: UGT-HP4
Primary metabolic pathway(s) [in vitro]	
Active Metabolites	Some metabolites appear pharmacologically active in vitro, but the clinical implications are not known.
Excretion	
Primary elimination pathways (% dose)	<ul style="list-style-type: none"> • Feces: 5% • Urine: 90% (2% unchanged riluzole)

* Unless otherwise stated, information in this table is based on pharmacokinetic studies of riluzole tablets.

† Information specific to TIGLUTIK

Specific Populations

Hepatic Impairment

Compared with healthy volunteers, the AUC of riluzole was approximately 1.7-fold greater in patients with mild chronic hepatic impairment (CP score A), and approximately 3-fold greater in patients with moderate chronic hepatic impairment (CP score B). The pharmacokinetics of riluzole have not been studied in patients with severe hepatic impairment (CP score C) [see *Use in Specific Populations (8.6)*].

Race

The clearance of riluzole was 50% lower in male Japanese subjects than in Caucasian subjects, after normalizing for body weight [see *Use in Specific Populations (8.7)*].

Gender

The mean AUC of riluzole was approximately 45% higher in female patients than male patients.

Smokers

The clearance of riluzole in tobacco smokers was 20% greater than in nonsmokers. *Geriatric Patients and Patients with Moderate to Severe Renal Impairment* Age 65 years or older and moderate to severe renal impairment do not have a meaningful effect on the pharmacokinetics of riluzole. The pharmacokinetics of riluzole in patients undergoing hemodialysis are unknown.

Drug Interaction Studies

Drugs Highly Bound to Plasma Proteins

Riluzole and warfarin are highly bound to plasma proteins. In vitro, riluzole did not show any displacement of warfarin from plasma proteins. Riluzole binding to plasma proteins was unaffected by warfarin, digoxin, imipramine and quinine at high therapeutic concentrations in vitro.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Riluzole was not carcinogenic in mice or rats when administered for 2 years at daily oral doses up to 20 and 10 mg/kg/day, respectively, which are approximately equal to the recommended human daily dose (RHDD, 100 mg) on a mg/m² basis.

Mutagenesis

Riluzole was negative in *in vitro* (bacterial reverse mutation (Ames), mouse lymphoma tk, chromosomal aberration assay in human lymphocytes), and in *in vivo* (rat cytogenetic and mouse micronucleus) assays.

N-hydroxyriluzole, the major active metabolite of riluzole, was positive for clastogenicity in the *in vitro* mouse lymphoma tk assay and in the *in vitro* micronucleus assay using the same mouse lymphoma cell line. N-hydroxyriluzole was negative in the HPRT gene mutation assay, the Ames assay (with and without rat or hamster S9), the *in vitro* chromosomal aberration assay in human lymphocytes, and the *in vivo* mouse

micronucleus assay.

Impairment of Fertility

When riluzole (3, 8, or 15 mg/kg) was administered orally to male and female rats prior to and during mating and continuing in females throughout gestation and lactation, fertility indices were decreased and embryoletality was increased at the high dose. This dose was also associated with maternal toxicity. The mid dose, a no-effect dose for effects on fertility and early embryonic development, is approximately equal to the RHDD on a mg/m² basis.

14 CLINICAL STUDIES

The efficacy of TIGLUTIK is based upon bioavailability studies comparing oral riluzole tablets to TIGLUTIK oral suspension [see *Clinical Pharmacology (12.3)*].

