

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

218637Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

RALDESY™ (trazodone hydrochloride) oral solution
Initial U.S. Approval: 1981

WARNING: SUICIDAL THOUGHTS and BEHAVIORS *See full prescribing information for complete boxed warning.*

- Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients. Closely monitor for clinical worsening and emergence of suicidal thoughts and behaviors (5.1).
- RALDESY is not approved for use in pediatric patients (8.4).

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

RALDESY is a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of major depressive disorder (MDD) in adults (1).

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

- Starting dosage: 150 mg orally in divided doses daily. May be increased by 50 mg per day every three to four days. Maximum dosage: 400 mg per day in divided doses (2.1).
- Administer RALDESY shortly after a meal or light snack (2.1).
- When discontinuing RALDESY, gradually reduce dose (2.5).

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

- Oral solution: 10 mg/mL

-----CONTRAINDICATIONS-----

- Concomitant use of monoamine oxidase inhibitors (MAOIs), or use within 14 days of stopping MAOIs (4).

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

- Serotonin Syndrome: Increased risk when co-administered with other serotonergic agents (e.g., SSRI, SNRI, triptans), but also when taken alone. If it occurs, discontinue RALDESY and initiate supportive treatment (5.2).
- Cardiac Arrhythmias: Increases the QT interval. Avoid use with drugs that also increase the QT interval and in patients with risk factors for prolonged QT interval (5.3).

- Orthostatic Hypotension and Syncope: Warn patients of risk and symptoms of hypotension (5.4).
- Increased Risk of Bleeding: Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), other antiplatelet drugs, warfarin, and other anticoagulants may increase this risk (5.5).
- Priapism: Cases of painful and prolonged penile erections and priapism have been reported. Immediate medical attention should be sought if signs and symptoms of prolonged penile erections or priapism are observed (5.6).
- Activation of Mania or Hypomania: Screen for bipolar disorder and monitor for mania or hypomania (5.7).
- Potential for Cognitive and Motor Impairment: Has potential to impair judgment, thinking, and motor skills. Advise patients to use caution when operating machinery (5.9).
- Angle-Closure Glaucoma: Avoid use of antidepressants, including RALDESY, in patients with untreated anatomically narrow angles (5.10).

-----ADVERSE REACTIONS-----

Most common adverse reactions (incidence $\geq 5\%$ and twice that of placebo) are: edema, blurred vision, syncope, drowsiness, fatigue, diarrhea, nasal congestion, weight loss (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Validus Pharmaceuticals LLC at 1-866-982-5438 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----DRUG INTERACTIONS-----

- CNS Depressants: RALDESY may enhance effects of alcohol, barbiturates, or other CNS depressants (7).
- CYP3A4 Inhibitors: Consider RALDESY dose reduction based on tolerability (2.5, 7).
- CYP3A4 Inducers: Increase in RALDESY dosage may be necessary (2.5, 7).
- Digoxin or Phenytoin: Monitor for increased digoxin or phenytoin serum levels (7).
- Warfarin: Monitor for increased or decreased prothrombin time (7).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 11/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Recommended Dosage
- 2.2 Screen for Bipolar Disorder Prior to Starting RALDESY
- 2.3 Switching to or from Monoamine Oxidase Inhibitor Antidepressant
- 2.4 Dosage Recommendations for Concomitant Use with Strong CYP3A4 Inhibitors or Inducers
- 2.5 Discontinuation of Treatment with RALDESY

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Suicidal Thoughts and Behaviors in Pediatric and Young Adult Patients
- 5.2 Serotonin Syndrome
- 5.3 Cardiac Arrhythmias
- 5.4 Orthostatic Hypotension and Syncope
- 5.5 Increased Risk of Bleeding
- 5.6 Priapism
- 5.7 Activation of Mania or Hypomania
- 5.8 Discontinuation Syndrome
- 5.9 Potential for Cognitive and Motor Impairment
- 5.10 Angle-Closure Glaucoma
- 5.11 Hyponatremia

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment

9 DRUG ABUSE AND DEPENDENCE

- 9.1 Controlled Substance
- 9.2 Abuse

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: SUICIDAL THOUGHTS and BEHAVIORS

Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors [see *Warnings and Precautions (5.1)*]. RALDESY is not approved for use in pediatric patients [see *Use in Specific Populations (8.4)*].

1 INDICATIONS AND USAGE

RALDESY™ is indicated for the treatment of major depressive disorder (MDD) in adults.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The initial dosage of RALDESY for the treatment of MDD in adults is 150 mg daily, taken orally, in divided doses. The dosage should be initiated at a low-dose and increased gradually, depending on clinical response and an tolerance. Occurrence of drowsiness may require the administration of a major portion of the daily dose at bedtime or a reduction of dosage [see *Dosage and Administration (2.5)*].

The dose may be increased by 50 mg daily every 3 to 4 days. The maximum recommended dosage for outpatients usually should not exceed 400 mg daily in divided doses. Inpatients (i.e., more severely depressed patients) may be given up to, but not in excess, of 600 mg daily in divided doses.

Administer RALDESY orally after a meal or light snack [see *Clinical Pharmacology (12.3)*].

2.2 Screen for Bipolar Disorder Prior to Starting RALDESY

Prior to initiating treatment with RALDESY or another antidepressant, screen patients for a personal or family history of bipolar disorder, mania, or hypomania [see *Warnings and Precautions (5.7)*].

2.3 Switching to or from Monoamine Oxidase Inhibitor Antidepressant

At least 14 days must elapse between discontinuation of a monoamine oxidase inhibitor (MAOI) antidepressant and initiation of RALDESY. In addition, at least 14 days must elapse after stopping RALDESY before starting an MAOI antidepressant [see *Contraindications (4)*, *Warnings and Precautions (5.2)*].

2.4 Dosage Recommendations for Concomitant Use with Strong CYP3A4 Inhibitors or Inducers

Coadministration with Strong CYP3A4 Inhibitors

Consider reducing RALDESY dose based on tolerability when RALDESY is coadministered with a strong CYP3A4 inhibitor [see *Drug Interactions (7.1)*].

Coadministration with Strong CYP3A4 Inducers

Consider increasing RALDESY dose based on therapeutic response when RALDESY is coadministered with a strong CYP3A4 inducer [see *Drug Interactions (7.1)*].

2.5 Discontinuation of Treatment with RALDESY

Adverse reactions may occur upon discontinuation of RALDESY [see *Warnings and Precautions (5.8)*]. Gradually reduce the dosage rather than stopping RALDESY abruptly whenever possible.

3 DOSAGE FORMS AND STRENGTHS

RALDESY (10 mg/mL) Oral Solution: Clear, colorless solution

4 CONTRAINDICATIONS

RALDESY is contraindicated in patients taking, or within 14 days of stopping, monoamine oxidase inhibitors (MAOIs), including MAOIs such as linezolid or intravenous methylene blue, because of an increased risk of serotonin syndrome [see *Warnings and Precautions (5.2)*, *Drug*

5 WARNINGS AND PRECAUTIONS

5.1 Suicidal Thoughts and Behaviors in Pediatric and Young Adult Patients

In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients and over 4,500 pediatric patients, the incidence of suicidal thoughts and behaviors in antidepressant-treated patients age 24 years and younger was greater than in placebo-treated patients. There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied. There were differences in absolute risk of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors per 1,000 patients treated are provided in Table 1.

Table 1: Risk Differences of the Number of Cases of Suicidal Thoughts or Behaviors in the Pooled Placebo-Controlled Trials of Antidepressants in Pediatric and Adult Patients

Age Range (years)	Drug-Placebo Difference in Number of Patients of Suicidal Thoughts or Behaviors per 1,000 Patients Treated
	Increases Compared to Placebo
<18	14 additional patients
18-24	5 additional patients
	Decreases Compared to Placebo
25-64	1 fewer patient
≥65	6 fewer patients

It is unknown whether the risk of suicidal thoughts and behaviors in pediatric and young adult patients extends to longer-term use, i.e., beyond four months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with MDD that antidepressants delay the recurrence of depression and that depression itself is a risk factor for suicidal thoughts and behaviors.

Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing RALDESY, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

5.2 Serotonin Syndrome

SSRIs, including RALDESY, can precipitate serotonin syndrome, a potentially life-threatening condition. The risk is increased with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort) and with drugs that impair metabolism of serotonin, i.e., MAOIs [see *Contraindications (4)*, *Drug Interactions (7.1)*]. Serotonin syndrome can also occur when these drugs are used alone.

Serotonin syndrome signs and symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

The concomitant use of RALDESY with MAOIs is contraindicated. In addition, do not initiate RALDESY in a patient being treated with MAOIs such as linezolid or intravenous methylene blue. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection). If it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking RALDESY, discontinue RALDESY before initiating treatment with the MAOI [see *Contraindications (4)*, *Drug Interactions (7.1)*].

Monitor all patients taking RALDESY for the emergence of serotonin syndrome. Discontinue treatment with RALDESY and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of RALDESY with other serotonergic drugs is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms.

5.3 Cardiac Arrhythmias

Clinical studies indicate that trazodone hydrochloride may be arrhythmogenic in patients with preexisting cardiac disease. Arrhythmias identified include isolated PVCs, ventricular couplets, tachycardia with syncope, and torsade de pointes. Postmarketing reports, including torsade de pointes have been reported at doses of 100 mg or less with the immediate-release trazodone hydrochloride tablets. RALDESY should also be avoided in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and the presence of congenital prolongation of the QT interval. RALDESY is not recommended for use during the initial recovery phase of myocardial infarction. Caution should be used when administering RALDESY to patients with cardiac disease

and such patients should be closely monitored, since antidepressant drugs (including RALDESY) may cause cardiac arrhythmias [see *Adverse Reactions (6.2)*].

