PRIOR AUTHORIZATION POLICY

POLICY: Attention Deficit Hyperactivity Disorder Non-Stimulant Medications Prior Authorization Policy

- Intuniv® (guanfacine extended-release tablets – Shire, generic)
- Kapvay® (clonidine hydrochloride extended-release tablets – Concordia, generic)
- Onyda™ XR (clonidine hydrochloride extended-release oral suspension – Tris)
- Strattera® (atomoxetine capsules – Eli Lilly, generic)
- Qelbree® (viloxazine extended-release capsules – Supernus)

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OVERVIEW

Atomoxetine capsules (Strattera, generic), guanfacine extended-release (ER) tablets (Intuniv, generic), clonidine ER tablets (Kapvay, generic), Onyda XR, and Qelbree are non-stimulant medications approved for the **treatment of attention deficit hyperactivity disorder** (ADHD).[1-5]

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, clonidine ER tablets, and Onyda XR, alpha agonists, are approved for use in children and adolescents 6 to 17 years of age with ADHD.[2,3,5] Guanfacine ER tablets, clonidine ER tablets, and Onyda XR 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.[6,7] 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of atomoxetine capsules (Strattera, generic), clonidine ER tablets (Kapvay, generic), guanfacine ER tablets (Intuniv, generic), Onyda XR, and Qelbree. All approvals are provided for the duration noted below.

Automation: An age edit is in place such that a patient 6 to 18 years of age will be approved at the point of service. For a patient < 6 or > 18 years of age, coverage will be determined by Prior Authorization criteria.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of atomoxetine capsules (Strattera, generic), clonidine ER tablets (Kapvay, generic), Onyda XR, or guanfacine ER tablets (Intuniv, generic) is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Attention Deficit Hyperactivity Disorder.** Approve for 1 year 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 1 year if the patient has symptoms of attention deficit hyperactivity disorder (e.g., inattention, hyperactivity).

II. Coverage of Qelbree is recommended in those who meet the following criteria:

FDA-Approved Indication

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of atomoxetine capsules (Strattera, generic), clonidine ER tablets (Kapvay, generic), guanfacine ER tablets (Intuniv, generic), or Qelbree is not recommended in the following situations:

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.[8] 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 resulted in further improvement.[9,10] 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.[11] 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.[12] 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.[13] 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.[21] A 2013 Ethics, Law, and Humanities Committee position paper, endorsed by the American Academy of Neurology, 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[14], Alzheimer's disease[15], schizophrenia[16,17], and Parkinson's disease.[18] However, atomoxetine has not demonstrated clinical benefit.

5. **Long-Term Combination Therapy (i.e., > 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.[19,20] Short-term drug therapy (2 months or less) with both atomoxetine and CNS stimulant medications is allowed for transitioning the patient to only one drug. Guanfacine ER tablets, clonidine ER tablets, and Onyda XR 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.[2,3,5] 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.[22] 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).[23] Additional controlled trials with atomoxetine are needed. Data with guanfacine ER tablets, clonidine ER tablets, or Qelbree are lacking.

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).[24] Atomoxetine did not demonstrate efficacy for weight reduction in patients with schizophrenia (n = 37) treated with antipsychotics (clozapine or olanzapine).[25] 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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4. Qelbree® extended-release capsules [prescribing information]. Rockville, MD: Supernus; April 2022.
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