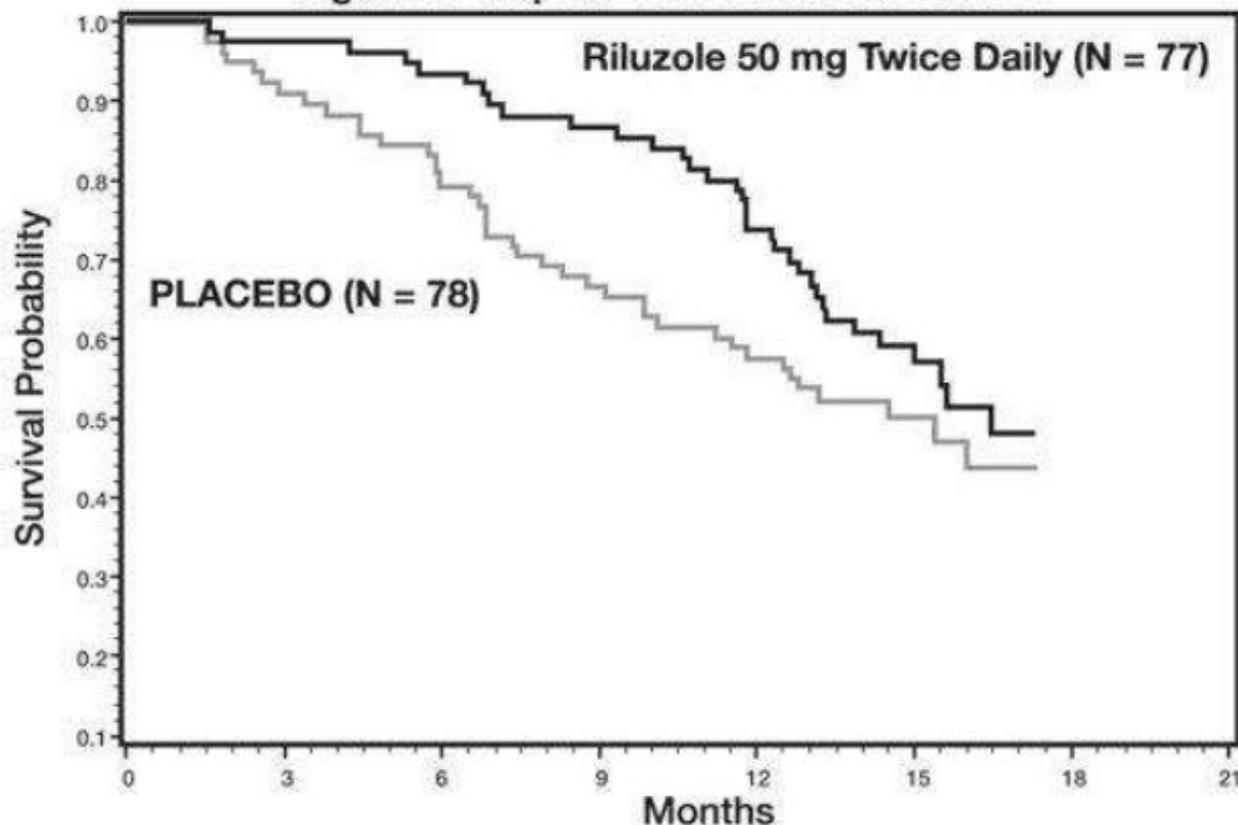
The efficacy of riluzole was demonstrated in two studies (Study 1 and 2) that evaluated 50 mg riluzole oral tablets twice daily in patients with amyotrophic lateral sclerosis (ALS). Both studies included patients with either familial or sporadic ALS, disease duration of less than 5 years, and baseline forced vital capacity greater than or equal to 60% of normal.

Study 1 was a randomized, double-blind, placebo-controlled clinical study that enrolled 155 patients with ALS. Patients were randomized to receive riluzole 50 mg twice daily (n=77) or placebo (n=78) and were followed for at least 13 months (up to a maximum duration of 18 months). The clinical outcome measure was time to tracheostomy or death.

The time to tracheostomy or death was longer for patients receiving riluzole compared to placebo. There was an early increase in survival in patients receiving riluzole compared to placebo. Figure 1 displays the survival curves for time to death or tracheostomy. The vertical axis represents the proportion of individuals alive without tracheostomy at various times following treatment initiation (horizontal axis). Although these survival curves were not statistically significantly different when evaluated by the analysis specified in the study protocol (Logrank test p=0.12), the difference was found to be significant by another appropriate analysis (Wilcoxon test p=0.05). As seen in Figure 1, the study showed an early increase in survival in patients given riluzole. Among the patients in whom the endpoint of tracheostomy or death was reached during the study, the difference in median survival between the riluzole 50 mg twice daily and placebo groups was approximately 90 days.

Figure 1. Time to Tracheostomy or Death in ALS Patients in Study 1 (Kaplan-Meier Curves)

