HUB Instructions Regarding Letters of Medical Necessity

Some payers may require that the prescribing physician document a patient's medical necessity for the treatment to get insurance coverage for the agent. The following letter is only intended as a sample Letter of Medical Necessity that outlines the information a payer may request. Health plan requirements may vary, so the prescriber should refer to the prior authorization or coverage information specific to their patient's health plan before completing a Letter of Medical Necessity. Use of this letter does not guarantee coverage or reimbursement for the drug.

This information is presented for informational purposes only and is not intended to provide reimbursement or legal advice. Providers are encouraged to contact third-party payers for specific information about their coverage policies. For support, call 866-524-6546.

The provider should refer to the full prescribing information when determining whether RALDESY™ (trazodone hydrochloride) oral solution is medically appropriate for the patient. It is the sole responsibility of the healthcare provider to include the proper information and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

Make sure you have the following for an efficient submission of your Letter of Medical Necessity:

- Patient's insurance policy/ID number
- Case ID number if a decision has already been rendered
- Patient's full name, plan identification number, and date of birth
- A brief medical history, including diagnosis, allergies, existing comorbidities, and *International Classification of Diseases* (*ICD*) code(s)
- Clinical support for your recommendation
- Your office contact information

For support in person or by phone, call 866-524-6546.

Please see Indications and Important Safety Information, including BOXED WARNING, at the end of this sample letter.

[Please note – this sample letter is intended to support the development of a Letter of Medical Necessity. Providers and their staff are responsible for confirming a diagnosis, establishing a treatment plan, and preparing the content and appropriate supporting materials for individual patients. The letter should be on the physician's letterhead and have his or her practice name and contact information.]

[Contact name of Pharmacy Director or other payer representative]
[Contact title]
[Name of health insurance company]
[Address]
[City, State ZIP]

RE: Letter of Medical Necessity for RALDESY™ (trazodone hydrochloride) oral solution

Patient: [Patient name]
Date of birth: [Date]
Group/policy number: [Number]
Policyholder: [Policyholder's name]
Diagnosis: [Insert diagnosis]

Dear [Contact name]:

I am writing on behalf of my patient, [Patient name], to [Document medical necessity] for treatment with RALDESY™ (trazodone hydrochloride) oral solution, a medication that is approved by the US Food and Drug Administration (FDA) for the treatment of major depressive disorder in adults. [Patient name] has a diagnosis of [Insert diagnosis], and I believe RALDESY™ is medically necessary for the treatment of [Patient name]'s [Insert diagnosis] as prescribed. On behalf of the patient, I am requesting approval for the use of and subsequent payment for RALDESY™.

On November 26, 2024, the FDA approved RALDESY™ 10 mg/mL for the treatment of major depressive disorder in adults, and it is the only liquid formulation approved by the FDA for this indication.[1] RALDESY™ is a selective serotonin reuptake inhibitor 5-HT_2 receptor antagonist.[1] RALDESY™ is AB rated by the FDA for bioequivalence to immediate-release tablet formulations of trazodone hydrochloride.[2]

The liquid formulation of RALDESY™ allows for ease of swallowing. Literature shows that dysphagia and depressive disorders may worsen one another, while dysphagia is associated with significant disease burden and morbidity.[3,4] The risk for swallowing difficulties, including dysphagia, increases with age, affecting an estimated 10% to 33% of older adults.[4]

Patients with difficulty swallowing may often alter oral medications, such as by cutting or crushing a tablet or opening a capsule to remove the contents.[5] However, modifying a medication's dosage form may change the absorption, distribution, metabolism, or elimination profile of the medication, which may lead to unintended consequences, such as reducing efficacy or toxicity.[5] In addition, using alternative medication formulations that use a calibrated oral syringe may help reduce errors in administering medications. Furthermore, patients taking oral medications often cite taste as a reason for difficulty taking medications, which may lead to noncompliance.[6] The palatable neutral flavor of RALDESY™ may allow patients to take their medication as prescribed.

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. RALDESY is not approved for use in pediatric patients.

Patient Medical History and Diagnosis

[Provide a brief medical history, including diagnosis, allergies, existing comorbidities, and *International Classification of Diseases* (*ICD*) code(s).]

[Discuss rationale for using <product name> vs other treatments. Insert your recommendation summary here, including your professional opinion of your patient's likely prognosis or disease progression without treatment.]

Based on the above, as well as the enclosed medical records, which offer additional support for the formulary exception request for [Product name], I respectfully request that [Payer name] cover [Product name] as prescribed for [Patient name].

Please refer to the prescribing information enclosed [and any appropriate supporting documents] for further details, and please don't hesitate to contact me if you have any further questions regarding this request. [Insert appropriate contact information.]

Thank you for your prompt attention to this matter.

Sincerely,

[Prescriber's name], [Credential]

cc: [Patient name]

Optional Enclosures: RALDESY™ prescribing information (PI), clinical notes and records, [variable published literature].

