BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/19/16**
SECTION: DRUGS	**LAST REVIEW DATE: 11/15/18**
	LAST CRITERIA REVISION DATE: 11/15/18
	ARCHIVE DATE:

EVEKEO™ (amphetamine sulfate) oral tablet
AMPHETAMINE SULFATE oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

EVEKEO™ (amphetamine sulfate) oral tablet
AMPHETAMINE SULFATE oral tablet (cont.)

Criteria:

- **Criteria for initial therapy**: Evekeo (amphetamine sulfate) or Amphetamine Sulfate is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. **For a confirmed diagnosis of Attention Deficit Disorder with Hyperactivity,** individual is 3 years of age or older who has failure, contraindication or intolerance from a trial of each of the following:
   - Immediate release mixed amphetamine/dextroamphetamine salt
   - Immediate release dextroamphetamine

2. **For a confirmed diagnosis of Narcolepsy,** individual is 6 years of age or older who has failure, contraindication or intolerance from a trial of each of the following:
   - Immediate release mixed amphetamine/dextroamphetamine salt
   - Immediate release dextroamphetamine
   - Methylphenidate
   - Modafinil or armodafinil

3. **For a confirmed diagnosis of Exogenous Obesity ALL** of the following:
   - Individual is 12 years of age or older
   - Benefit plan design must include weight loss as a covered benefit
   - Has failed alternative therapy, e.g., repeated diets, group programs and other drugs
   - Has failure, contraindication or intolerance to immediate release methamphetamine
   - Evekeo to be used as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction

4. **ALL** of the following baseline tests have been completed before initiation of treatment:
   - Assessment for pre-existing cardiac disease
   - Assessment for risk of abuse
   - Assessment for pre-existing psychiatric disorder such as depression, history of suicide, bipolar disorder, or psychotic disorder

5. There are **NO** contraindications.
   - Contraindications include:
     - Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines
     - Agitated states
     - Individuals with a history of drug abuse
     - During or within 14 days following the administration of monoamine oxidase inhibitors

Initial approval duration:
ADHD & Narcolepsy: 6 months
Exogenous Obesity: 1 month

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- **Continuation of coverage (renewal request):** Evekeo (amphetamine sulfate) or Amphetamine Sulfate is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual's condition has responded while on therapy
    - Response is defined as:
        - For ADHD:
            - Adult and Child: Achieved and maintains at least a 50% reduction from baseline in core symptoms of hyperactivity, impulsivity, and attention
            - Child: Achieved and maintains at least a 50% improvement from baseline in SKAMP rating scale
        - For Narcolepsy:
            - Achieved and maintains an improvement in daytime sleepiness and alertness over baseline and reduced number of cataplexy episode (if it was present)
            - Achieved and maintains an improvement in the Epworth Sleepiness Scale (ESS) score of 7or less
        - For Exogenous Obesity:
            - Achieved and maintains at least a 10% reduction in weight

2. Individual has been adherent with the medication

3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications as listed in the criteria for initial therapy section
    - Significant adverse effect such as:
        - Seizure
        - Serotonin Syndrome
        - Development of psychotic or manic symptoms

4. There are no significant interacting drugs

Renewal duration:
ADHD & Narcolepsy: 12 months
Exogenous Obesity: 6 month

Description:

Evekeo (amphetamine sulfate) and Amphetamine Sulfate is indicated for the treatment of individuals 3 years of age or older with Attention Deficit Hyperactivity Disorder (ADHD); for the treatment of individuals 12 years or age or older with narcolepsy; and for the short term treatment (a few weeks) of individuals 12 years of age or older with exogenous obesity as an adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy such as repeated diets, group programs, and other drugs.

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Narcolepsy is a chronic neurologic disorder of the central nervous system characterized by the brain's inability to control sleep-wake cycles, resulting in excessive daytime sleepiness (EDS) and intermittent bouts of rapid eye movement (REM) sleep during wakefulness. At various times throughout the day, individuals with narcolepsy experience irresistible and sudden bouts of sleep, which can last from a few seconds to several minutes. In addition to EDS, other major symptoms of narcolepsy include cataplexy (a sudden loss of voluntary muscle tone), hypnagogic hallucinations (vivid dream-like images or hallucinations during sleep onset or upon waking), and sleep paralysis (brief episodes of total paralysis, also during sleep onset or upon waking). Most individuals experience poor sleep quality that can involve frequent awakenings during nighttime sleep, and other sleep disorders. Sleep may be disrupted by insomnia, vivid dreaming, sleep talking, acting out while dreaming, and periodic leg movements.

