See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Brexiprazole (Rexulti®) is an atypical antipsychotic.

FDA approved indication
- Use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD)
- Treatment of schizophrenia

Policy/Criteria
*Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria*

It is the policy of health plans affiliated with Centene Corporation® that Rexulti is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Major Depressive Disorder (must meet all):
      1. Diagnosis of major depressive disorder;
      2. Failure of THREE antidepressants (e.g., SSRI, SNRI, TCA, bupropion, mirtazapine, etc.) from at least TWO different classes at maximum indicated doses, each trialed for ≥ 4 weeks, unless member is unable to satisfy this requirement due to clinically significant adverse effects or has contraindication(s) to multiple antidepressants;
      3. Failure of ≥ 4 week trial of aripiprazole, used concurrently with an antidepressant, at maximum indicated doses, unless member experiences clinically significant adverse effects or has contraindication(s) to aripiprazole;
         *Aripiprazole requires prior authorization; if criterion #3 has NOT been met, but member has met criteria 1 & 2, reviewer MUST recommend the use of aripiprazole concurrently with an antidepressant, enter a 12 month approval for aripiprazole in the pharmacy benefit system (allow all tablet strength and 1 tablet/day) and inform prescriber of this approval*;
      4. Rexulti will be used concurrently with an antidepressant;
      5. Request does not exceed 3 mg per day and health plan approved daily quantity limit.
   
   Approval duration: 12 months

   B. Schizophrenia (must meet all):
      1. Diagnosis of schizophrenia;
      2. Member meets one of the following (a or b):
a. Failure of three of the following generic atypical antipsychotics: risperidone, quetiapine, olanzapine, or ziprasidone at maximum indicated doses, each trialed for ≥ 4 weeks, unless member experiences clinically significant adverse effects or has contraindication(s) to all relevant generic atypical antipsychotics;
b. Member has diabetes mellitus or BMI > 30;
3. Failure of ≥ 4 week trial of aripiprazole at maximum indicated doses, unless member experiences clinically significant adverse effects or has contraindication(s) to aripiprazole;

*Aripiprazole requires prior authorization; if criterion #3 has NOT been met, but member has met criteria 1 & 2, reviewer MUST recommend the use of aripiprazole, enter a 12 month approval for aripiprazole in the pharmacy benefit system (allow all tablet strength and 1 tablet/day) and inform prescriber of this approval*

4. Request does not exceed 4 mg per day and health plan approved daily quantity limit. Approval duration: 12 months

C. Other diagnoses/indications – Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy
A. All Indications (must meet all):
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently on Rexulti for an FDA approved indication (MDD or schizophrenia), has received this medication for ≥ 30 days, and is responding positively to therapy;
2. If request is for a dose increase, new dose does not exceed FDA approved maximum recommended dose for the relevant indication and health plan approved daily quantity limit.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PMN.53 if requested indication is NOT listed under section III

(Diagnoses/Indications for which coverage is NOT authorized)

Approval duration: 12 months

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Dementia-related psychosis
B. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy - CP.PMN.53 or evidence of coverage documents

IV. Appendices/General Information
Appendix A: Abbreviation Key
BMI: body mass index
CrCl: creatinine clearance
CYP: cytochrome P450
MDD: major depressive disorder
NMS: neuroleptic malignant syndrome
SNRI: serotonin-norepinephrine reuptake inhibitors
SSRI: selective serotonin reuptake inhibitors
TCA: tricyclic antidepressants

V. Dosage and Administration
- Administer Rexulti once daily with or without food

<table>
<thead>
<tr>
<th>Indication</th>
<th>Starting Dose</th>
<th>Recommended Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD</td>
<td>0.5 mg/day or 1 mg/day</td>
<td>2 mg/day</td>
<td>3 mg/day</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>1 mg/day</td>
<td>2 to 4 mg/day</td>
<td>4 mg/day</td>
</tr>
</tbody>
</table>

- *Moderate to Severe Hepatic Impairment (Child-Pugh score ≥7):* Maximum recommended dosage is 2 mg once daily for patients with MDD and 3 mg once daily for patients with schizophrenia
- *Moderate, Severe or End-Stage Renal Impairment [creatinine clearance (CrCl) < 60 mL/minute]:* Maximum recommended dosage is 2 mg once daily for patients with MDD and 3 mg once daily for patients with schizophrenia
- *Known cytochrome P450 (CYP) 2D6 Poor Metabolizers:* Reduce the usual dosage by half

VI. Product Availability
Rexulti is supplied as tablets in the following strengths: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg.

VII. Workflow Document

VIII. References

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.
Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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