Trazodone hydrochloride prolongs the QT/QT_c interval. The use of RALDESY should be avoided in patients with known QT prolongation or in combination with other drugs that are inhibitors of CYP3A4 (e.g., itraconazole, clarithromycin, voriconazole), or known to prolong QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin). Concomitant administration of drugs may increase the risk of cardiac arrhythmia [see *Drug Interactions (7.1)*].

5.4 Orthostatic Hypotension and Syncope

Hypotension, including orthostatic hypotension and syncope has been reported in patients receiving trazodone hydrochloride. Concomitant use with an antihypertensive may require a reduction in the dose of the antihypertensive drug.

5.5 Increased Risk of Bleeding

Drugs that interfere with serotonin reuptake inhibition, including RALDESY, increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), other antiplatelet drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to drugs that interfere with serotonin reuptake have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages.

Inform patients about the risk of bleeding associated with the concomitant use of RALDESY and antiplatelet agents or anticoagulants. For patients taking warfarin, carefully monitor coagulation indices when initiating, titrating, or discontinuing RALDESY .

5.6 Priapism

Cases of priapism (painful erections greater than 6 hours in duration) have been reported in males receiving trazodone hydrochloride tablets. Priapism, if not treated promptly, can result in irreversible damage to the erectile tissue. Males who have an erection lasting greater than 4 hours, whether painful or not, should immediately discontinue the drug and seek emergency medical attention [see *Adverse Reactions (6.2)*, *Overdosage (10)*].

RALDESY should be used with caution in males who have conditions that might predispose them to priapism (e.g., sickle cell anemia, multiple myeloma, or leukemia), or in men with anatomical deformation of the penis (e.g., angulation, cavernosal fibrosis, or Peyronie's disease).

5.7 Activation of Mania or Hypomania

In patients with bipolar disorder, treating a depressive episode with RALDESY or another antidepressant may precipitate a mixed/manic episode. Activation of mania/hypomania has been reported in a small proportion of patients with major affective disorder who were treated with antidepressants. Prior to initiating treatment with RALDESY, screen patients for any personal or family history of bipolar disorder, mania, or hypomania [see *Dosage and Administration (2.3)*].

5.8 Discontinuation Syndrome

Adverse reactions after discontinuation of serotonergic antidepressants, particularly after abrupt discontinuation, include: nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible [See *Dosage and Administration (2.6)*].

5.9 Potential for Cognitive and Motor Impairment

RALDESY™ may cause somnolence or sedation and may impair the mental and/or physical ability required for the performance of potentially hazardous tasks. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that the drug treatment does not affect them adversely.

5.10 Angle-Closure Glaucoma

The pupillary dilation that occurs following use of many antidepressant drugs including RALDESY may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy. Avoid use of antidepressants, including RALDESY, in patients with untreated anatomically narrow angles.

5.11 Hyponatremia

Hyponatremia may occur as a result of treatment with SNRIs and SSRIs, including RALDESY. Cases with serum sodium lower than 110 mmol/L have been reported. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. In many cases, this hyponatremia appears to be the

result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

In patients with symptomatic hyponatremia, discontinue RALDESY and institute appropriate medical intervention. Elderly patients, patients taking diuretics, and those who are volume-depleted may be at greater risk of developing hyponatremia with SSRIs and SNRIs [see *Use in Specific Populations* (8.5)].

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Suicidal Thoughts and Behaviors in Pediatric and Young Adult Patients [see *Boxed Warning and Warnings and Precautions* (5.1)]
- Serotonin Syndrome [see *Warnings and Precautions* (5.2)]
- Cardiac Arrhythmias (see *Warnings and Precautions* (5.3))
- Orthostatic Hypotension and Syncope [see *Warnings and Precautions* (5.4)]
- Increased Risk of Bleeding [see *Warnings and Precautions* (5.5)]
- Priapism [see *Warnings and Precautions* (5.6)]
- Activation of Mania or Hypomania [see *Warnings and Precautions* (5.7)]
- Discontinuation Syndrome [see *Warnings and Precautions* (5.8)]
- Potential for Cognitive and Motor Impairment [see *Warnings and Precautions* (5.9)]
- Angle-Closure Glaucoma [see *Warnings and Precautions* (5.10)]
- Hyponatremia [see *Warnings and Precautions* (5.11)]

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.

The safety of RALDESY for the treatment of MDD in adults is based on studies of trazodone hydrochloride tablets. Below is a display of adverse reactions of trazodone hydrochloride tablets from those studies.

Table 2: Common Adverse Reactions Occurring in $\geq 2\%$ of Trazodone hydrochloride Tablets-treated Patients and Greater than the Rate of Placebo-Treated Patients as Observed in Controlled Clinical Studies

	Inpatients		Outpatients	
	Trazodone hydrochloride N=142	Placebo N=95	Trazodone hydrochloride N=157	Placebo N=158
Allergic				
Skin Condition/Edema	3%	1%	7%	1%
Autonomic				
Blurred Vision	6%	4%	15%	4%
Constipation	7%	4%	8%	6%
Dry Mouth	15%	8%	34%	20%
Cardiovascular				
Hypertension	20%	1%	1%	*
Hypotension	7%	1%	4%	0
Syncope	3%	2%	5%	1%
CNS				
Confusion	5%	0	6%	8%
Decreased Concentration	3%	2%	1%	0
Disorientation	2%	0	*	0
Dizziness/Light-Headedness	20%	5%	28%	15%
Drowsiness	24%	6%	41%	20%
Fatigue	11%	4%	6%	3%
Headache	10%	5%	20%	16%
Nervousness	15%	11%	6%	8%
Gastrointestinal				
Abdominal/Gastric Disorder	4%	4%	6%	4%
Diarrhea	0	1%	5%	1%
Nausea/Vomiting	10%	1%	13%	10%
Musculoskeletal				
Aches/Pains	6%	3%	5%	3%
Neurological				
Incoordination	5%	0	2%	*
Tremors	3%	1%	5%	4%
Other				
Eyes Red/Tired/Itching	3%	0	0	0
Head Full-Heavy	3%	0	0	0
Malaise	3%	0	0	0
Nasal/Sinus Congestion	3%	0	6%	3%

Weight Gain	1%	0	5%	2%
Weight Loss	*	3%	6%	3%

Other adverse reactions occurring at an incidence of <2% with the use of trazodone hydrochloride in the controlled clinical studies: akathisia, allergic reaction, anemia, chest pain, delayed urine flow, early menses, flatulence, hallucinations/delusions, hematuria, hypersalivation, hypomania, impaired memory, impaired speech, impotence, increased appetite, increased libido, increased urinary frequency, missed periods, muscle twitches, numbness, paresthesia, retrograde ejaculation, shortness of breath, and tachycardia/palpitations. Occasional sinus bradycardia has occurred in long-term studies.

6.2 Postmarketing Experience

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

- Blood and lymphatic system disorders:** hemolytic anemia, leukocytosis
- Cardiac disorders:** cardiospasm, congestive heart failure, conduction block, orthostatic hypotension and syncope, palpitations, bradycardia, atrial fibrillation, myocardial infarction, cardiac arrest, arrhythmia, ventricular ectopic activity, including ventricular tachycardia and QT prolongation. Prolonged QT interval, torsade de pointes, and ventricular tachycardia have been reported at doses of 100 mg per day or less [see Warnings and Precautions (5.3)].
- Endocrine disorders:** inappropriate ADH syndrome
- Eye disorders:** diplopia
- Gastrointestinal disorders:** increased salivation, nausea/vomiting
- General disorders and administration site conditions:** chills, edema, unexplained death, weakness
- Hepatobiliary disorders:** cholestasis, jaundice, hyperbilirubinemia, liver enzyme alterations
- Investigations:** increased amylase
- Metabolism and nutrition disorders:** methemoglobinemia
- Nervous system disorders:** aphasia, ataxia, cerebrovascular accident, extrapyramidal symptoms, grand mal seizures, paresthesia, tardive dyskinesia, vertigo
- Psychiatric disorders:** abnormal dreams, agitation, anxiety, hallucinations, insomnia, paranoid reaction, psychosis, stupor
- Renal and urinary disorders:** urinary incontinence, urinary retention
- Reproductive system and breast disorders:** breast enlargement or engorgement, clitorism, lactation, priapism [see Warnings and Precautions (5.6)]
- Respiratory, thoracic and mediastinal disorders:** apnea
- Skin and subcutaneous tissue disorders:** alopecia, hirsutism, leukonychia, pruritus, psoriasis, rash, urticaria
- Vascular disorders:** vasodilation

7 DRUG INTERACTIONS

Table 3 displays clinically significant drug interactions with RALDESY.

