Rexulti (brexpiprazole)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Rexulti (brexpiprazole) is a second-generation atypical antipsychotic that modulates the action of dopamine and serotonin, neurotransmitters in the brain that influence mood and cognition. The FDA has approved Rexulti for the following indications:

1. Adjunctive treatment of major depressive disorder (MDD) in adults.
2. Treatment of schizophrenia in adults and pediatric patients ages 13 years and older.

3. Treatment of agitation associated with dementia due to Alzheimer's disease.
   Limitations of Use: Rexulti (brexpiprazole) is not indicated as an as needed ("prn") treatment for agitation associated with dementia due to Alzheimer's disease.

Rexulti is part of the larger class of second-generation antipsychotics, which includes drugs like aripiprazole (Abilify), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), and ziprasidone (Geodon). These medications all work in somewhat similar ways, but individual response and tolerance can vary. This means that if one does not respond well to one antipsychotic, they may still benefit from trying another with the same class. Selection of an antipsychotic often depends on multiple factors, including individual response to previous treatments, safety and tolerability of the drug, and individual considerations such as coexisting health conditions and potential drug interactions.

Despite the FDA approval of Rexulti (brexpiprazole) for the treatment of agitation associated with dementia due to Alzheimer's disease, like other antipsychotics, the package insert has a boxed warning for the increased risk of death in older adults with dementia-related psychosis. While Rexulti (brexpiprazole) is not approved for dementia-related psychosis without agitation in this population, psychosis and agitation can occur simultaneously and providers should use their judgement regarding appropriate use of antipsychotics in those with dementia.

Definitions

"Adjunct Therapy" is a treatment used together with the primary treatment. Its purpose is to assist the primary treatment.

"Agitation"is a state of excessive restlessness or emotional distress often characterized by behaviors such as pacing, yelling, or resistance.

"Atypical Antipsychotic" is a class of medications, also known as second-generation antipsychotics, that are primarily used to treat psychiatric conditions. Unlike the first-generation antipsychotics, these drugs are less likely to produce extrapyramidal side effects but more likely to cause weight gain and metabolic abnormalities.

"Major depressive disorder", also known as (MDD), is a psychiatric condition characterized by persistent low mood, low energy, or loss of interest in enjoyable activities causing substantial impairment in daily life. MDD is thought to be caused by a combination of genetic, environmental and psychological factors. Risk factors include family history, major life changes, certain medications, chronic health problems, and substance use disorders.

"Neuropsychiatric symptoms" are symptoms that originate from a disturbance in the brain and influence both neurological and psychiatric functionality. In the context of Alzheimer's disease, it may include symptoms such as agitation, depression, apathy, and psychosis.

"Neurotransmitter" is a molecule that sends signals from neurons to different parts of the body (e.g. muscles).

"Postpartum Psychosis" is a rare but serious mental health emergency characterized by sudden onset of psychotic symptoms shortly after childbirth. It is often characterized by acute onset of delusions, disorganized thoughts, hallucinations, and/or agitation. While it may occur as a manifestation of bipolar disorder, it can also present in patients without prior psychiatric history. Early recognition and treatment is critical due to risks to both mother and infant.

"Schizophrenia" is a psychiatric disorder involving chronic or recurrent psychosis and is commonly associated with impairments in social and occupational functioning.

Medical Necessity Criteria for Clinical Review

Initial Indication-Specific Criteria

Agitation associated with dementia due to Alzheimer's disease

The Plan considers Rexulti (brexpiprazole) medically necessary when ALL the following criteria are met for the applicable indication listed below:

1. Prescribed by a specialist[⇅] in Alzheimer's disease or a psychiatrist; *AND*

   [⇅]*To ensure member access to appropriate pharmacotherapy when clinical criteria are met but specialist availability is limited, an exception to the Rexulti (brexpiprazole) specialist requirement may be considered if there is inadequate access to specialists in the member's location. In such cases, Rexulti (brexpiprazole) may be prescribed by the member's primary care provider or other qualified clinician experienced in safely using this medication for agitation in Alzheimer's disease dementia, provided all other clinical criteria are documented and met.*
2. The member is 18 years of age or older; *AND*
3. The member has a confirmed diagnosis of Alzheimer's disease with documented agitation; *AND*
4. The member has demonstrated an inadequate response to or intolerance of non-pharmacological treatments for agitation, including but not limited to:
   a. Caregiver education and support; *and/or*
   b. Cognitive stimulation; *and/or*
   c. Exercise programs; *and/or*
   d. Group therapy; *and/or*
   e. Music therapy; *and/or*
   f. Redirecting; *and/or*
   g. Occupational therapy; *AND*
5. The member exhibits sufficient agitation behaviors (i.e., symptoms are severe, dangerous, and/or cause significant distress) warranting pharmacotherapy; *AND*

6. Rexulti (brexpiprazole) is NOT being used as an "as needed" treatment; *AND*
7. Clinical chart documentation is provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, Rexulti (brexpiprazole) will be approved for up to a lifetime.