Figure 1: Kaplan-Meier Survival Curves



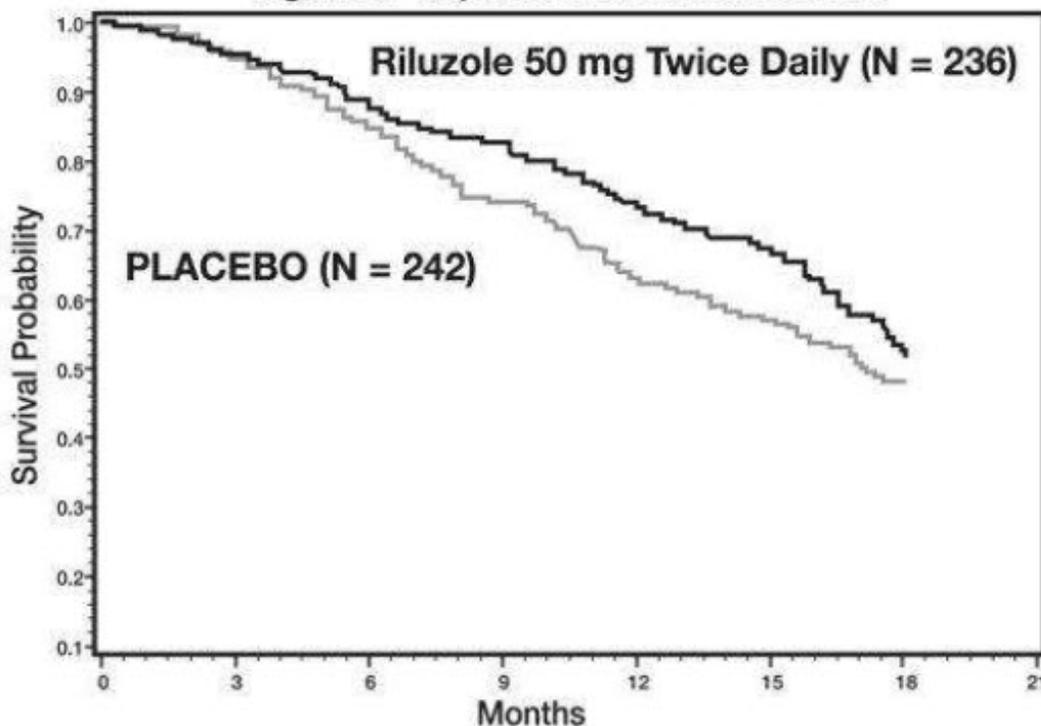
Study 2 was a randomized, double-blind, placebo-controlled clinical study that enrolled 959 patients with ALS. Patients were randomized to riluzole 50 mg twice daily (n=236) or placebo (n=242) and were followed for at least 12 months (up to a maximum duration of 18 months). The clinical outcome measure was time to tracheostomy or death.

The time to tracheostomy or death was longer for patients receiving riluzole compared to placebo. Figure 2 displays the survival curves for time to death or tracheostomy for patients randomized to either riluzole 100 mg per day or placebo. Although these survival curves were not statistically significantly different when evaluated by the analysis specified in the study protocol (Logrank test $p=0.076$), the difference was found to be significant by another appropriate analysis (Wilcoxon test $p=0.05$). Not displayed in Figure 2 are the results of riluzole 50 mg per day (one-half of the recommended daily dose), which could not be statistically distinguished from placebo, or the results of riluzole 200 mg per day (two times the recommended daily dose), which were not distinguishable from the 100 mg per day results. Among the patients in whom the endpoint of tracheostomy or death was reached during the study, the difference in median survival between riluzole and placebo was approximately 60 days.

Although riluzole improved survival in both studies, measures of muscle strength and neurological function did not show a benefit.

Figure 2. Time to Tracheostomy or Death in ALS Patients in Study 2 (Kaplan-Meier Curves)

Figure 2: Kaplan-Meier Survival Curves



16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

TIGLUTIK (50 mg/10 mL) oral suspension is supplied in amber glass bottles closed with child-resistant tamper evident screw caps. Each bottle contains 300 mL of oral suspension and is intended for multi-dose use, NDC 70726-0303-2.

TIGLUTIK is supplied in a carton, NDC 70726-0303-1, containing:

- Two bottles, each containing 300 mL oral suspension
- Two 10 mL oral syringes
- Two syringe bottle adapters
- Two syringe tip caps
- Prescribing Information, including Instructions for Use

16.2 Storage and Handling

Store at 20-25°C (68-77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature], and protect from bright light. Do not freeze. Store upright.

Use within 15 days after initially opening of each bottle. Discard any unused TIGLUTIK remaining after 15 days of first opening of the bottle.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Instructions for Use).

Administration Instructions

Instruct patients to discard any unused TIGLUTIK after 15 days of opening the bottle. If the patient requires administration of TIGLUTIK via PEG tube, refer the patient/caregiver to the Instructions for Use for steps on how to take/give TIGLUTIK.

Hepatic Injury

Advise patients that TIGLUTIK can cause liver injury, which can be fatal. Inform patients of the clinical signs or symptoms suggestive of hepatic dysfunction (e.g., unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine) and to contact a healthcare provider promptly if these signs or symptoms occur [see *Warnings and Precautions (5.1)*].

Neutropenia

Advise patients that TIGLUTIK can cause neutropenia, and to report to their healthcare provider if they have a fever [see *Warnings and Precautions (5.2)*].

Interstitial Lung Disease

Advise patients that TIGLUTIK can cause interstitial lung disease, and to report to their healthcare provider if they have respiratory symptoms (e.g., dry cough and difficult or labored breathing) [see *Warnings and Precautions (5.3)*].

Pregnancy

Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during TIGLUTIK therapy [see *Use in Specific Populations (8.1)*].