Table 3: Clinically Significant Drug Interactions with RALDESY

Monoamine Oxidase Inhibitors (MAOIs)	
Clinical Impact:	The concomitant use of MAOIs and serotonergic drugs including RALDESY increases the risk of serotonin syndrome.
Intervention:	RALDESY is contraindicated in patients taking MAOIs, including MAOIs such as linezolid or intravenous methylene blue [see Contraindications (4), Dosage and Administration (2.3, 2.4), and Warnings and Precautions (5.2)].
Other Serotonergic Drugs	
Clinical Impact:	The concomitant use of serotonergic drugs, including RALDESY and other serotonergic drugs increases the risk of serotonin syndrome.
Intervention:	Monitor patients for signs and symptoms of serotonin syndrome, particularly during RALDESY initiation. If serotonin syndrome occurs, consider discontinuation of RALDESY and/or concomitant serotonergic drugs [see Warnings and Precautions (5.2)].
Antiplatelet Agents and Anticoagulants	
Clinical Impact:	Serotonin release by platelets plays an important role in hemostasis. The concurrent use of an antiplatelet agent or anticoagulant with RALDESY may potentiate the risk of bleeding.
Intervention:	Inform patients of the increased risk of bleeding with the concomitant use of RALDESY and antiplatelet agents and anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio (INR) when initiating or discontinuing RALDESY [see Warnings and Precautions (5.5)].
Strong CYP3A4 Inhibitors	
Clinical Impact:	The concomitant use of RALDESY and strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of RALDESY alone.

Intervention:	If RALDESY is used with a potent CYP3A4 inhibitor, the risk of adverse reactions, including cardiac arrhythmias, may be increased and a lower dose of RALDESY should be considered [see <i>Dosage and Administration (2.5), Warnings and Precautions (5.3)</i>].
Strong CYP3A4 Inducers	
Clinical Impact:	The concomitant use of RALDESY and strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of RALDESY alone.
Intervention:	Patients should be closely monitored to see if there is a need for an increased dose of RALDESY when taking CYP3A4 inducers [see <i>Dosage and Administration (2.5)</i>].
Digoxin and Phenytoin	
Clinical Impact:	Digoxin and phenytoin are narrow therapeutic index drugs. Concomitant use of RALDESY can increase digoxin or phenytoin concentrations.
Intervention:	Measure serum digoxin or phenytoin concentrations before initiating concomitant use of RALDESY. Continue monitoring and reduce digoxin or phenytoin dose as necessary.
Central Nervous System (CNS) Depressants	
Clinical Impact:	RALDESY may enhance the response CNS depressants.
Intervention:	Patients should be counseled that RALDESY may enhance the response to alcohol, barbiturates, and other CNS depressants.
QT Interval Prolongation	
Clinical Impact:	Concomitant use of drugs that prolong the QT interval may add to the QT effects of RALDESY and increase the risk of cardiac arrhythmia.
Intervention:	Avoid the use of RALDESY in combination with other drugs known to prolong QTc [see <i>Warnings and Precautions (5.3)</i>].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antidepressants during pregnancy. Healthcare providers should encourage patients to enroll by calling the National Pregnancy Registry for Antidepressants at 1-866-961-2388 or visiting online at <https://womensmentalhealth.org/research/pregnancyregistry/antidepressants/>.

Risk Summary

Published prospective cohort studies, case series, and case reports over several decades with trazodone hydrochloride tablets use in pregnant women have not identified any drug-associated risks of major birth defects, miscarriage, or other adverse maternal or fetal outcomes (see *Data*). There are risks associated with untreated depression in pregnancy (see *Clinical Considerations*). Trazodone hydrochloride has been shown to cause increased fetal resorption and other adverse effects on the fetus in the rat when given at dose levels approximately 7.3 to 11 times the maximum recommended human dose (MRHD) of 400 mg/day in adults on a mg/m² basis. There was also an increase in congenital anomalies in the rabbit at approximately 7.3 to 22 times the MRHD on a mg/m² basis (see *Data*).

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryofetal risk

Women who discontinue antidepressants during pregnancy are more likely to experience a relapse of major depression than women who continue antidepressants. This finding is from a prospective, longitudinal study of 201 pregnant women with a history of major depressive disorder who were euthymic and taking antidepressants at the beginning of pregnancy. Consider the risk of untreated depression when discontinuing or changing treatment with antidepressant medication during pregnancy and postpartum.

Data

Human Data

While available studies cannot definitively establish the absence of risk, published data from prospective cohort studies, case series, and case reports over several decades have not identified an association with trazodone use during pregnancy and major birth defects, miscarriage, or other adverse maternal or fetal outcomes. All available studies have methodological limitations, including small sample size and inconsistent comparator groups.

Animal Data

No teratogenic effects were observed when trazodone was given to pregnant rats and rabbits during the period of organogenesis at oral doses up to 450 mg/kg/day. This dose is 11 and 22 times, in rats and rabbits, respectively, the maximum recommended human dose (MRHD) of 400 mg/day in adults on a mg/m² basis. Increased fetal resorption and other adverse effects on the fetus in rats at 7.3 to 11 times the MRHD and increase in congenital anomalies in rabbits at 7.3 to 22 times the MRHD on a mg/m² basis were observed. No further details on these studies are available.

8.2 Lactation

Risk Summary

Data from published literature report the transfer of trazodone into human milk. There are no data on the effect of trazodone on milk production. Limited data from postmarketing reports have not identified an association of adverse effects on the breastfed child. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for RALDESY and any potential adverse effects on the breastfed child from RALDESY or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness of RALDESY in the pediatric patients have not been established.

Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric patients [see *Boxed Warning, Warnings and Precautions (5.1)*].

8.5 Geriatric Use

Reported clinical literature and experience with trazodone has not identified differences in responses between geriatric and younger patients. However, as experience with trazodone hydrochloride in geriatric patients is limited, RALDESY should be used with caution in these patients.

Serotonergic antidepressants have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse reaction [see *Warnings and Precautions (5.11)*].

8.6 Renal Impairment

Trazodone has not been studied in patients with renal impairment. RALDESY should be used with caution in this population.

8.7 Hepatic Impairment

Trazodone has not been studied in patients with hepatic impairment. RALDESY should be used with caution in this population.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Trazodone hydrochloride is not a controlled substance.

9.2 Abuse

Although trazodone hydrochloride has not been systematically studied in preclinical or clinical studies for its potential for abuse, no indication of drug-seeking behavior was seen in the clinical studies with trazodone hydrochloride.

10 OVERDOSAGE

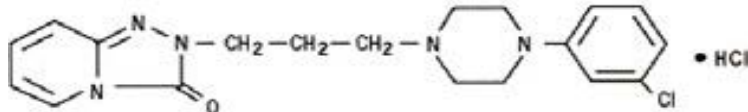
Death from overdose has occurred in patients ingesting trazodone and other CNS depressant drugs concurrently (alcohol; alcohol and chloral hydrate and diazepam; amobarbital; chlordiazepoxide; or meprobamate).

The most severe reactions reported to have occurred with overdose of trazodone alone have been priapism, respiratory arrest, seizures, and ECG changes, including QT prolongation. The reactions reported most frequently have been drowsiness and vomiting. Overdosage may cause an increase in incidence or severity of any of the reported adverse reactions.

There is no specific antidote for trazodone hydrochloride overdose. Consider contacting the Poison Help line 1-888-222-1222 or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

RALDESY contains trazodone hydrochloride, a selective serotonin reuptake inhibitor and 5HT₂ receptor antagonist. Trazodone hydrochloride is a triazolopyridine derivative designated as 2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-1,2,4-triazolo [4,3-a]pyridin-3(2H)-one hydrochloride. It is a white odorless crystalline powder which is freely soluble in water. The structural formula is represented



as follows:

Molecular Formula: C₁₉H₂₂ClN₅O • HCl

Molecular Weight: 408.33

RALDESY Oral Solution: Each mL contains 10 mg of Trazodone Hydrochloride, USP equivalent to 9.1 mg of trazodone base. The following inactive ingredients: disodium edetate, glycerin, ortho phosphoric acid, propyl gallate, propylene glycol, purified water, sodium benzoate, sorbitol, and sucralose. The pH of the oral solution is 3.8 to 4.8.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of trazodone's antidepressant action is unclear, but is thought to be related to its enhancement of serotonergic activity in the CNS. Trazodone is both a selective serotonin reuptake inhibitor (SSRI) and a 5HT₂ receptor antagonist and the net result of this action on serotonergic transmission and its role in trazodone's antidepressant effect is unknown.

12.2 Pharmacodynamics

Preclinical studies have shown that trazodone selectively inhibits neuronal reuptake of serotonin (K_i = 367 nM) and acts as an antagonist at 5-HT_{2A} (K_i = 35.6 nM) serotonin receptors. Trazodone is also an antagonist at several other monoaminergic receptors including 5-HT_{2B} (K_i = 78.4 nM), 5-HT_{2C} (K_i = 224 nM), α_{1A} (K_i = 153 nM), α_{2C} (K_i = 155 nM) receptors and it is a partial agonist at 5-HT_{1A} (K_i = 118 nM) receptor.

Trazodone antagonizes alpha 1-adrenergic receptors, a property which may be associated with postural hypotension.

12.3 Pharmacokinetics

No clinically significant difference in pharmacokinetics of trazodone was observed between RALDESY and immediate-release trazodone hydrochloride tablet administered under fed conditions.

Absorption

Peak plasma levels occur approximately one hour after administration under fed conditions.

Effect of Food

Ingestion of a high-fat meal with RALDESY lowers mean C_{max} of trazodone by 31% and increases mean AUC by 8%. Median T_{max} was similar between fed and fasted conditions.

