

PRIOR AUTHORIZATION POLICY

POLICY: Attention Deficit Hyperactivity Disorder Non-Stimulant Medications

- Intuniv® (guanfacine extended-release tablets – Shire Pharmaceuticals, generics)
- Kapvay® (clonidine hydrochloride extended-release tablets – Shionogi Pharma, Inc., generics)
- Strattera® (atomoxetine capsules – Eli Lilly and Company, generics)

APPROVAL DATE: 07/24/2019

OVERVIEW

Currently, there are three non-stimulant medications approved for the treatment of attention deficit/hyperactivity disorder (ADD/ADHD): atomoxetine (Strattera, generics), guanfacine extended-release tablets (Intuniv, generics), and clonidine extended-release tablets (Kapvay, generics).¹⁻³ Atomoxetine, a selective norepinephrine reuptake inhibitor, is indicated for the treatment of ADHD in children ≥ 6 years of age, adolescents, and adults.¹ Guanfacine extended-release tablets and clonidine extended-release tablets, both of which are alpha agonists, are approved for use in children and adolescents aged 6 to 17 years with ADHD.²⁻³ Guanfacine extended-release tablets and clonidine extended-release tablets are indicated for use as monotherapy, or as adjunctive therapy to stimulant medications.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of atomoxetine, guanfacine extended-release tablets (Intuniv, generics), and clonidine extended-release tablets (Kapvay, generics). All approvals are provided for the duration noted below.

Automation: An age edit targeting patients < 6 or > 18 years of age is recommended. Therefore, patients between the ages of 6 and 18 years will be approved at the point-of-service. For patients < 6 or > 18 years of age, coverage will be determined by prior authorization criteria.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of atomoxetine (Strattera, generics), guanfacine extended-release tablets (Intuniv, generics), or clonidine extended-release tablets (Kapvay, generics) is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

- 1. Attention Deficit/Hyperactivity Disorder.** Approve for 3 years if the patient is ≥ 6 years of age.

Other Uses with Supportive Evidence

- 2. Pervasive Developmental Disorders (e.g., autism spectrum disorder, Asperger's disorder).** Approve for 3 years in patients with symptoms of attention deficit hyperactivity disorder (e.g., inattention, hyperactivity).

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.^{4,5} However, there is evidence to support use of these agents (e.g., stimulants, Atomoxetine, guanfacine extended-release tablets, clonidine extended-release tablets) in this patient population.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Atomoxetine (Strattera, generics), guanfacine extended-release tablets (Intuniv, generics), and clonidine extended-release tablets (Kapvay, generics) have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 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.⁶ Additional studies with atomoxetine are needed. There are no data with guanfacine extended-release tablets or clonidine extended-release tablets.
- 2. Depression without Attention Deficit/Hyperactivity Disorder.** Limited information is available on atomoxetine's use for 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.^{7,8} 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.⁹ 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.¹⁰ There are no data with guanfacine extended-release tablets or clonidine extended-release tablets.
- 3. Fibromyalgia.** In case reports, atomoxetine was effective in reducing fatigue and pain in fibromyalgia syndrome.¹¹ Well-controlled trials with atomoxetine are needed to establish safety and efficacy. There are no data with guanfacine extended-release tablets or clonidine extended-release tablets.
- 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.¹⁹ 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 disease¹², Alzheimer disease¹³, schizophrenia^{14,15}, and Parkinson's disease¹⁶. However, atomoxetine has not demonstrated clinical benefit.
- 5. Long-Term Combination Therapy (i.e., > 2 months) with atomoxetine (Strattera, generics) and Central Nervous System (CNS) Stimulants used for the Treatment of Attention Deficit/Hyperactivity Disorder (e.g., mixed amphetamine salts extended-release capsules [Adderall XR[®], generics], methylphenidate extended-release tablets, methylphenidate immediate-release tablets).** Currently, data do not support using atomoxetine and CNS stimulant medications concomitantly.^{17,18} 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

extended-release tablets and clonidine extended-release 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

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.²⁰ 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).²¹ Additional controlled trials with atomoxetine are needed. There are no data with guanfacine extended-release tablets or clonidine extended-release tablets.
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).²² Atomoxetine did not demonstrate efficacy for weight reduction in patients with schizophrenia (n = 37) treated with antipsychotics (clozapine or olanzapine).²³ Additional studies are needed.
8. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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