PHARMACY COVERAGE GUIDELINE

ADHANSIA XR™ (methylphenidate hydrochloride extended release)
APTENSIO XR™ (methylphenidate hydrochloride extended release)
AZSTARYS™ (serdexmethylphenidate and dexmethylphenidate)
DAYTRANA® (methylphenidate) transdermal patch
JORNAY PM™ (methylphenidate hydrochloride extended release)
Methylphenidate ER
Methylphenidate Pad transdermal patch

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Adhansia XR, Aptensio XR, Azstarys, Daytrana, Jornay PM, methylphenidate ER or methylphenidate pad are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Psychiatrist

2. Individual is 6 years of age or older

3. A confirmed diagnosis of Attention Deficit Hyperactivity Disorder (ADHD)

4. Individual has failure, contraindication per FDA label, or intolerance to a trial of **ONE** drug from **BOTH** of the following:
    a. A generic extended release methylphenidate **OR** a generic extended release dexmethylphenidate (such as generic Concerta, generic Metadate CD and generic Ritalin LA, dexmethylphenidate ER)
    b. Generic dextroamphetamine with amphetamine extended release **OR** generic extended release dextroamphetamine **OR** Vyvanse (lisdexamfetamine)

5. Request for **brand** Daytrana: Individual has failure, contraindication per FDA label, or intolerance to the **generic methylphenidate pad**

6. There is no history of risky, harmful, non-medical or inappropriate use of these and other substances that might be unhealthy, hazardous, or a problem (i.e., multiple providers, multiple pharmacies, or multiple controlled substances)

7. There are no known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, or other serious heart problems

8. There is no history of uncontrolled pre-existing psychiatric mood disorder such as depression history of suicide, bipolar disorder, or psychotic disorder

9. There are **NO** FDA-label contraindications:
    a. Known hypersensitivity to methylphenidate products
    b. Currently using or use within the preceding 14 days a monoamine oxidase inhibitor (MAOI)
    c. **Additional for Daytrana and generic methylphenidate pad only:**
        i. Marked anxiety, tension, or agitation
        ii. Glaucoma
        iii. Tics or a family history or diagnosis of Tourette's syndrome

10. There are no significant interacting drugs

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Adhansia XR, Aptensio XR, Azstarys, Daytrana, Jornay PM, methylphenidate ER or methylphenidate pad is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

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1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Psychiatrist

2. Request for continuation of **brand** Daytrana: Individual has failure, contraindication per FDA label, or intolerance to the **generic methylphenidate pad**

3. Individual's condition responded while on therapy with response is defined as **TWO** of the following:
    a. Achieved and maintains at least a 50% reduction from baseline in core symptoms of hyperactivity, impulsivity, and attention
    b. Achieved and maintains at least a 50% improvement from baseline in SKAMP rating scale
    c. Improved attention and social skills
    d. No aggressive behaviors

4. Individual has been adherent with the medication

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Development of psychotic or manic symptoms or other serious psychiatric events
        ii. Peripheral vasculopathy, including Raynaud's phenomenon
        iii. Priapism
        iv. Serious cardiovascular event such as stroke, or myocardial infarction
        v. **Additional for Daytrana and generic methylphenidate pad only:**
            1. Chemical leukoderma or signs of skin depigmentation
            2. Contact sensitization with erythema, edema, papules, & vesicles that has not improved within 48 hours or has spread beyond the patch site

6. There is no history of risky, harmful, non-medical or inappropriate use of these and other substances that might be unhealthy, hazardous, or a problem (i.e., multiple providers, multiple pharmacies, or multiple controlled substances)

7. There is no history of uncontrolled pre-existing psychiatric mood disorder such as depression, history of suicide, bipolar disorder, or psychotic disorder

8. There are no significant interacting drugs

Renewal duration: 12 months

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- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Adhansia XR (methylphenidate), Aptensio XR (methylphenidate), Azstarys (serdexmethylphenidate and dexmethylphenidate) capsule, Daytrana (methylphenidate transdermal system), Jornay PM (methylphenidate), and methylphenidate ER are a central nervous system stimulants indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years of age and older.

How methylphenidate exerts its therapeutic benefit in the treatment of ADHD is unknown. Methylphenidate is a known central nervous system (CNS) stimulant. Methylphenidate is a racemic mixture of the d- and l-isomers. The d-isomer is more pharmacologically active than the l-isomer. Methylphenidate is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space. Methylphenidate is available in numerous formulations that includes short acting, intermediate acting, and long acting preparations. Dexmethylphenidate is the more pharmacologic active d-enantiomer of racemic methylphenidate and is thought to block reuptake of norepinephrine and dopamine into the presynaptic neuron like methylphenidate. Serdexmethylphenidate is a prodrug of dexmethylphenidate that is converted to dexmethylphenidate in the gastrointestinal tract.