Distribution

Trazodone is 89% to 95% protein bound *in vitro* at concentrations attained with therapeutic doses in humans.

Metabolism

In vitro studies in human liver microsomes show that trazodone is metabolized, via oxidative cleavage, to an active metabolite, m-chlorophenylpiperazine (mCPP) by CYP3A4. Other metabolic pathways that may be involved in the metabolism of trazodone have not been well characterized. Trazodone is extensively metabolized; less than 1% of an oral dose is excreted unchanged in the urine.

Elimination

The average terminal elimination half-life of RALDESY under fed state is 18 hours.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No drug- or dose-related occurrence of carcinogenesis was evident in rats receiving trazodone in daily oral doses up to 7.3 times the maximum recommended human dose (MRHD) of 400 mg/day in adults on a mg/m² basis.

Mutagenesis

No genotoxicity studies were conducted with trazodone.

Impairment of Fertility

Trazodone has no effect on fertility in rats at doses up to 7.3 times the MRHD in adults on a mg/m² basis.

14 CLINICAL STUDIES

The efficacy of RALDESY for the treatment of MDD in adults is based on studies of trazodone hydrochloride tablets.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

RALDESY™ contains 10 mg/mL of trazodone hydrochloride. It is a clear, colorless solution and is supplied as:

150 mL amber glass bottle

- NDC 30698-455-03 with child-resistant cap along with a 10 mL calibrated oral dosing syringe and bottle adapter.

150 mL white, opaque, high-density polyethylene (HDPE) bottle

- NDC 30698-455-02 with child-resistant cap along with a 10 mL calibrated oral dosing syringe and bottle adapter.

300 mL amber glass bottle

- NDC 30698-455-04 with child-resistant cap along with a 10 mL calibrated oral dosing syringe and bottle adapter.

300 mL white, opaque, HDPE bottle

- NDC 30698-455-01 with child-resistant cap along with a 10 mL calibrated oral dosing syringe and bottle adapter.

The bottle, bottle adapter and the dosing syringe are placed in a carton.

Storage and Handling

Store at 20°C to 25°C (68°F to 77°F). Excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Protect from light. Discard any unused RALDESY remaining in the bottle 20 days after first opening the bottle.

17 PATIENT COUNSELING INFORMATION

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

Suicidal Thoughts and Behaviors

Advise patients and caregivers to look for the emergence of suicidality, especially early during treatment and when the dosage is adjusted up or down and instruct them to report such symptoms to the healthcare provider [see *Box Warning and Warnings and Precautions* (5.1)].

Dosage and Administration

Advise patients that RALDESY should be taken shortly after a meal or light snack. Advise patients regarding the importance of following dosage titration instructions [see *Dosage and Administration* (2)].

Serotonin Syndrome

Caution patients about the risk of serotonin syndrome, particularly with the concomitant use of RALDESY with other serotonergic drugs including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's Wort, and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid). Patients should contact their health care provider or report to the emergency room if they experience signs or symptoms of serotonin syndrome [see *Warnings and Precautions* (5.2) and *Drug Interactions* (7)].

Increased Risk of Bleeding

Inform patients about the concomitant use of RALDESY with aspirin, NSAIDs, other antiplatelet drugs, warfarin, or other anticoagulants because the combined use of drugs that interfere with serotonin reuptake and these medications has been associated with an increased risk of bleeding. Advise them to inform their health care providers if they are taking or planning to take any prescription or over-the-counter medications that increase the risk of bleeding [see *Warnings and Precautions* (5.5)].

Activation of Mania or Hypomania

Advise patients and their caregivers to observe for signs of activation of mania/hypomania and instruct them to report such symptoms to the healthcare provider [see *Warnings and Precautions* (5.7)].

Discontinuation Syndrome

Advise patients not to abruptly discontinue RALDESY and to discuss any tapering regimen with their healthcare provider. Adverse reactions can occur when RALDESY is discontinued [see *Warnings and Precautions* (5.8)].

Concomitant Medications

Advise patients to inform their health care providers if they are taking, or plan to take any prescription or over-the-counter medications since there is a potential for interactions [see *Drug Interactions* (7.1)].

Pregnancy

Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during therapy with RALDESY. Advise patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to RALDESY during pregnancy [see *Use in Special Populations* (8.1)].

Manufactured for and distributed by:

Validus Pharmaceuticals LLC
Parsippany, NJ 07054

MEDICATION GUIDE
RALDESY™ (ral DEH see)
(trazodone hydrochloride)
oral solution

What is the most important information I should know about RALDESY?

RALDESY can cause serious side effects, including:

- **Increased risk of suicidal thoughts or actions.** RALDESY and other antidepressant medicines increase the risk of suicidal thoughts and actions in people 24 years of age and younger, **especially within the first few months of treatment or when the dose is changed. RALDESY is not for use in children.**

- o **Depression and other mental illnesses are the most important causes of suicidal thoughts and actions.**

How can I watch for and try to prevent suicidal thoughts and actions?

- o Pay close attention to any changes, especially sudden changes in mood, behaviors, thoughts, or feelings if you develop suicidal thoughts or actions. This is very important when an antidepressant medicine is started or when the dose is changed.
- o Call your healthcare provider right away to report new or sudden changes in mood, behavior, thoughts or feelings, or if you develop suicidal thoughts or actions.
- o Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

Call a healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:

- attempts to commit suicide
- thoughts about suicide or dying
- feeling agitated, restless, angry, or irritable
- other unusual changes in behavior and mood
- acting on dangerous impulses
- new or worse depression
- trouble sleeping
- acting aggressive or violent
- a new or worse anxiety or panic attacks
- an increase in activity or talking more than what is normal for you

See **“What are the possible side effects of RALDESY?”** for more information about side effects.

What is RALDESY?

RALDESY is a prescription medicine used in adults to treat major depressive disorder (MDD). It is not known if RALDESY is safe and effective for use in children.

Who should not take RALDESY?

Do not take RALDESY if you:

- are taking, or have stopped taking within the last 14 days, a medicine called Monoamine Oxidase Inhibitor (MAOI), including the antibiotic linezolid and intravenous methylene blue

Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI, including the antibiotic linezolid or intravenous blue.

Do not start taking an MAOI for at least 14 days after you stop treatment with RALDESY.

Before taking RALDESY tell your healthcare provider about all of your medical conditions, including if you:

- have or have a family history of heart problems, including fast or slow heartbeat, or changes in the electrical activity of your heart (QT prolongation)
- have ever had a heart attack
- have or have had bleeding problems
- are male and have conditions that may cause a prolonged or painful erection (priapism) such as sickle cell anemia, multiple myeloma, leukemia, or a deformed penis
- have or have a family history of bipolar disorder, mania, or hypomania
- have high pressure in the eye (glaucoma)
- have low sodium levels in your blood
- are pregnant or plan to become pregnant. It is not known if RALDESY will harm your unborn baby. Talk to your healthcare provider about the risks to you or your unborn baby if you take RALDESY during pregnancy.
 - o Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with RALDESY.
 - o There is a pregnancy registry for females who are exposed to RALDESY during pregnancy. The purpose of this registry is to collect information about the health of females exposed to RALDESY and their baby. If you become pregnant during treatment with RALDESY, talk to your healthcare provider about registering with the National

Pregnancy Registry for Antidepressants. You can register by calling 1-866-961-2388 or visiting online at <https://womensmentalhealth.org/research/pregnancyregistry/antidepressants/>.

- are breastfeeding or plan to breastfeed. RALDESY passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with RALDESY.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

RALDESY and some other medicines may affect each other causing serious side effects. RALDESY may affect the way other medicines work and other medicines may affect the way RALDESY works.

Especially tell your healthcare provider if you take:

- MAOIs
- medicines used to treat migraine headache called triptans
- medicines used to treat mood, anxiety, psychotic or thought disorders, including tricyclic antidepressants, lithium, selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), buspirone, or antipsychotics
- tramadol, fentanyl, or other opioids
- over-the-counter supplements such as tryptophan or St. John's Wort
- medicines used to treat high blood pressure
- medicines used to treat irregular heartbeats
- medicines that affect blood clotting such as aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin or other blood thinners
- digoxin
- medicines used to treat seizures or convulsions
- diuretics

Ask your healthcare provider if you are not sure if you are taking any of these medicines. Your healthcare provider can tell you if it is safe to take RALDESY with your other medicines.

Do not start or stop any other medicines during treatment with RALDESY without talking to your healthcare provider first. Stopping RALDESY suddenly may cause you to have serious side effects. See, **“What are the possible side effects of RALDESY?”**

Know the medicines you take. Keep a list of them to show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take RALDESY?

See the detailed Instructions for Use that comes with RALDESY for information on how to take RALDESY oral solution.

- Take RALDESY exactly as your healthcare provider tells you. Your healthcare provider may need to change your dose of RALDESY until it is the right dose for you.
- If you feel sleepy after taking RALDESY, talk to your healthcare provider. Your healthcare provider may change your dose or the time of day you take your RALDESY.
- Take RALDESY after a meal or light snack.
- Do not stop taking RALDESY without talking to your healthcare provider.
- If you take too much RALDESY, call your healthcare provider, your Poison Help Line at 1-800-222-1222, or go to the nearest hospital emergency room right away.

What should I avoid while taking RALDESY?

