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Coverage Policy Number **IP0217**

Attention Deficit Hyperactivity Disorder Non-Stimulant Medications

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following attention deficit hyperactivity disorder non-stimulant medications:

- **Qelbree®** (viloxazine extended-release capsules)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Viloxazine (Qelbree) is considered medically necessary when the following are met:

1. **Attention Deficit Hyperactivity Disorder (ADHD).** Individual meets **ALL** of the following criteria (A, B, and C):
    A. Individual is 6 years of age or older
    B. Documented diagnosis of attention deficit hyperactivity disorder (ADHD)
    C. Individual meets the preferred covered alternative(s) criteria as indicated in the table below

Coverage varies across plans and requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Employer Group Non-Covered Products and Preferred Covered Alternatives by Drug List:

Non-Covered Product	Standard / Performance	Value / Advantage	Cigna Total Savings	Legacy
Qelbree (viloxazine extended-release capsules) [may be opened and sprinkled or swallowed whole]	There is documentation of **ONE** of the following (A or B): A. The individual has had an inadequate response, contraindication, or is intolerant to atomoxetine (generic for Strattera) B. Individual has an inability to swallow capsules/tablets			

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Viloxazine (Qelbree) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Binge-Eating Disorder.** In one 10-week, placebo-controlled study in outpatients with binge-eating disorder (n = 40), atomoxetine was associated with a significantly greater reduction in binge-eating episode frequency vs. placebo.[7] Additional studies with atomoxetine are needed. There are no data with guanfacine ER tablets, clonidine ER tablets, or Qelbree.

2. **Depression Without Attention Deficit/Hyperactivity Disorder.** Limited information is available on the use of atomoxetine for the treatment of major depressive disorder. In three case reports and one case series in 15 patients with depressive disorders, adding atomoxetine to a selective serotonin reuptake inhibitor (SSRI) resulted in further improvement.[8,9] However, in a published controlled trial, patients with major depressive disorder (without ADHD) [n =276] were treated with sertraline at doses up to 200 mg/day.[10] Patients who continued to experience depressive symptoms (n = 146) were then randomly assigned to either treatment with atomoxetine 40 to 120 mg/day or placebo for an additional 8 weeks. There was no difference between the atomoxetine/sertraline and placebo/sertraline treatment groups in mean change in depressive symptom severity or in the number of patients whose depressive symptoms remitted (40.3% vs. 37.8%, respectively; P = 0.865). Atomoxetine did not improve clinically significant depression in patients with Parkinson disease (n = 55) in one study.[11] There are no data with guanfacine ER tablets, clonidine ER tablets, or Qelbree.

3. **Fibromyalgia.** In case reports, atomoxetine was effective in reducing fatigue and pain in fibromyalgia syndrome.[12] Well-controlled trials with atomoxetine are needed to establish safety and efficacy. There are no data with guanfacine ER tablets, clonidine ER tablets, or Qelbree.

4. **Improve Cognitive Function (or Neuroenhancement).** The use of prescription medication to augment cognitive or affective function in otherwise healthy individuals (also known as neuroenhancement) is increasing in adult and pediatric populations.[20] A 2013 Ethics, Law, and Humanities Committee position paper, endorsed by the American Academy of Neurology (AAN) indicates that based on currently available data and the balance of ethics issues, neuroenhancement in children and adolescents without a diagnosis of a neurologic disorder is not justifiable. The prescription of neuroenhancements is inadvisable due to numerous social, developmental, and professional integrity issues. Several studies have evaluated atomoxetine for cognitive function in various patient populations, including patients with Huntington disease[12], Alzheimer's disease[14], schizophrenia[15,16], and Parkinson's disease.[17] However, atomoxetine has not demonstrated clinical benefit.

5. **Long-Term Combination Therapy (for example, > 2 months) with atomoxetine (Strattera, generic) and Central Nervous System (CNS) Stimulants used for the Treatment of Attention Deficit/Hyperactivity Disorder (e.g., mixed amphetamine salts ER capsules [Adderall XR®, generic], methylphenidate ER tablets, methylphenidate immediate-release tablets).** Currently, data do not support using atomoxetine and CNS stimulant medications concomitantly.[18,19] Short-term drug therapy (2 months or less) with both atomoxetine and CNS stimulant medications are allowed for transitioning the patient to only one drug. Guanfacine ER tablets and clonidine ER tablets are indicated for use as monotherapy or as adjunctive therapy to CNS stimulant medications; therefore, long-term combination therapy with either agent and CNS stimulants is appropriate.[2-3] Qelbree labeling does not address combination use with CNS stimulants at this time.[4]

6. **Nocturnal Enuresis.** In case reports, children with ADHD and other comorbid psychiatric diagnoses who had nocturnal enuresis and were treated with atomoxetine had resolution of their enuresis.[21] In one controlled trial in pediatric patients (n = 87) with nocturnal enuresis, atomoxetine increased the average number of dry nights per week by 1.47 vs. 0.60 for placebo (P = 0.01).[22] Additional controlled trials with atomoxetine are needed. There are no data with guanfacine ER tablets, clonidine ER tablets, or Qelbree.

7. **Weight Loss.** In one 12-week, placebo-controlled study in obese women (n = 30), atomoxetine resulted in a mean -3.7% loss vs. 0.2% gain with placebo when combined with a hypocaloric diet (500 kcal/day deficit).[23] Atomoxetine did not demonstrate efficacy for weight reduction in patients with schizophrenia (n = 37) treated with antipsychotics (clozapine or olanzapine).[24] Additional studies are needed.

Background

Overview

Atomoxetine capsules (Strattera, generic), guanfacine extended-release (ER) tablets (Intuniv, generic), clonidine ER tablets (Kapvay, generic), and Qelbree are non-stimulant medications approved for the **treatment of attention deficit hyperactivity disorder** (ADHD).[1-4]

Atomoxetine capsules, a selective norepinephrine reuptake inhibitor, and Qelbree, a selective norepinephrine reuptake inhibitor, are indicated for the treatment of ADHD in children ≥ 6 years of age, adolescents, and adults.[1,4] Guanfacine ER tablets and clonidine ER tablets, both alpha agonists, are approved for use in children and adolescents 6 to 17 years of age with ADHD.[2,3] Guanfacine ER tablets and clonidine ER tablets are indicated for use as monotherapy or as adjunctive therapy to stimulant medications.

Clinical Efficacy

Patients with pervasive developmental disorders who have symptoms of ADHD respond to ADHD medications at a reduced rate compared with typically developing peers and often with undesirable side effects.[5,6] However, there

is evidence to support use of these agents (e.g., stimulants, atomoxetine capsules, guanfacine ER tablets, and clonidine ER tablets) in this patient population.

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