UnitedHealthcare Pharmacy  
Clinical Pharmacy Programs

<table>
<thead>
<tr>
<th>Program Number</th>
<th>2019 P 3065-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program</td>
<td>Step Therapy</td>
</tr>
<tr>
<td>Medication</td>
<td>Rexulti (brexpiprazole)</td>
</tr>
<tr>
<td>Effective Date</td>
<td>6/1/2019; N/A</td>
</tr>
</tbody>
</table>

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) and for the treatment of schizophrenia.

   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.

   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 Seroquel XR prior to the coverage of 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):

         [Table continues with detailed criteria]

© 2019 UnitedHealthcare Services, Inc.
1
i. risperidone  
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. 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-

4. 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-

5. 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:
<table>
<thead>
<tr>
<th>Program</th>
<th>Step Therapy - Rexulti® (brexpiprazole)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change Control</strong></td>
<td></td>
</tr>
<tr>
<td>11/2015</td>
<td>New program.</td>
</tr>
<tr>
<td>5/2016</td>
<td>Added criteria for members stable on Rexulti therapy post inpatient admission or new to the plan.</td>
</tr>
<tr>
<td>7/2016</td>
<td>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&amp;T recommendation. Added Indiana and West Virginia coverage information.</td>
</tr>
<tr>
<td>8/2016</td>
<td>Removed the word “please” from the request to document drug, date and duration of previous medication trials. Updated references. Added California coverage information.</td>
</tr>
<tr>
<td>10/2016</td>
<td>Added criteria for “all other diagnoses.” Updated references.</td>
</tr>
<tr>
<td>2/2017</td>
<td>Annual review. Added reauthorization criteria to allow for continuation of coverage. Updated references.</td>
</tr>
<tr>
<td>3/2019</td>
<td>Annual review. Updated references.</td>
</tr>
</tbody>
</table>