Amphetamine, immediate release forms of mixed salts of amphetamine/dextroamphetamine, dextroamphetamine, methamphetamine, many methylphenidate products, Provigil (modafinil) and Nuvigil (armodafinil) are effective for treatment of daytime sleepiness due to narcolepsy and are FDA-approved for use for this disorder. Many of these agents are available as a generic formulation.

ADHD is one of the most commonly diagnosed neurobehavioral disorders of childhood. It is more frequently diagnosed in males than in females. ADHD is characterized by inattention, hyperactivity that exceeds the usual developmental pattern, and impulsivity that impair activities of daily living. Comorbidities are also common and may include mood disorder, anxiety disorder, substance abuse, tics, learning difficulties, and disruptive behaviors such as oppositional defiance or conduct disorder. Symptoms can persist into adolescence and into adulthood.

The published literature suggests that central nervous system (CNS) stimulant medications are considered first line therapy in uncomplicated ADHD. Methylphenidate or mixed Amphetamine salts, or Dextroamphetamine are often recommended as first line therapy. Evidence for the use of Methylphenidate is derived from well-designed efficacy and safety trials. Due to limited number of trial information the strength of evidence for the other stimulants is ranked as fair.

When one stimulant fails to manage the condition due to an inadequate response or intolerable adverse effects occur, it is suggested to change to another one of the first line stimulants within a different class. Approximately 50% of individuals not responding to one stimulant may respond to the other. It is further suggested that if two first line stimulants are ineffective, non-stimulant medications may be added or used as mono-therapy. Use of non-stimulant medications may also be beneficial in situations such as concerns about substance abuse or diversion, tic disorder, impulsivity, sleep problems, anxiety, psychosis, aggression, or cardiac abnormalities associated with use of stimulants. Non-stimulant medications may include Atomoxetine, Clonidine, or Guanfacine.

There are many agents available with brand and generic options for the treatment of ADHD. Several agents are available as both immediate acting and long acting formulations. Comparative trials of stimulant medications are lacking, but it is apparent that all stimulant medications have similar effects and adverse effects and given the extensive evidence of efficacy and safety, they still remain agent first choice. There are clinically meaningful differences in dosing, time to onset, route, duration of action, and cost among the various compounds. Sustained-release formulations of stimulants may show benefit over immediate release forms at specific times of day depending on the pharmacokinetics of the specific formulation used, but overall differences on safety and efficacy are not found.

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For individuals with swallowing difficulties, many capsule forms of extended release stimulants can be opened and sprinkled onto food. Liquid formulations are also available and some products have a chewable dosage form that can be used.

Adult individuals with a body mass index (BMI) of 25-29.9 kg/m^2 are considered overweight and those with a BMI of $\geq$ 30 kg/m^2 are considered obese. Diet and exercise are the preferred methods for losing weight and there are several drugs that are FDA-approved as adjuncts to diet and exercise for weight loss. Amphetamines are non-catecholamine, sympathomimetic amines with CNS stimulant activity. Drugs in this class when used in the treatment of obesity are commonly referred to as "anorectics" or "anorexigenics." The mechanism of action of such drugs in treating obesity has not been established, however they act primarily to cause appetite suppression. Other CNS actions or metabolic effects may be involved. Methamphetamine is also FDA-approved for short-term treatment of obesity. Coverage of Evekeo for exogenous obesity is dependent upon benefit plan design that includes weight loss as a covered benefit.

Definitions:

Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale
The SKAMP rating scale is a validated 13-item teacher-rated scale that assesses manifestations of ADHD in a classroom setting. The SKAMP rating scale consists of 13 items rated on a 7-point impairment scale (0 = normal to 6 = maximal impairment). The combined scores for the SKAMP are obtained by summing the values of all 13 items.

