Medication Policy Manual

Policy No: dru425

Topic: High-Cost Oral Antipsychotics:

- asenapine (Saphris®)
- brexpiprazole (Rexulti®)
- cariprazine (Vraylar™)
- iloperidone (Fanapt®)
- lurasidone (Latuda®)
- paliperidone (oral) (Invega®, generic paliperidone)
- quetiapine ER (oral) (generic, Seroquel XR®)

Date of Origin: October 9, 2015

Committee Approval Date: October 13, 2017

Next Review Date: October 2018

Effective Date: November 1, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Asenapine (Saphris®), brexpiprazole (Rexulti®), cariprazine (Vraylar™), iloperidone (Fanapt®), lurasidone (Latuda®), paliperidone oral (Invega®, generic paliperidone), and quetiapine extended-release (ER) oral (Seroquel XR®, generic quetiapine ER) are oral antipsychotics used to treat schizophrenia. Many of these medications may also be used to treat other conditions such as bipolar disorder, Tourette's syndrome, agitation with autistic disorder, and as an add-on treatment to antidepressant medications for treatment of major depressive disorder (MDD).

This policy does not apply to injectables, such as aripiprazole (Abilify Maintena®, Aristada®), olanzapine (Zyprexa Relprevv®), paliperidone (Invega Sustenna®, Invega Trinza®), or risperidone (Risperdal Consta®).

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Policy/Criteria

I. Most contracts require prior authorization approval of oral high-cost antipsychotics prior to coverage. Oral high-cost antipsychotics may be considered medically necessary when at least two low-cost generic antipsychotics listed in Appendix 1 have been ineffective, are not tolerated, or are contraindicated.

II. Administration and Authorization Period

A. Regence considers oral high-cost antipsychotics medications in this policy to be self-administered medications.

B. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

Position Statement

- There are many generic atypical antipsychotic options available, of which generic olanzapine, quetiapine, risperidone, and ziprasidone are the lowest cost.
- Higher-cost antipsychotics, asenapine, brexpiprazole, cariprazine, iloperidone, lurasidone, paliperidone, and quetiapine ER, have not been established as superior in safety or efficacy relative to low-cost generic or preferred oral atypical antipsychotics but are more costly.
- There is a large body of evidence that indicates atypical antipsychotics are effective in certain conditions; however, because individual studies are unreliable, it cannot be determined if there is a clinically meaningful difference between individual medications. [1,2]
- No atypical antipsychotic has been shown to have an overall superior safety profile; however, individual medications differ in the incidence and severity of specific adverse events. [1,2]
- Appendix 1 includes examples of numerous low-cost, generically available treatment options for each diagnosis that high-cost antipsychotics are commonly used to treat.

Clinical Efficacy

SCHIZOPHRENIA

- Atypical antipsychotics, including low-cost generics, are all considered to be effective for treatment of schizophrenia. [1,2]
  - With the exception of clozapine, there is no reliable evidence that one atypical antipsychotic is more effective than another. [1,2,5] Multiple systematic reviews and meta-analyses have been published to describe the comparative efficacy between atypical antipsychotics; however, these analyses are all based on low quality, unreliable evidence. Overall, the evidence for atypical antipsychotics in all conditions is considered generally low quality due to high attrition rates (up to 60%), small sample size, and lack of clinically meaningful endpoints.[1,2,5]
- Antipsychotics are recognized by guidelines as being effective for the treatment of schizophrenia. Atypical antipsychotics are generally preferred over first-generation (typical) antipsychotics due to the lower incidence of extrapyramidal side effects and tardive dyskinesia.[6-9]

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- Guidelines recommend that treatment selection be guided by factors such as previous treatment response, adverse event profile, patient preference, route of administration, comorbid medical conditions and potential drug-drug interactions.[6-9]
- Guidelines recognize the superior efficacy of clozapine; however, due to risk of potentially serious blood dyscrasias, it is recommended only for treatment refractory disease.[6-9]

BIPOLAR DISORDER

- Various atypical antipsychotics, including low-cost generics, have been studied for the treatment of bipolar disorder; however, there is insufficient evidence to determine comparable efficacy between products.[1,2]
- Guidelines recommend the use of generic mood stabilizers, as follows: [10-14]
  - For manic or mixed episodes, lithium carbonate or valproic acid with or without an antipsychotic as the preferred first-line treatment options. Carbamazepine and oxcarbazepine are listed as alternatives to lithium carbonate and valproic acid.
  - For depressive episodes, lithium with or without an antidepressant or lamotrigine as the preferred first-line treatment.

MAJOR DEPRESSIVE DISORDER (MDD)

- Two large, comprehensive systematic reviews concluded that no atypical antipsychotic had evidence of providing a significant long-term benefit as an adjunct to antidepressants in treatment resistant depression.[1,2]
- Antidepressants such as selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), mirtazapine and bupropion, are recommended by guidelines as first line treatment for patients with major depressive disorder.[15]
- Because all antidepressants generally have similar efficacy, guidelines indicate choice of therapy should be guided by other factors such as adverse event profiles, half-life, potential drug-drug interactions, prior response and patient preference.[15]
- Guidelines recommend dose optimization, followed by transition to another antidepressant or augmentation with a second antidepressant, lithium carbonate, thyroid hormone, or an atypical antipsychotic.[15]

AUTISTIC DISORDER

- There is limited evidence for the efficacy of pharmacotherapy in autistic disorder; however, SSRIs and atypical antipsychotics are used to alleviate some of the associated symptoms.[1,2,4,16]
- Two large, comprehensive systematic reviews concluded there is insufficient evidence to draw a conclusion regarding the efficacy of atypical antipsychotics for the treatment of autistic disorder.[1,2]
- Aripiprazole and risperidone have an FDA indication for irritability associated with autistic disorder.[3]

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Safety

- There is a general lack of useful data on the relative overall safety and tolerability of the atypical antipsychotics.
- Individual products vary in variety and severity of adverse events.[3]
- The most common adverse events to this class of medications are: [1-3]
  * Movement disorders and restlessness
  * Anticholinergic effects including sedation, blurry vision and dry mouth
  * Metabolic complications including weight gain, increased lipids and increased blood glucose
- Generally, treatments are selected based on side effect profiles and the impact on the patient's existing health status.[6-14]
- Use of atypical antipsychotics for dementia-related psychosis is associated with an increased risk of death and all medications in this class have a boxed warning with regard to use in this indication.[3]

Appendix 1: Lowest-Cost Generic Medication Alternatives [a]

Class	Low-Cost Generic Preferred Alternatives
Atypical antipsychotics	– aripiprazole (generic Abilify®) – clozapine (generic Clozaril®) – olanzapine (generic Zyprexa®) – quetiapine (generic Seroquel®) – risperidone (generic Risperdal®) – ziprasidone (generic Geodon®)

[a] Based on FDA-approval or guidelines. [3,6-16]

Cross References
None

Codes	Number	Description
N/A		

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Revision History

Revision Date	Revision Summary
10/13/2017	No change to criteria with this annual update.
12/16/2016	Change step therapy from two low-cost generic options (including oral antipsychotics, mood stabilizers, or antidepressants) to two low-cost generic oral antipsychotics.
10/14/2016	Remove aripiprazole from the policy

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