References:

1. RALDESY. Prescribing information. Validus Pharmaceuticals LLC; 2024.
2. US Food and Drug Administration. Orange Book Cumulative Supplement 11. FDA Law Blog. Updated November 2024. Accessed March 6, 2025. https://www.thefdalawblog.com/wp-content/uploads/2024/12/obcs_2024_11.pdf
3. Khayyat YM, Abdul Wahab RA, Natto NK, Al Wafi AA, Al Zahrani AA. Impact of anxiety and depression on the swallowing process among patients with neurological disorders and head and neck neoplasia: systemic review. *Egypt J Neurol Psychiatry Neurosurg*. 2023;59:75. doi:10.1186/s41983-023-00674-y
4. Thiyagalingam S, Kulinski AE, Thorsteinsdottir B, Shindelar KL, Takahashi PY. Dysphagia in older adults. *Mayo Clin Proc*. 2021;96(2):488-497. doi:10.1016/j.mayocp.2020.08.001
5. Harnett A, Byrne S, O'Connor J, Lyons D, Sahm LJ. Adult patients with difficulty swallowing oral dosage forms: a systematic review of the quantitative literature. *Pharmacy (Basel)*. 2023;11(5):167. doi:10.3390/pharmacy11050167

6. Shariff ZB, Dahmash DT, Kirby DJ, Missaghi S, Rajabi-Siahboomi A, Maidment ID. Does the formulation of oral solid dosage forms affect acceptance and adherence in older patients? A mixed methods systematic review. *J Am Med Dir Assoc*. 2020;21(8):1015-1023.e8. doi:10.1016/j.jamda.2020.01.108

RAL-516-25

IMPORTANT SAFETY 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. RALDESY is not approved for use in pediatric patients.

INDICATIONS AND USAGE

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

ADMINISTRATION

Administer RALDESY orally after a meal or light snack.

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.

WARNINGS AND PRECAUTIONS

Suicidal Thoughts and Behaviors in Pediatric and Young Adult 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. 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.

Serotonin Syndrome: Selective serotonin reuptake inhibitors (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. Serotonin syndrome can also occur when these drugs are used alone. 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. 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. 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.

Cardiac Arrhythmias: RALDESY should 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.

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.

Increased Risk of Bleeding: 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.

Priapism: 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).

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.

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.

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 machinery, including automobiles,until they are reasonably certain that the drug treatment does not cause them drowsiness.

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.

Hyponatremia: Hyponatremia may occur as a result of treatment with SSRIs and serotonin and norepinephrine reuptake inhibitors (SNRIs), 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 Full Prescribing Information for additional warnings and precautions associated with RALDESY.*

ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling: Suicidal Thoughts and Behaviors in Pediatric and Young Adult Patients, Serotonin Syndrome, Cardiac Arrythmias, Orthostatic Hypotension and Syncope, Increased Risk of Bleeding, Priapism, Activation of Mania or Hypomania, Discontinuation Syndrome, Potential for Cognitive and Motor Impairment, Angle-Closure Glaucoma and Hyponatremia.

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

See Full Prescribing Information for additional adverse reactions associated with RALDESY.

DRUG INTERACTIONS

Monoamine Oxidase Inhibitors (MAOIs): RALDESY is contraindicated in patients taking MAOIs, including MAOIs such as linezolid or intravenous methylene blue.

Other Serotonergic Drugs: 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.

Antiplatelet Agents and Anticoagulants: 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.

Strong CYP3A4 Inhibitors: 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.

Strong CYP3A4 Inducers: Patients should be closely monitored to see if there is a need for an increased dose of RALDESY when taking CYP3A4 inducers.

Digoxin and Phenytoin: Patient serum digoxin or phenytoin concentrations should be measured before initiating concomitant use of RALDESY. Continue monitoring and reduce digoxin or phenytoin dose as necessary.

Central Nervous System (CNS) Depressants: Patients should be counseled that RALDESY may enhance the response to alcohol, barbiturates, and other CNS depressants.

QT Interval Prolongation: Avoid the use of RALDESY in combination with other drugs known to prolong QT. *See Full Prescribing Information for additional potential drug interactions associated with RALDESY.*

USE IN SPECIFIC POPULATIONS

Pregnancy: There are risks associated with untreated depression in pregnancy. 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/m^2 basis.

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/.

Lactation: 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.

Pediatric Use: Safety and effectiveness of RALDESY in pediatric patients have not been established. Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric patients.

Geriatric Use: Serotonergic antidepressants have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse reaction.

Renal Impairment: RALDESY should be used with caution in this population.

Hepatic Impairment: RALDESY should be used with caution in this population.

DOSAGE FORMS AND STRENGTHS

RALDESY (10 mg/mL) Oral Solution: Clear, colorless solution. RALDESY is available only by prescription.

OVERDOSAGE

Death from overdose has occurred in patients concurrently ingesting trazodone and other CNS depressant drugs (e.g., 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 at 1-888-222-1222 or a medical toxicologist for additional overdose management recommendations.

Please see Full Prescribing Information including Boxed WARNING at www.raldesy.com.

Validus PHARMACEUTICALS LLC