- **Do not** drive, operate heavy machinery, or do other dangerous activities until you know how RALDESY affects you. RALDESY can cause sleepiness or may affect your ability to make decisions, think clearly, or react quickly.
- **Do not** drink alcohol or take other medicines that make you sleepy or dizzy during treatment with RALDESY until you talk with your healthcare provider. RALDESY may make your sleepiness or dizziness worse if you drink alcohol or take other medicines that cause sleepiness or dizziness.

What are the possible side effects of RALDESY?

RALDESY can cause serious side effects, including:

- See **“What is the most important information I should know about RALDESY?”**

Serotonin syndrome. A potentially life-threatening problem called serotonin syndrome can happen when you take RALDESY with certain other medicines. See **“Who should not take RALDESY?”** **Call your healthcare provider or go to the nearest hospital emergency room right away** if you have any of the following signs and symptoms of serotonin syndrome:

- | | |
|---|--|
| o agitation | o flushing |
| o seeing or hearing things that are not real (hallucinations) | o high body temperature (hyperthermia) |

- o confusion
- o coma
- o fast heartbeat
- o changes in blood pressure
- o sweating
- o shaking (tremors), stiff muscles, or muscle twitching
- o loss of coordination
- o seizures
- o nausea, vomiting, diarrhea
- o dizziness

- **Changes in the electrical activity of your heart (QT prolongation).** Call your healthcare provider right away if you have any of the following symptoms: abnormal heartbeats, dizziness, feel lightheaded or faint.
- **Low blood pressure and fainting.** Low blood pressure can happen when you change positions from sitting to standing or laying down. You may feel dizzy, lightheaded, or faint.
- **Increased risk of bleeding.** Taking RALDESY with aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), warfarin, or blood thinners may add to this risk. Tell your healthcare provider right away about any unusual bleeding or bruising.
- **Painful erection lasting for more than 6 hours (priapism).** If you have an erection that lasts more than 4 hours, get medical help right away.
- **Manic episodes.** Manic episodes may happen in people with bipolar disorder who take RALDESY. Symptoms may include:
 - o greatly increased energy
 - o racing thoughts
 - o unusually grand ideas
 - o talking more or faster than usual
 - o severe problems sleeping
 - o reckless behavior
 - o excessive happiness or irritability
- **Discontinuation syndrome.** Suddenly stopping RALDESY may cause you to have serious side effects. Your healthcare provider may want to decrease your dose slowly. Symptoms may include:
 - o nausea
 - o sweating
 - o changes in your mood
 - o irritability and agitation
 - o dizziness
 - o electric shock feeling (paresthesia)
 - o tremor
 - o anxiety
 - o confusion
 - o headache
 - o tiredness
 - o problems sleeping
 - o hypomania
 - o ringing in the ears (tinnitus)
 - o seizures
- **Eye problems (angle-closure glaucoma).** RALDESY can cause a type of eye problem called angle-closure glaucoma in people with certain eye conditions. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are. Call your healthcare provider if you have changes in your vision, eye pain, or swelling or redness in or around the eye.
- **Low sodium in your blood (hyponatremia).** Low sodium levels in your blood that may be serious and may cause death, can happen during treatment with RALDESY. Elderly people and people who take certain medicines may be at greater risk for this. Signs and symptoms may include:
 - o headache
 - o difficulty concentrating
 - o memory changes
 - o confusion
 - o weakness and unsteadiness on your feet, which can lead to falls

In more severe or sudden cases, signs and symptoms include:

- o seeing or hearing things that are not real (hallucinations)
- o fainting
- o seizures
- o coma
- o stopping breathing (respiratory arrest)

The most common side effects of RALDESY include:

- swelling
- blurred vision
- fainting
- sleepiness
- tiredness
- diarrhea
- stuffy nose
- weight loss

These are not all of the possible side effects of RALDESY.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store RALDESY?

- Store RALDESY at room temperature between 68°F to 77°F (20°C to 25°C).
- RALDESY comes in a bottle with a child-resistant cap.
- Keep RALDESY out of the light.

- Throw away (discard) RALDESY 20 days after first opening the bottle.
- Safely throw away medicine that is out of date or no longer needed.

Keep RALDESY and all medicines out of the reach of children

General information about the safe and effective use of RALDESY.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use RALDESY for a condition for which it was not prescribed. Do not give RALDESY to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about RALDESY that is written for health professionals.

What are the ingredients in RALDESY?

Active ingredient: trazodone hydrochloride, USP

Inactive ingredients: disodium edetate, glycerin, ortho phosphoric acid, propyl gallate, propylene glycol, purified water, sodium benzoate, sorbitol, and sucralose.

Manufactured for and distributed by:

Validus Pharmaceuticals LLC

Parsippany, NJ 07054

For more information, go to www.RALDESY.com or call **Validus Pharmaceuticals LLC at 1-866-982-5438**.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

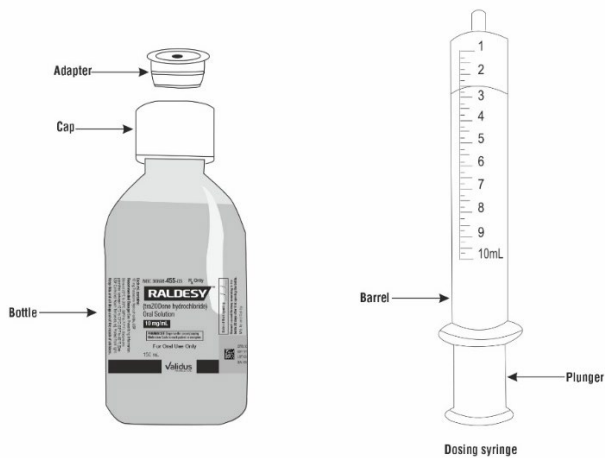
Issued: 11/2024

INSTRUCTIONS FOR USE
RALDESY™ (ral DEH see)
(trazodone hydrochloride)
oral solution

This Instructions for Use contains information on how to take RALDESY.

Read this Instructions for Use before you start taking RALDESY for the first time and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

Supplies needed to take RALDESY



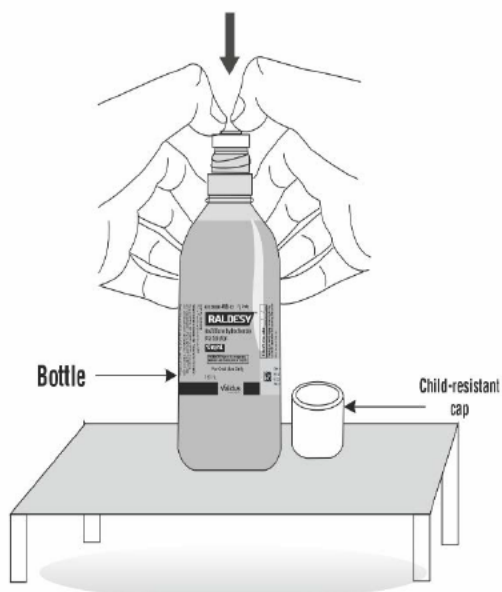
Each carton of RALDESY contains:

- 1 bottle of RALDESY oral solution
- 1 plastic adapter
- One 10 mL oral dosing syringe

Important Information You Need to Know Before Taking RALDESY

- For oral use only (taken by mouth).
- Use the plastic adapter and oral dosing syringe that comes in the carton. If you did not receive the plastic adapter and oral dosing syringe, contact your pharmacist.
- Ask your pharmacist how to measure your prescribed doses.
- Take RALDESY exactly as prescribed by your healthcare provider. **Do not** stop taking RALDESY without first talking to your healthcare provider.
- Take RALDESY after a meal or light snack.
- Check the expiration date on the bottle. If you have not opened the RALDESY bottle, **do not** use RALDESY if the expiration date on the bottle has passed. Contact your healthcare provider or pharmacist.
- **Do not** use RALDESY 20 days after first opening the bottle.

Preparing the RALDESY bottle



Step 1. Remove the child-resistant cap by pushing it **firmly** down and turning it counterclockwise (to the left), as shown on the top of the child-resistant cap.

Note: Save the child-resistant cap so you can close the bottle after each use.

Step 2. Hold the open bottle upright on a table and push the ribbed end of the plastic adapter firmly into the neck of the bottle as far as you can.

Step 3. Put the child-resistant cap back on the bottle to make sure the plastic adapter has been fully inserted into the neck of the bottle.

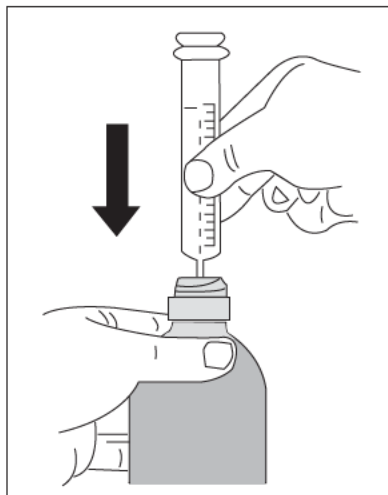
Note: You may not be able to push the plastic adapter all the way down, but it will be forced into the bottle when you put the child-resistant cap back on.

Now the bottle is ready to use with the oral dosing syringe.

Do not remove the adapter. The plastic adapter must always stay in the bottle. The child-resistant cap should seal the bottle in between use.

Write the date of first opening the RALDESY bottle.