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, impulsivity that impair activities of daily living, and/or inattention that occur in more than one setting and affect function (e.g., academic, social, emotional, etc.). The symptoms must not be better accounted for by another mental disorder.

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 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.

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Treatment goals include improved relationships with parents, teachers, siblings, or peers (e.g., plays without fighting at recess); improved academic performance (e.g., completes academic assignments); and improved rule following (e.g., does not talk back to the teacher).

Response to treatment is demonstrated by objective measurement of reduction in core symptoms and/or improvement in target goals (e.g., 40-50% reduction in core symptoms compared with baseline and decreased proportion of missing assignments from 60% to 20%. Core symptoms can be monitored through the use of ADHD-specific rating scales and target symptoms can be monitored through a daily report card or periodic narrative reports from the child's teacher.

Treatment failure is defined by lack of satisfactory improvement in core symptoms of ADHD at the maximum dose or the occurrence of intolerable adverse effects. It is important to differentiate lack of response from rebound effects as the medication wears off. With lack of response there is no improvement in core symptoms. With rebound, there is an initial improvement in core symptoms, but near the end of the expected duration of action, there may be a recurrence or worsening of symptoms.

When one stimulant fails to manage the condition due to an inadequate response, it is suggested to change to another one of the first line stimulants. Approximately 50% of individuals not responding to one stimulant may respond to the other as side effects may occur with one type of stimulant but not another.

It is further suggested that if first line stimulants are ineffective, non-stimulant medications may be added or used as monotherapy. Use of non-stimulant medications may be beneficial in situations such as concerns about substance abuse or diversion, tic disorder, sleep problems, anxiety, psychosis, aggression, or cardiac abnormalities associated with use of stimulants. Non-stimulant medications may include atomoxetine, clonidine, guanfacine, and antidepressants (e.g., tricyclic antidepressants, bupropion, selective serotonin reuptake inhibitors).

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.

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.

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Definitions:

Attention Deficit Hyperactivity Disorder (ADHD)

- ADHD types:
  - Inattentive Type, *at least 6* of the following symptoms must have persisted for *at least 6 months*
    - Lack of attention to details/careless mistakes
    - Lack of sustained attention
    - Poor listener
    - Failure to follow through on tasks
    - Poor organization
    - Avoids tasks requiring sustained mental effort
    - Loses things
    - Easily distracted
    - Forgetful
  - Hyperactive-Impulsive Type, *at least 6* of the following symptoms must have persisted for *at least 6 months*
    - Fidgeting/squirming
    - Leaving seat
    - Inappropriate running/climbing
    - Difficulty with quiet activities
    - "On the go"
    - Excessive talking
    - Blurting answers
    - Can't wait turn
    - Intrusive
  - Combined Type requires both inattentive and hyperactive-impulsive criteria to be met

ADHD medications – stimulants: [Note may not be a complete list]

Methylphenidate-type products:		
Methylphenidate		
Aptensio XR	ER Cap 24 h	10, 15, 20, 30, 40, 50, 60 mg
Concerta	ER Tab	18, 27, 36, 54 mg
Daytrana	Transdermal	10 mg/9 hr, 15 mg/9 hr, 20 mg/9 hr, 30 mg/ 9 hr
Metadate CD	ER Cap	10, 20, 30, 40, 50, 60 mg
Metadate ER	ER Tab	20 mg
Methylin	Tab chewable	2.5, 5, 10 mg
	Solution	5 mg / 5 mL, 10 mg / 5 mL
Methylphenidate	Tab	5, 10, 20 mg
	Tab chewable	2.5, 5, 10 mg
	Solution	5 mg /5 mL, 10 mg / 5 mL
Methylphenidate ER	ER Tab	10, 18, 20, 27, 36, 54 mg

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Methylphenidate ER	ER Tab 24 h	18, 27, 36, 54 mg
Methylphenidate ER (CD)	ER Cap	10, 20, 30, 40, 50, 60 mg
Methylphenidate ER (LA)	ER Cap 24 h	20, 30, 40 mg
Quillivant XR	ER Suspension	25 mg / 5 mL
Ritalin	Tab	5, 10, 20 mg
Ritalin LA	ER Cap 24 h	10, 20, 30, 40, 60 mg
Ritalin SR	ER Tab	20 mg
Dexmethylphenidate		
Dexmethylphenidate	Tab	2.5, 5, 10 mg
Dexmethylphenidate ER	ER Cap 24 h	5, 10, 15, 30, 40 mg
Focalin	Tab	2.5, 5, 10 mg
Focalin XR	ER Cap 24 h	5, 10, 15, 20, 25, 30, 35, 40 mg
Listing does not imply formulary status or need for precertification or need step-therapy		