1. Getting started on assignments for classroom periods
2. Sticking with tasks or activities for the allotted time
3. Attending to an activity or a discussion of the class
4. Stopping and making transition to the next period
5. Interacting with other children
6. Interacting with the teacher or aide
7. Remaining quiet according to classroom rules
8. Staying seated according to classroom rules
9. Completing assigned work
10. Performing work accurately
11. Being careful and neat while writing or drawing
12. Complying with the teacher's usual requests or directions
13. Following the rules established for the classroom

Epworth Sleepiness Scale (ESS)
The ESS subjectively measures sleepiness as it occurs in ordinary life situations. It can be used to screen for excessive sleepiness or to follow an individual's subjective response to an intervention. A score greater than ten is consistent with excessive sleepiness.

Sitting and standing	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points

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	High chance of dozing	3 points
Watching television	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points
	High chance of dozing	3 points
Sitting inactive in a public place	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points
	High chance of dozing	3 points
Sitting for an hour as a passenger in a car	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points
	High chance of dozing	3 points
Lying down in the afternoon to rest	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points
	High chance of dozing	3 points
Sitting and talking to another person	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points
	High chance of dozing	3 points
Sitting quietly after lunch (no alcohol at lunch)	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points
	High chance of dozing	3 points
Sitting in a car, stopped for a few minutes due to traffic	No chance of dozing	0 points
	Slight chance of dozing	1 point
	Moderate chance of dozing	2 points
	High chance of dozing	3 points
Total points:		
Score assessment: 1-6 points: Normal sleep 7-8 points: Average sleepiness 9-24 points: Abnormal (possibly pathologic) sleepiness		

Resources:

Evekeo. Package Insert. Revised by manufacturer 02/2015; accessed 04-21-2016. Revised by manufacturer 09/2016; accessed 04-08-2017. Revised by manufacturer 10/2016; accessed 03-14-2018.

Evekeo product information accessed 05-01-18 at DailyMed:
https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f469fb38-0380-4621-9db3-a4f429126156

UpToDate: Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/attention-deficit-hyperactivity-disorder-in-children-and-adolescents-overview-of-treatment-and-prognosis?search=adhd&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H197690673

UpToDate: Attention deficit hyperactivity disorder in children and adolescents: Clinical features and diagnosis. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/attention-deficit-hyperactivity-disorder-in-children-and-adolescents-clinical-features-and-diagnosis?search=adhd&source=search_result&selectedTitle=4~150&usage_type=default&display_rank=4

UpToDate: Attention deficit hyperactivity disorder in children and adolescents: Treatment with medications. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/attention-deficit-hyperactivity-disorder-in-children-and-adolescents-treatment-with-medications?search=adhd&source=search_result&selectedTitle=5~150&usage_type=default&display_rank=5

UpToDate: Attention deficit hyperactivity disorder in adults: Epidemiology, pathogenesis, clinical features, course, and diagnosis. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/attention-deficit-hyperactivity-disorder-in-adults-epidemiology-pathogenesis-clinical-features-course-assessment-and-diagnosis?search=adhd&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2

UpToDate: Pharmacotherapy for adult attention deficit hyperactivity disorder. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/pharmacotherapy-for-adult-attention-deficit-hyperactivity-disorder?search=adhd&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3

UpToDate: Narcolepsy in children. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/narcolepsy-in-children?search=narcolepsy&source=search_result&selectedTitle=3~117&usage_type=default&display_rank=3

UpToDate: Clinical features and diagnosis of narcolepsy in adults. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-features-and-diagnosis-of-narcolepsy-in-adults?search=narcolepsy&source=search_result&selectedTitle=1~117&usage_type=default&display_rank=1

UpToDate: Treatment of narcolepsy in adults. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-narcolepsy-in-adults?search=narcolepsy&source=search_result&selectedTitle=2~117&usage_type=default&display_rank=2

UpToDate: Quantifying sleepiness. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/quantifying-sleepiness?search=Maintenance%20of%20Wakefulness%20Test&source=search_result&selectedTitle=1~9&usage_type=default&display_rank=1

UpToDate: Obesity in adults: Drug therapy. Current through Apr, 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/obesity-in-adults-drug-therapy?topicRef=5371&source=see_link

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.