Adjunct Therapy of Major depressive disorder

Medical Necessity Criteria for Initial Authorization

1. The member is 18 years of age or older; *AND*
2. The member has a diagnosis of major depressive disorder; *AND*
3. The member has demonstrated an inadequate response to at least 8-weeks of antidepressant therapy (e.g., delayed-release duloxetine, escitalopram, fluoxetine, extended-release paroxetine, sertraline, or extended-release venlafaxine); *AND*
4. Rexulti (brexpiprazole) is being prescribed for use as an adjunct to an antidepressant (e.g., delayed-release duloxetine, escitalopram, fluoxetine, extended-release paroxetine, sertraline, or extended-release venlafaxine); *AND*
5. The member is unable to use or has tried and failed TWO (2) of the following:
    a. Aripiprazole; *and/or*
    b. Olanzapine; *and/or*
    c. Quetiapine; *AND*
6. Clinical chart documentation is provided for review to substantiate the above listed requirements.

Postpartum Psychosis

1. The requested medication is prescribed by or in consultation with a psychiatrist; *AND*
2. The member has postpartum psychosis as evidenced by ONE (1) of the following:
    a. New onset psychotic symptoms (e.g., delusions, disorganized thoughts, hallucinations, agitation, bizarre behavior) in the postpartum period; *or*
    b. Bipolar disorder with postpartum psychotic symptoms; *or*
    c. Primary mental disorder with psychotic symptoms during the peripartum period; *AND*
3. Clinical chart documentation is provided for review to substantiate the above listed requirements.

Schizophrenia

1. The requested medication is prescribed by or in consultation with a psychiatrist; *AND*
2. The member is 13 years of age or older; *AND*

3. The member has a diagnosis of schizophrenia; *AND*
4. The member is unable to use or has adequately tried and failed at least a one month trial to THREE (3) of the following:
    a. Aripiprazole (Abilify); *and/or*
    b. Asenapine (Saphris); *and/or*
    c. Lurasidone (Latuda); *and/or*
    d. Olanzapine (Zyprexa); *and/or*
    e. Paliperidone (Invega); *and/or*
    f. Quetiapine (Seroquel); *and/or*
    g. Risperidone (Risperdal); *and/or*
    h. Ziprasidone (Geodon); *AND*
5. Clinical chart documentation is provided for review to substantiate the above listed requirements.

<u>If the above prior authorization criteria are met, Rexulti (brexpiprazole) will be approved for up to a lifetime.</u>

Experimental or Investigational / Not Medically Necessary

Rexulti (brexpiprazole) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Acute Mania / Bipolar 1 Disorder. There are not enough high-quality studies to support the safety and efficacy of Rexulti (brexpiprazole) for the management of acute mania/bipolar 1 disorder. In two open-label studies, there was no statistically significant difference between brexpiprazole and placebo in the primary outcome of change in the Young Mania Rating Scale total score.
- Alcohol Use Disorders (AUD). There are not enough high-quality studies to support the safety and efficacy of Rexulti (brexpiprazole) for the management of AUD.
- Attention Deficit Hyperactivity Disorder (ADHD). There is only one randomized controlled study that assessed Rexulti (Brexpipazole) for the management of ADHD. When combined with a stimulant, there was no benefit of adjunct Rexulti (brexpipazole) in those who were stimulant-naive and prior stimulant non-responders.
- Borderline Personality Disorder (BPD). There are not enough high-quality studies to support the safety and efficacy of Rexulti (brexpiprazole) for the management of BPD. Studies are mixed, with one phase-two randomized controlled study found no statistically significant difference between Rexulti (Brexpiprazole) and placebo in the Zanarini Rating scale for BPD (ZAN-BPD). Another 12-week randomized controlled trial found a significant interaction between treatment and time on the ZAN-BPD between Rexulti (Brexpiprazole) and placebo but not on the self-reported version of the ZAN-BPD.

- Irritability Associated With Autism Spectrum Disorder (ASD). There are not enough high-quality studies to support the safety and efficacy of Rexulti (brexpiprazole) for the management of ASD. One 8-week randomized controlled trial did not find a difference between Rexulti (Brexpiprazole) and placebo on the Aberrant Behavior Checklist-Irritability subscale, and the Clinical Global Impressions-Severity scale.
- Post Traumatic Stress Disorder (PTSD). There are very few high-quality studies to support the safety and efficacy of Rexulti (brexpiprazole) for the management of PTSD. While there is some data to support the use of Rexulti (brexpiprazole) for the management of PTSD, studies have only shown benefit when combined with sertraline. When used on its own, Rexulti (brexpiprazole) provides no benefit. One randomized controlled trial found only Rexulti (brexpiprazole) with sertraline was effective compared to sertraline monotherapy, Rexulti (brexpiprazole) monotherapy or placebo. Sertraline is commonly used in PTSD, and negative findings complicate the interpretation of these results.

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