UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 3065-12
Program	Step Therapy
Medication	Rexulti (brexpiprazole)
P&T Approval Date	11/2015, 5/2016, 8/2016, 10/2016, 2/2017, 3/2018, 3/2019, 3/2020, 6/2021, 6/2022, 7/2023
Effective Date	10/1/2023; Oxford only: N/A

1. **Background:**
Step Therapy programs are utilized to encourage the use of lower cost alternatives for certain therapeutic classes. Rexulti (brexpiprazole) is FDA approved for use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD), for the treatment of schizophrenia, and for the treatment of agitation associated with dementia due to Alzheimer's disease.

For the treatment of schizophrenia, treatment guidelines recommend the use of any atypical antipsychotic (with the exception of clozapine) as first-line. The use of adjunctive atypical antipsychotics in the treatment of major depressive disorder is reserved for those who fail to demonstrate response to adequate trials of antidepressant monotherapy. Antipsychotics are recommended for the treatment of agitation associated with dementia due to Alzheimer's disease only in patients with severe symptoms.

This program requires a member to try two atypical antipsychotics (aripiprazole plus the choice of at least one of the following: risperidone, olanzapine, ziprasidone, quetiapine IR or Seroquel XR) before providing coverage for Rexulti for schizophrenia. For major depressive disorder, this program requires the trial of two adequate antidepressant trials (at least two trials from different antidepressant classes) as well as an atypical antipsychotic prior to the coverage of Rexulti. For agitation associated with dementia, this program requires a trial of a selective serotonin reuptake inhibitor (SSRI) and an atypical antipsychotic prior to providing coverage for Rexulti. If a member has a prescription for Rexulti in the claims history within the previous 12 months, the claim will automatically process.

2. **Coverage Criteria [a]:**

Initial Authorization

A. **Rexulti** will be approved based on **one** of the following criteria:

1. Diagnosis of schizophrenia and history of failure, contraindication, or intolerance to **both** of the following:

a. aripiprazole (Document date and duration tried)

-AND-

b. At least **one** of the following (Document date, duration and drug tried):

i. risperidone

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ii. olanzapine
iii. quetiapine IR or XR
iv. ziprasidone

-OR-

2. Diagnosis of major depressive disorder, and used in combination with an antidepressant, and history of failure, contraindication, or intolerance to **all** of the following:

   a. At least **one** selective serotonin reuptake inhibitor (SSRI) (Document date, duration and drug tried).

   -AND-

   b. At least **one** of the following: serotonin norepinephrine reuptake inhibitor (SNRI), mirtazapine, or bupropion (Document date, duration and drug tried).

   -AND-

   c. At least **one** of the following atypical antipsychotics approved by the FDA for the adjunctive treatment of major depressive disorder with an antidepressant (Document drug, date and duration tried):

      i. olanzapine
      ii. aripiprazole
      iii. quetiapine extended-release

   -OR-

3. Diagnosis of agitation associated with dementia due to Alzheimer's disease, and history of failure, contraindication, or intolerance to **all** of the following:

   a. At least **one** selective serotonin reuptake inhibitor (SSRI) (Document date, duration and drug tried).

   -AND-

   b. At least **one** of the following (Document date, duration and drug tried).

      i. aripiprazole
      ii. risperidone
      iii. olanzapine
      iv. quetiapine IR or XR
      v. ziprasidone

   -OR-

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4. Treatment with Rexulti was initiated at a recent behavioral inpatient admission (discharge within the past 3 months) and the member is currently stable on therapy. (Document date of discharge from inpatient admission).

-OR-

5. All of the following:

   a. The member is new to the plan (as evidenced by coverage effective date of less than or equal to 120 days).
   b. The member is currently stabilized on Rexulti.

-OR-

6. All other diagnoses (not specified above):

   a. History of failure, contraindication or intolerance to aripiprazole and quetiapine. (Document the diagnosis, date and duration of trial for each preferred product).

Authorization will be issued for 12 months.

Reauthorization

A. Documentation of positive clinical response.

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Programs:

- Supply limits may also be in place.
- Prior Authorization/Medical Necessity may be in place.
- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.

4. References:

1. Rexulti [package insert]. Rockville, MD: Otsuka Pharmaceutical Co.; May 2023.
2. American Psychiatric Association. Practice Guideline for the Treatment of Patients with Schizophrenia Third Edition. 2021. Available at: https://psychiatryonline.org/doi/book/10.1176/appi.books.9780890424841
3. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder, Third Edition. 2010. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf
4. Nelson, C. Unipolar depression in adults: Treatment with second-generation antipsychotics. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on April 28, 2022).

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5. American Family Physician. Pharmacological Management of Agitation in Patients with Dementia. 2021. Available at: https://www.aafp.org/pubs/afp/issues/2021/0700/p91.html

Program	Step Therapy - Rexulti® (brexpiprazole)
Change Control	
11/2015	New program.
5/2016	Added criteria for members stable on Rexulti therapy post inpatient admission or new to the plan.
7/2016 8/2016	Removed requirement for diagnosis of schizophrenia (in background section) for those that are new to the plan and stable on Rexulti to align with clinical intent that anyone new to the plan who is stable on therapy remain on therapy per P&T recommendation. Added Indiana and West Virginia coverage information.
10/2016	Removed the word "please" from the request to document drug, date and duration of previous medication trials. Updated references. Added California coverage information.
2/2017	Added criteria for "all other diagnoses." Updated references.
3/2018	Annual review. Added reauthorization criteria to allow for continuation of coverage. Updated references.
3/2019	Annual review. Updated references.
3/2020	Annual review. Updated references.
6/2021	Annual review. Updated references.
6/2022	Annual review. Updated references.
7/2023	Annual review. Updated references, updated background and coverage criteria sections with new indication for agitation associated with Alzheimer's.

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