Preparing the dose of RALDESY oral solution

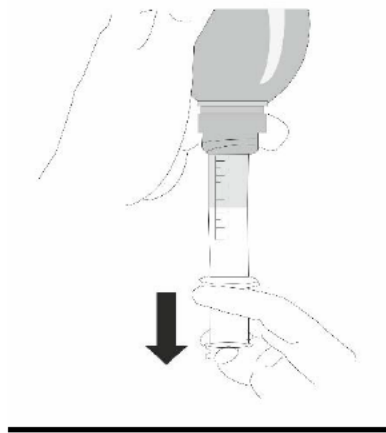


Step 4. Push down and turn the child-resistant cap to the left to open the bottle.

Note: Always replace the cap after use.

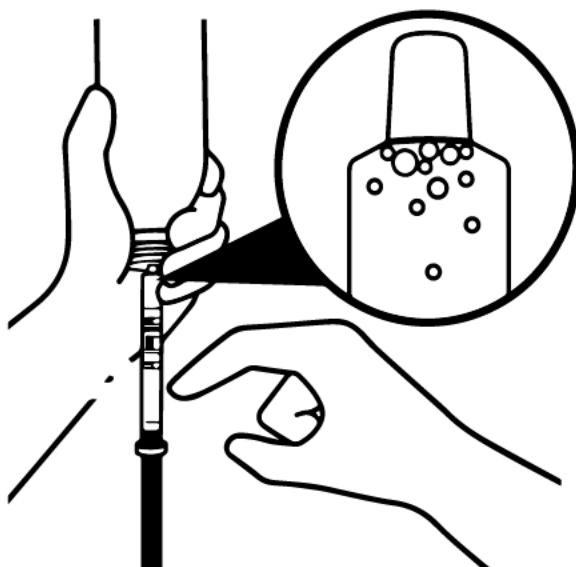
Step 5. Check that the plunger is all the way down inside the barrel of the oral dosing syringe.

Step 6. Keep the bottle upright and push the tip of the oral dosing syringe **firmly** into the plastic adapter.



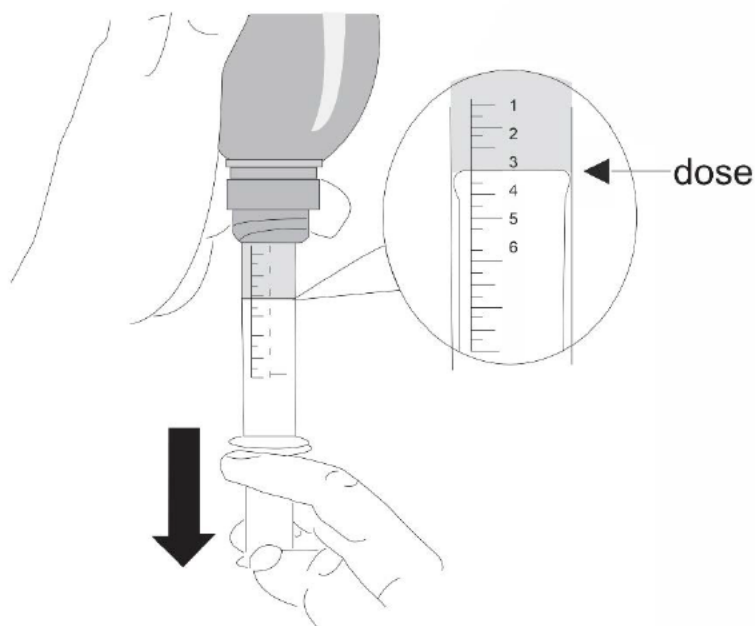
Step 7. Hold the syringe in place and carefully turn the bottle upside down.

Step 8. Slowly pull down the plunger to fill the oral dosing syringe slightly past your prescribed dose line to help remove any air bubbles.



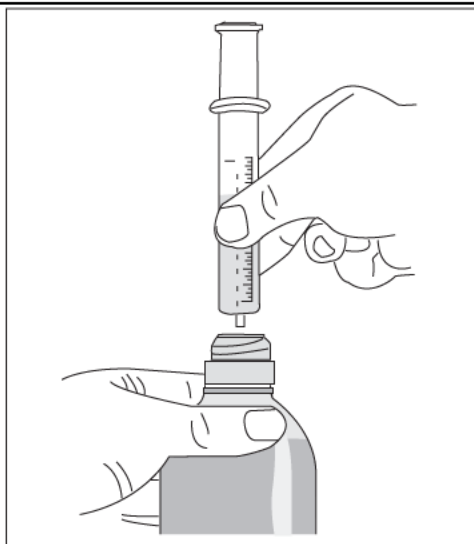
Step 9. Tap oral dosing syringe to move air bubbles to the top. Doing this helps set the correct dose.

Step 10. Push the plunger back slowly just far enough to completely push out any large or small air bubbles that may be trapped in the oral dosing syringe.



Step 11. Slowly pull the plunger down until the top edge of the plunger is level with the marker on the syringe barrel for the prescribed dose.

Note: If the prescribed dose is more than 10 mL, you will need to refill the oral dosing syringe to make up the full dose.



Step 12. Carefully turn the bottle upright. Take out the oral dosing syringe by gently twisting it out of the plastic adapter. The plastic adapter should stay in the bottle.

Taking the dose of RALDESY oral solution



Note: Sit up straight while taking RALDESY.

Step 13. Place the oral dosing syringe gently into your mouth. Push the plunger **slowly** until the plunger moves all of the medicine out of the oral dosing syringe.

Step 14. Swallow all of the medicine.

Step 15. Close the bottle by screwing the child-resistant cap back on the bottle after use. Make sure the child-resistant cap is tightly closed.

Step 16. Cleaning: After use, rinse the oral dosing syringe with warm water and allow it to dry thoroughly.

Step 17. Throw away (discard): Safely throw away medicine that is expired or no longer needed. Do not throw away any medicine down the sink or in your household trash. Ask your pharmacist how to throw away medicines you no longer use.

Storing RALDESY

- Store RALDESY at room temperature between 68°F to 77°F (20°C to 25°C).
- RALDESY comes in a bottle with a child-resistant cap.
- Keep RALDESY out of the light.
- Throw away (discard) RALDESY 20 days after first opening the bottle.
- Safely throw away medicine that is out of date or no longer needed.

Keep RALDESY and all medicines out of the reach of children.

Manufactured for and distributed by:

Validus Pharmaceuticals LLC
Parsippany, NJ 07054

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Approved: 11/2024

RALDESY (traZODone hydrochloride) Oral Solution 10 mg/mL - 150mL Amber Glass Carton

