Antidepressants: Pharmacy Medical Necessity Criteria for Brands

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Replaces  N/A

*This policy is managed through the Pharmacy benefit.

Policy

Branded SSRI, SNRI and any second generation antidepressant when used to treat depression) may be considered medically necessary when there has been a trial and failure of at least two generically available second generation antidepressants.

Note: For diagnosis of diabetic peripheral neuropathy, chronic musculoskeletal pain or fibromyalgia. (See Related Policies.)

Related Policies

5.01.521  Pharmacologic Treatment of Neuropathy, Fibromyalgia and Seizure Disorders
5.01.605  Medical Necessity Criteria for Pharmacy Edits

Policy Guidelines

Single Source Branded SSRI, SNRI and any other Single Source Brand (SSB) second generation antidepressants may be covered under the following circumstances:

- Patients with Depressive Disorders that have had a trial and failure of at least two generically available second generation antidepressants (examples of, but not limited to; fluoxetine, sertraline, venlafaxine, bupropion, mirtazapine).
- Patients with Anxiety Disorders that have had a trial and failure of at least two generically available SSRIs, or at least one generically available SSRI and one generically available SNRI (examples of, but not limited to; SSRI: citalopram, escitalopram, paroxetine, fluoxetine, sertraline…SNRI: duloxetine, venlafaxine).

Coding

This policy is managed through the Pharmacy benefit.
Pathophysiology of Depression

While the pathology of depression is far from completely understood, it is apparent that both heredity and environmental factors play a part. Genetic microarray techniques are being used to identify candidate genes, with the hope of developing a pharmacogenomic approach to predicting which drugs will be most effective in each patient. However, this knowledge is still in its infancy, and its practical application will be some time in the future. For now, practitioners must continue using empiric approaches to treatment, both pharmacologic and otherwise.

Disease Burden

More than 18 million Americans suffer from depression. Over 15% will experience at least one major depressive episode during their lifetimes. Exact prevalence rates are difficult to determine because of the extent to which depression goes unreported. It occurs twice as frequently in women as in men. A recent meta-analysis showed that depressed persons have a 1.5-2 fold increased risk of mortality.

In 2000, the economic burden of depression in the U.S. was estimated to be $83.1 billion. Indirect costs include related mortality and morbidity, as well as significant amounts of absenteeism and presenteeism that can impact workplace productivity. Quality of life of patients and those around them also suffer.

Pharmacotherapy

A recent overview of the various treatment modalities used in depression was provided in *Lancet* by Ebmeier et al. Treatments include a variety of cognitive behavioral approaches, psychotherapy, treatment with antidepressant medications and in severely resistant cases, electroconvulsive therapy. Of the nonpharmacologic treatment modalities, cognitive behavioral approaches have the best supporting evidence. Drugs used to treat depression include selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs) and several agents with combinations of serotonergic, noradrenergic and dopaminergic activity.

This policy applies to the following medications:
- Single Source Branded (SSB) SSRI (selective serotonin reuptake inhibitor), SNRI (serotonin/norepinephrine reuptake inhibitor) and any other Single Source Brand (SSB) second generation antidepressants (antidepressants other than tricyclic and MAOI agents).

Scope

Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer services representative to determine whether there are any benefit limitations applicable to this service or supply. This policy does not apply to Medicare Advantage.

Benefit Application

This policy applies to all pharmacy benefit contracts that include Pharmacy Prior Authorization Edits.
Rationale

Current evidence from head-to-head comparative trials of second-generation antidepressants, systematic reviews, and meta-analyses indicates these agents are of comparable efficacy and effectiveness as measured by HAM-D or MADRS response (>50% improvement), though one study reported a statistically superior but modest improvement in MADRS score with escitalopram compared to citalopram. Overall, the data support for a meaningful difference is not compelling.

Evidence from four small comparative effectiveness trials failed to provide compelling evidence of the superiority of escitalopram. In the one study that showed a statistically significant difference in the primary endpoint (change from baseline in MADRS score), the effect size was modest, and p value was barely significant.

Two longer-term (≥6 month) efficacy and safety studies of duloxetine (Cymbalta) have been published, and the manufacturer supplied data on two unpublished trials. Although not compelling, evidence now supports the relative safety of longer-term (6 month to 1 year) use of duloxetine for the treatment of major depressive disorder. Other evidence also shows comparable efficacy with venlafaxine and comparable onset of effect with escitalopram.

A meta-analysis of 117 small randomized controlled trials including 25,928 patients compared 12 “new generation” antidepressants for efficacy and tolerability. The authors concluded that escitalopram and sertraline offered the best combination of efficacy and patient acceptability. Of the two, they felt that sertraline might be the best choice when starting treatment, because it has the best balance between efficacy, safety and cost. Although well-designed, this study is limited by the size and heterogeneity of the individual trials that were included. In particular, the evidence supporting superiority of escitalopram over citalopram is based on 5 small trials, all of which were manufacturer-sponsored. There is no clinical reason to expect a meaningful difference between these two agents, assuming that the doses of the S-isomer are equal.

A similar meta-analysis of 203 studies yielded no substantial differences among agents. The authors concluded that the body of existing evidence does not favor selection of one particular antidepressant over the others based on efficacy or effectiveness.

U.S. guidelines for the treatment of adults with depression from the American Psychiatric Association recommend use of antidepressants as preferred initial treatment or as a part of a preferred initial treatment regimen for most patients with any level of severity of MDD. Initial choice of medication should consider anticipated side effects, safety or tolerability of side effects for individual patients, patient preference, quantity and quality of clinical trial data, and cost. Based on these factors, the APA indicates SSRIs, desipramine, nortriptyline, bupropion, venlafaxine, and mirtazapine are likely to be effective for most patients.

