MEDICAL MUTUAL®

Drug Policy

Policy:	Attention Deficit Hyperactivity Disorder (ADHD) Non-Stimulant Medications Intuniv (guanfacine ER) Kapvay (clonidine hydrochloride ER) Qelbree (viloxazine) Strattera (atomoxetine)	Annual Review Date: 05/19/2022 Last Revised Date: 05/19/2022

OVERVIEW

Currently, there are four non-stimulant medications approved for the treatment of attention deficit/hyperactivity disorder (ADD/ADHD): viloxazine (Qelbree), atomoxetine (Strattera, generics), guanfacine extended-release tablets (Intuniv, generics), and clonidine extended-release tablets (Kapvay, generics). Atomoxetine and viloxazine are selective norepinephrine reuptake inhibitors indicated for the treatment of ADHD in children ≥ 6 years of age and adolescents up to age 17. Atomoxetine is also indicated for the treatment of ADHD in adults. 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. Guanfacine extended-release tablets and clonidine extended-release tablets are indicated for use as monotherapy, or as adjunctive therapy to stimulant medications.

POLICY STATEMENT

This policy involves the use of Intuniv, Kapvay, Qelbree, Strattera, and generics. Prior authorization is recommended for pharmacy benefit coverage of Intuniv, Kapvay, Qelbree, Strattera, and generics. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Intuniv, Kapvay, Qelbree, Strattera, and generics is recommended in those who meet the following criteria:

1. **Attention Deficit/Hyperactivity Disorder (ADHD/ADD)**
   Criteria. *Approve if the patient meets the following criteria (a AND b):*
   a. The patient is 6 years of age or older; AND
   b. One of the following conditions is met (i OR ii OR iii OR iv OR v):
      i. The request is for a generic product (i.e. atomoxetine, guanfacine ER, or clonidine ER); OR

ii. If the request is for brand name Strattera, the patient has tried generic atomoxetine AND brand Strattera is being requested due to a formulation difference in inactive ingredient(s) [e.g. difference in dyes, fillers, preservatives] between brand Strattera and generic atomoxetine which, per the prescriber, would result in a significant allergy or serious adverse reaction; OR

iii. If the request is for brand name Intuniv, the patient meets has tried generic guanfacine ER AND brand Intuniv is being requested due to a formulation difference in inactive ingredient(s) [e.g. difference in dyes, fillers, preservatives] between brand Intuniv and generic guanfacine ER which, per the prescriber, would result in a significant allergy or serious adverse reaction; OR

iv. If the request is for brand name Kapvay, the patient has tried generic clonidine ER AND brand Kapvay is being requested due to a formulation difference in inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between brand Kapvay and generic clonidine ER which, per the prescriber, would result in a significant allergy or serious adverse reaction; OR

v. If the request is for Qelbree, the patient has tried at least one generic stimulant medication (examples include methylphenidate, etc.) AND at least one generic non-stimulant medication (examples include atomoxetine, guanfacine ER, clonidine ER).

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Atomoxetine (Strattera, generics), viloxazine (Qelbree), 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. (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. Additional studies with atomoxetine are needed. There are no data with guanfacine extended-release tablets or clonidine extended-release tablets.

2. **Depression without ADD/ADHD.** 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. 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. 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. 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. 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. 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, Alzheimer disease, schizophrenia, and Parkinson's disease. However, atomoxetine has not demonstrated clinical benefit.

5. **Long-Term Combination Therapy (i.e., > 2 months) of atomoxetine (Strattera, generics) and Central Nervous System (CNS) Stimulants used for the Treatment of ADD/ADHD (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. 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.

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. 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). 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). Atomoxetine did not demonstrate efficacy for weight reduction in patients with schizophrenia (n = 37) treated with antipsychotics (clozapine or olanzapine). 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.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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