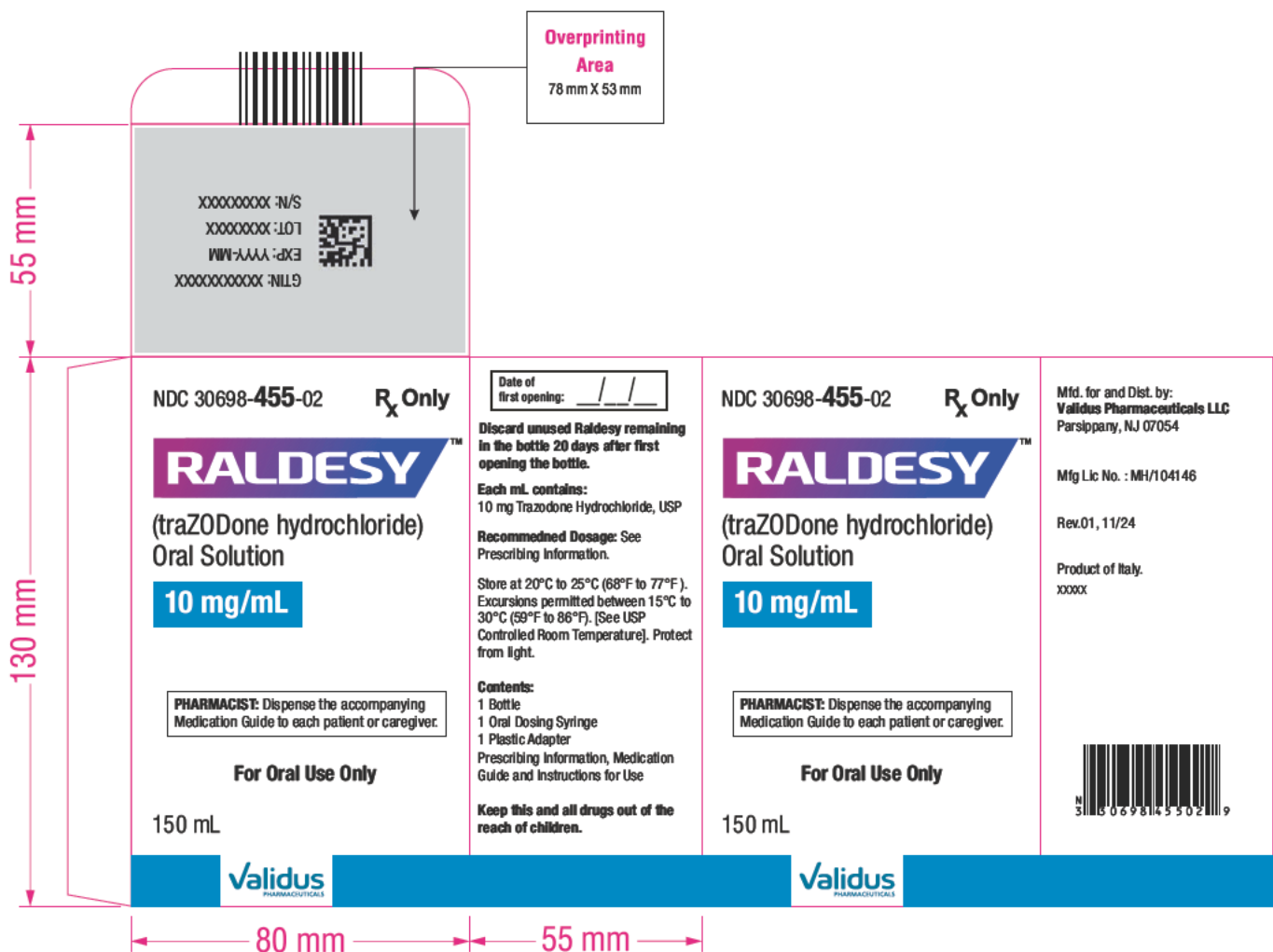


85 X 60 X 145 mm (Actual Size)

Pharma Code XXXXX



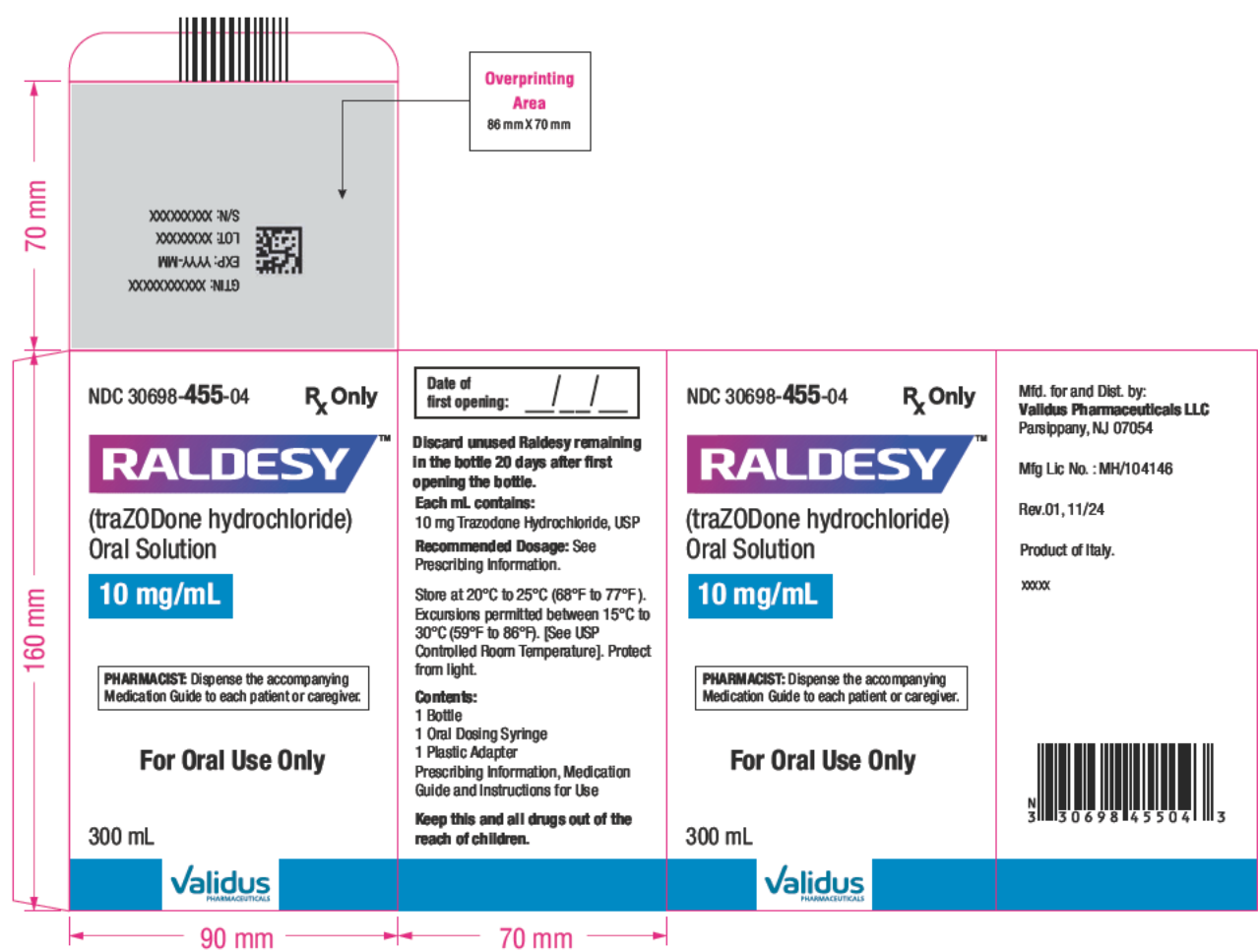
RALDESY (traZODone hydrochloride) Oral Solution 10 mg/mL - 150mL HDPE Carton



80 X 55 x 130 mm (Actual Size)
Pharma Code XXXXX



RALDESY - (traZODone hydrochloride) Oral Solution 10 mg/mL - 300mL Amber Glass - Carton

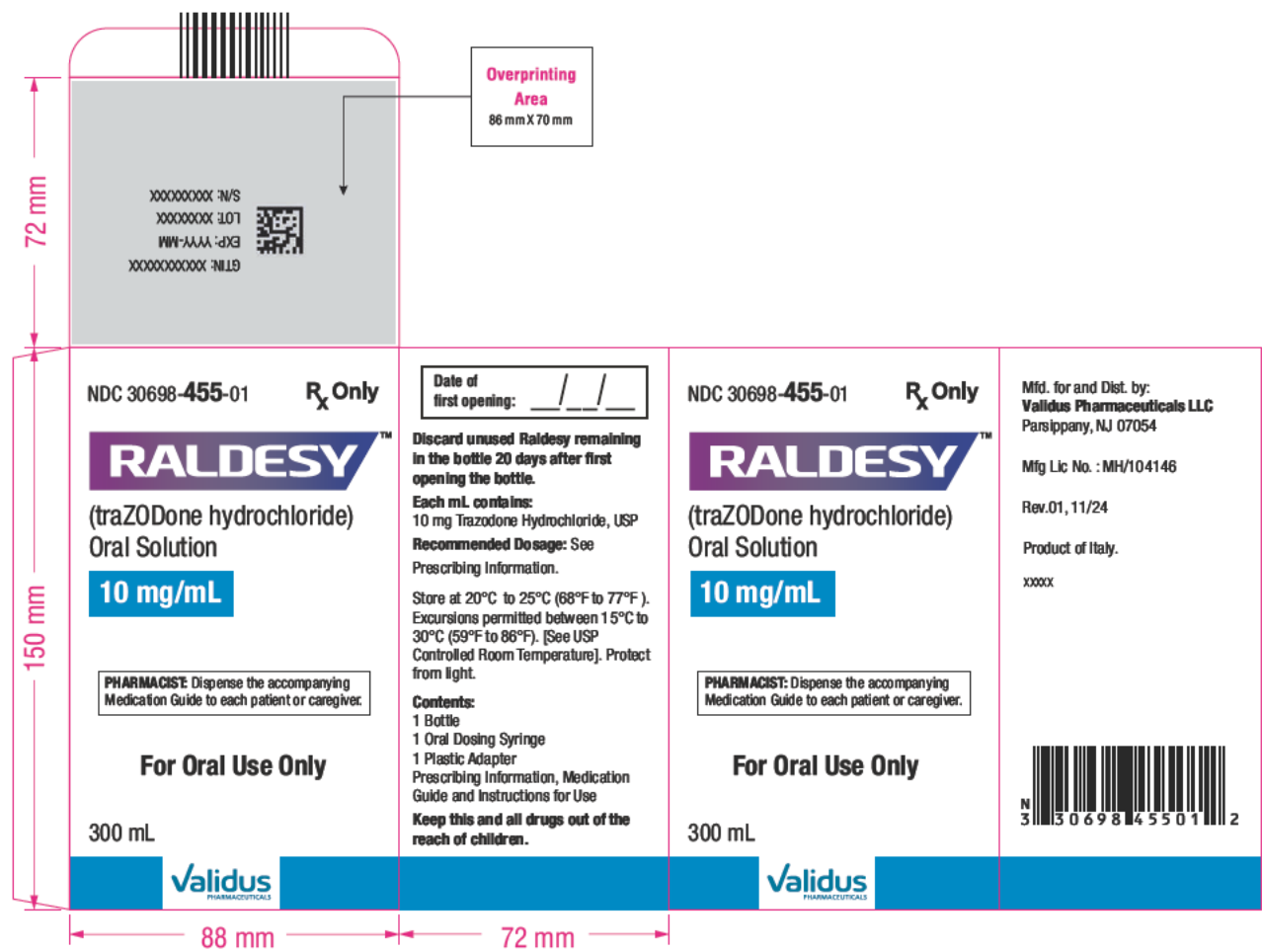


90 X 70 X 160 mm (Actual Size)
Pharma Code XXXXX



(b) (4)