2009 Update
A literature search was performed for March 2009 through December 2009. No published randomized studies were found that would change the policy statements.

2011 Update
Updated to incorporate reference to newly U.S. Food and Drug Administration (FDA-approved indication for Cymbalta in chronic musculoskeletal pain). No other significant updates to the literature were found.

2012 Update
Updated to allow for recent availability of generic escitalopram; thus, trial of generic citalopram is no longer a specific requirement for access to Lexapro. No other significant updates to the literature were found.

2014 Update
Updated to include newly available generic duloxetine and Khedezla, a new venlafaxine extended release
product. No other significant changes to the literature were found at this time.

2015 Update
Expanded the indication of Major Depressive Disorder to Depressive Disorders; Expanded the indication of Generalized Anxiety Disorder to Anxiety Disorders. Updated these new expanded indications with separate criteria: For patients with Depressive Disorders, trial and failure of at least two generically available second generation antidepressants; or patients with Anxiety Disorders, trial and failure of at least two generically available SSRIs, or at least one generically available SSRI and one generically available SNRI.

2016 Update
A literature search was performed for April 1, 2015 through December 6, 2016. No published randomized studies were found that would change existing policy statements.

References


74. Criteria reviewed and approved by the P&T Committee September 26, 2006.


Appendix

N/A

History

<table>
<thead>
<tr>
<th>Date</th>
<th>Reason</th>
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<tbody>
<tr>
<td>12/13/05</td>
<td>Add to Prescription Drug Section - New Policy—effective January 1, 2006.</td>
</tr>
<tr>
<td>08/08/06</td>
<td>Replace Policy - Policy reviewed with literature search by Pharmacy and Therapeutic Committee on July 25, 2006. Policy statement updated with exenatide and thiazolidinediones added as medically necessary; Policy Guidelines and Rationale sections updated; references added.</td>
</tr>
<tr>
<td>05/08/07</td>
<td>Replace Policy - Policy statement for exenatide updated with additional criteria; Policy Guidelines updated to reflect addition to policy statement. Reviewed by P&amp;T on March 27, 2007.</td>
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<tr>
<td>06/12/07</td>
<td>Replace Policy - Policy statement on coverage criteria for exenatide (Byetta®), sitagliptin and esomeprazole (Nexium®) expanded; medically necessary indications for 5HT3 antagonists, Actiq® and Fentora™ added to policy statement. Policy Guidelines updated and Rationale updated; references added</td>
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<tr>
<td>12/11/07</td>
<td>Replace Policy - Policy reviewed with literature search by Pharmacy and Therapeutic Committee on May 15, 2007.Policy statement updated to include Pregabalin as either medically necessary or investigational under the criteria. Acyclovir, famciclovir and valacyclovir as medically necessary under criteria. References added.</td>
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</table>
04/08/08 Replace Policy - Policy updated with literature search by Pharmacy. Policy statement was updated to include fibromyalgia as a medically necessary indication under Pregabalin. References added.
12/16/08 Replace Policy - Policy updated with literature search by Pharmacy. Policy statement updated to include the use of leukotriene modifiers for the treatment of allergic rhinitis refractory to nasal corticosteroids under the medically necessary indication.
02/10/09 New PR Policy PR.5.01.520 - Policy information regarding antidepressants deleted from PR.5.01.605 and addressed in this new policy.
01/12/10 Replace Policy - Policy reviewed with literature search; no change to the policy statement. References added.
05/10/11 Replace Policy - Medically necessary policy statement on branded SSRI, SSNI and second generation antidepressants updated to require trial and failure two generic antidepressants as a condition to be met, where it was previously only one; chronic musculoskeletal pain has been added as an exception to the investigational indications for use of duloxetine (Cymbalta®). Title changed to “Antidepressants: Pharmacy Medical Necessity Criteria for Brands.” Reviewed by P&T in March 2011.
09/11/12 Replace policy. Policy updated with literature review. Policy Guidelines section updated to allow for recent availability of generic escitalopram; thus, trial of generic citalopram is no longer a specific requirement for access to Lexapro.
07/08/13 Replace policy. Policy Guidelines updated with Desvenlafaxine, a recently released second-generation SSRI used for treating depression, which may be approved following the failure of two generics, one being venlafaxine. Clarification was added to the policy that it is managed through the member’s pharmacy benefit; this is now listed in the header and within the coding section.
12/04/13 Replace policy. Policy section updated with Khedezla™ added to the list of SSRIs which may be approved when criteria are met.
03/10/14 Replace policy. Cymbalta removed from the scope of policy; prior authorization is no longer required. (NOTE: This is a non-formulary medication; therefore, prior authorization would be required for closed formulary.)
10/13/14 Interim update. Clarification made that policy applies to branded SSRI (selective serotonin reuptake inhibitor) and second generation antidepressants (antidepressants other than tricyclic and MAOI agents) from a single source.
07/14/15 Annual Review. Policy updated with literature review. The following updates were performed: Expanded the indication of Major Depressive Disorder to Depressive Disorders; Expanded the indication of Generalized Anxiety Disorder to Anxiety Disorders; Updated these new expanded indications with separate criteria: For patients with Depressive Disorders, trial and failure of at least two generically available second generation antidepressants, and for patients with Anxiety Disorders, trial and failure of at least two generically available SSRIs, or at least one generically available SSRI and one generically available SNRI.
10/13/15 Interim Update. Requirements of venlafaxine trial for Pristiq, Khedezla or Desvenlafaxine we removed. All brand antidepressants will have same criteria of any 2 generics first. No change to policy statement.
12/13/16 Annual review. No published randomized studies were found that would change existing policy statements. Minor correction was made to the 2015 update, i.e. addition of “trial and failure of a generically available SNRI.”

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200 Independence Avenue SW, Room 509F, HHH Building
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