Lactation

Advise patients to notify their healthcare provider if they are breastfeeding or intend to breastfeed during TIGLUTIK therapy [see *Use in Specific Populations (8.2)*].

Manufactured for:

ITF Pharma, Inc.

850 Cassatt Road, Suite 350

Berwyn, PA 19312 USA

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PRINCIPAL DISPLAY PANEL - 300 mL Bottle Carton

NDC 70726-0303-1

R_x only

Tiglutik[®]

riluzole

oral suspension

50 mg/10 mL (5 mg/mL)

For Oral Administration
Shake gently before use

Contents of this package:

- Two bottles, each containing 300 mL
- Two 10 mL oral syringes
- Two syringe bottle adapters
- Two syringe tip caps
- One Prescribing Information, including Instructions for Use

This product is a liquid suspension and is supplied with syringes for oral administration. Before use, please read the enclosed Prescribing Information.

600 mL (two bottles/300 mL each)
Not To Be Dispensed Separately

NDC 70726-0303-1

Rx only



Tiglutik[®]

riluzole
oral suspension
50 mg/10 mL (5 mg/mL)



For Oral Administration

Shake gently before use

This product is a liquid suspension and is supplied with syringes for oral administration. Before use, please read the enclosed Prescribing Information.

Contents of this package:

- Two bottles, each containing 300 mL
- Two 10 mL oral syringes
- Two syringe bottle adapters
- Two syringe tip caps
- One Prescribing Information, including Instructions for Use



Manufactured for:
ITF Pharma, Inc.
Berwyn, PA 19312 USA
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TOC122019

600 mL (two bottles/300 mL each)

Not To Be Dispensed Separately

For Oral Administration



50 mg/10 mL (5 mg/mL)
oral suspension
riluzole
Tiglutik[®]



Rx only
NDC 70726-0303-1

NDC 70726-0303-1

Rx only



Tiglutik[®]

riluzole
oral suspension
50 mg/10 mL (5 mg/mL)



Contains: TIGLUTIK[®] 50 mg/10 mL (5 mg/mL) oral suspension is a slightly brown, opaque, homogeneous suspension when mixed, containing 50 mg of riluzole per 10 mL of suspension.

Storage and Use: The bottle must be gently shaken for at least 30 seconds by continuously rotating the bottle 180° until the visual appearance of the suspension is homogeneous.

Store TIGLUTIK[®] at controlled room temperature between 20°-25°C (68°-77°F), excursions permitted to 15°-30°C (59°-86°F) and protect from bright light. Do not freeze. Store upright.

Once opened, the bottle of TIGLUTIK[®] should be used within 15 days. Keep bottle tightly closed

For Oral Administration

Shake gently before use

This product is a liquid suspension and is supplied with syringes for oral administration. Before use, please read the enclosed Prescribing Information.

between each use.

Dosage: The recommended dose is 10 mL of TIGLUTIK® oral suspension, containing 50 mg of riluzole, taken orally twice daily, every 12 hours.

Before use, please read the enclosed Prescribing Information.

Pharmacist: Please dispense TIGLUTIK® using the two 300 mL bottles enclosed, without breaking open bottle seals.

Keep out of reach of children.

600 mL (two bottles/300 mL each)

Not To Be Dispensed Separately

TIGLUTIK

riluzole liquid

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:70726-0303
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
RILUZOLE (UNII: 7LJ087RS6F) (RILUZOLE - UNII:7LJ087RS6F)	RILUZOLE	50 mg in 10 mL

Inactive Ingredients

Ingredient Name	Strength
SORBITOL (UNII: 506T60A25R)	
POLYOXYL 20 CETOSTEARYL ETHER (UNII: YRC528SWUY)	
MAGNESIUM ALUMINUM SILICATE (UNII: 6M3P64V0NC)	
WATER (UNII: 059QF0KO0R)	
SACCHARIN SODIUM (UNII: SB8ZUX40TY)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
DIMETHICONE (UNII: 92RU3N3Y1O)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
XANTHAN GUM (UNII: TTV12P4NEE)	

Product Characteristics

Color	brown (slightly brown, opaque)	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
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1	NDC:70726-0303-1	2 in 1 CARTON	09/21/2018	
1	NDC:70726-0303-2	300 mL in 1 BOTTLE, PLASTIC; Type 1: Convenience Kit of Co-Package		
Marketing Information				
Marketing Category	Application Number or Monograph Citation		Marketing Start Date	Marketing End Date
NDA	NDA209080		09/21/2018	

Labeler - EDW PHARMA, INC (080260470)

Registrant - EDW PHARMA, INC (080260470)

Establishment			
Name	Address	ID/FEI	Business Operations
Aphena Pharma Solutions		829739833	manufacture(70726-0303)

Revised: 2/2024

EDW PHARMA, INC