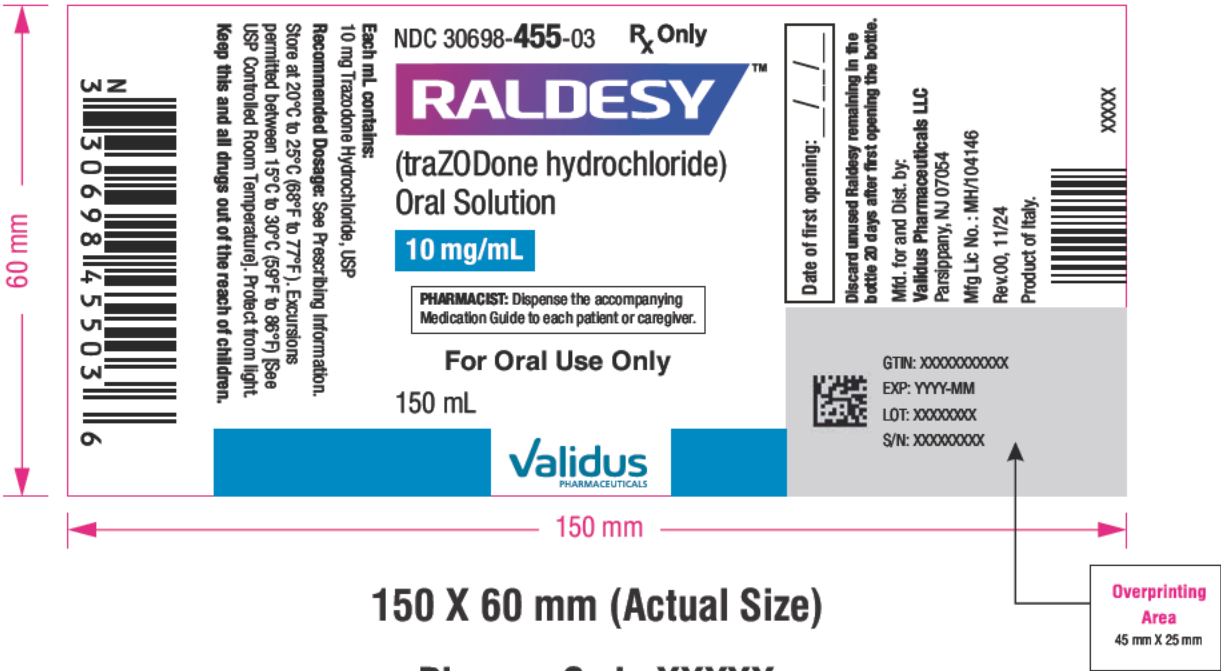
RALDESY - (traZODone hydrochloride) Oral Solution 10 mg/mL - 300mL HDPE - Carton



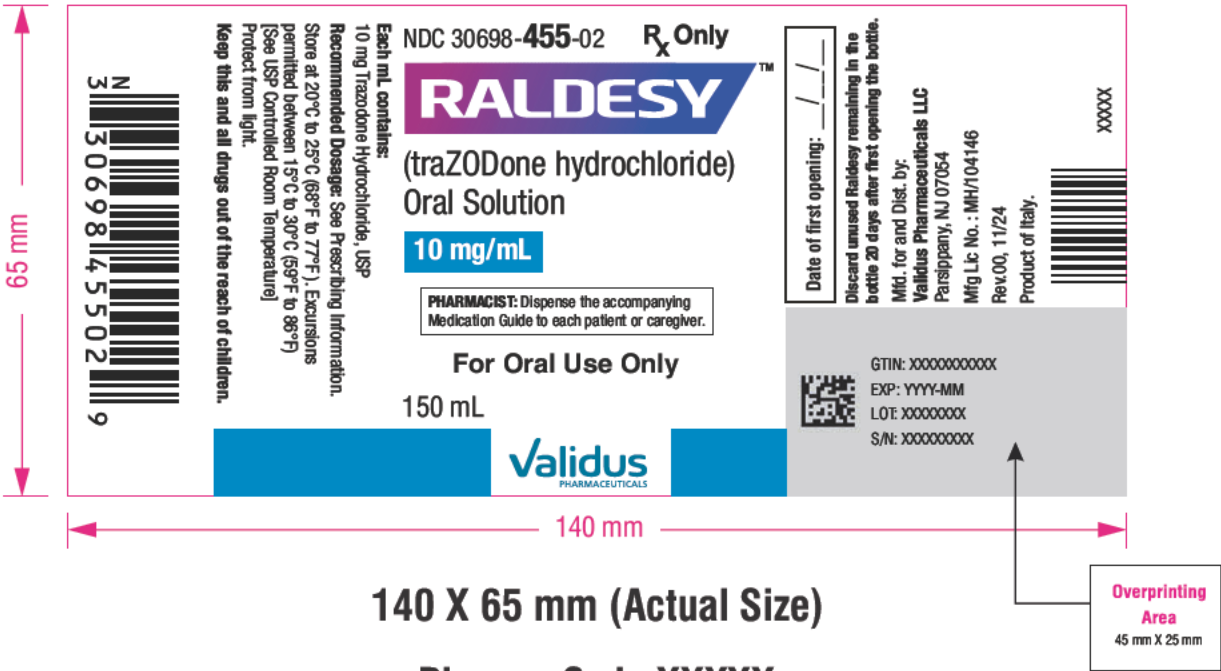
88 X 72 X 150 mm (Actual Size)
Pharma Code XXXXX



RALDESY (traZODone hydrochloride) Oral Solution 10 mg/mL - 150mL Amber Glass Bottle Label



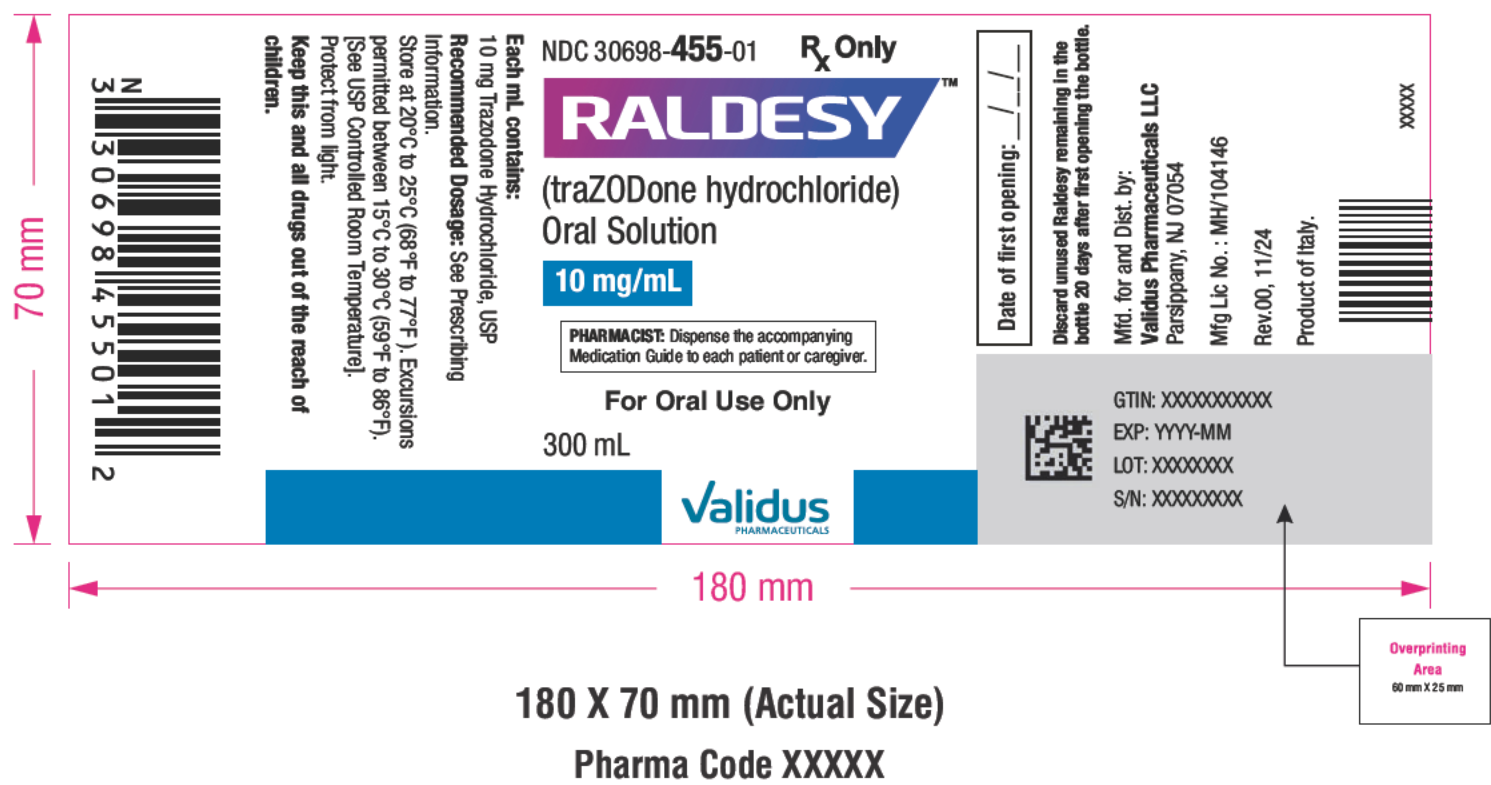
RALDESY (traZODone hydrochloride) Oral Solution 10 mg/mL - 150mL HDPE Bottle Label





(b) (4)

RALDESY (traZODone hydrochloride) Oral Solution 10 mg/mL - 300mL HDPE Label



(b) (4)

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

BERNARD A FISCHER
11/26/2024 10:08:59 AM