Amphetamine-type products:		
Amphetamine		
Adzenys XR-ODT	Tab ODT 24h	3.1, 6.3, 9.4, 12.5, 15.7, 18.8 mg
Dyanavel XR	Suspension	2.5 mg/mL
Evekeo	Tab	5, 10 mg
Mixed salts: Amphetamine (25%) / Dextroamphetamine (75%)		
Adderall	Tab	5, 7.5, 10,12.5, 15, 20, 30 mg
Adderall XR	ER Cap 24 h	5, 10, 15, 20, 25, 30 mg
Amphetamine / Dextroamphetamine	Tab	5, 7.5, 10,12.5, 15, 20, 30 mg
	ER Cap 24 h	5, 10, 15, 20, 25, 30 mg
Dextroamphetamine		
Dexedrine	ER Cap 24 h	5, 10, 15 mg
Dextroamphetamine	Tab	5, 10 mg
	Solution	5 mg / 5 mL
Dextroamphetamine ER	ER Cap 24 h	5, 10, 15 mg
ProCentra	Solution	5 mg / 5 mL
Zenzedi	Tab	2.5, 5, 7.5, 10, 15, 20, 30 mg
Lisdexamfetamine		
Vyvanse	Cap	10, 20, 30, 40, 50, 60, 70 mg
Methamphetamine		
Desoxyn	Tab	5 mg
Methamphetamine	Tab	5 mg
Listing does not imply formulary status or need for precertification or need step-therapy		

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ADHD medications – non-stimulants: [Note may not be a complete list]

Norepinephrine re-uptake inhibitor		
Atomoxatine (Strattera)	Cap	10, 18, 25, 40, 60, 80, 100 mg
Clonidine – central alpha-2 agonist		
Catapres	Tab	0.1, 0.2, 0.3 mg
Clonidine	Tab	0.1, 0.2, 0.3 mg
Clonidine ER	ER Tab 12 h	0.1 mg
Kapvay (clonidine ER)	ER Tab 12 h	0.1, 0.2 mg
Guanfacine – central alpha-2a agonist		
Guanfacine	Tab	1, 2 mg
Guanfacine ER	ER Tab 24 h	1, 2, 3, 4 mg
Intuniv (guanfacine ER)	ER Tab 24 h	1, 2, 3, 4 mg
Tenex	Tab	1, 2 mg
Listing does not imply formulary status or need for precertification or need step-therapy		

Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale:

- A validated 13-item teacher-rated scale that assesses manifestations of ADHD in a classroom setting
- The 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
- Subscale scores for attention (items 1-4), behavior (items 5-8), quality of work (items 9-11) and compliance (items 12-13) are obtained by summing the values of their corresponding items

	Impairment Scale 0-7
1. Getting started on assignments for classroom periods	1__2__3__4__5__6__7
2. Sticking with tasks or activities for the allotted time	1__2__3__4__5__6__7
3. Attending to an activity or a discussion of the class	1__2__3__4__5__6__7
4. Stopping and making transition to the next period	1__2__3__4__5__6__7
5. Interacting with other children	1__2__3__4__5__6__7
6. Interacting with the teacher or aide	1__2__3__4__5__6__7
7. Remaining quiet according to classroom rules	1__2__3__4__5__6__7
8. Staying seated according to classroom rules	1__2__3__4__5__6__7
9. Completing assigned work	1__2__3__4__5__6__7
10. Performing work accurately	1__2__3__4__5__6__7
11. Being careful and neat while writing or drawing	1__2__3__4__5__6__7
12. Complying with the teacher's usual requests or directions	1__2__3__4__5__6__7
13. Following the rules established for the classroom	1__2__3__4__5__6__7

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Resources:

Adhansia XR (methylphenidate) extended release capsule product information, revised by Adlon Therapeutics L.P. 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 07, 2022.

Aptensio XR (methylphenidate) extended release capsule product information, revised by Rhodes Pharmaceuticals L.P. 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 07, 2022.

Azstarys (serdexmethylphenidate and dexmethylphenidate) capsule product information, revised by Corium, Inc. 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 07, 2022.

Daytrana (methylphenidate) patch product information, revised by Noven Therapeutics, LLC 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 07, 2022.

Jornay PM (methylphenidate) extended release capsule product information, revised by Ironshore Pharmaceuticals, Inc. 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 07, 2022.

Methylphenidate extended release capsule product information, revised by SpecGx LLC. 01-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 09, 2022.

Krull KR. Attention deficit hyperactivity disorder in children and adolescents: Overview of treatment and prognosis. In: UpToDate, Augustyn M, Torchia MM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated February 03, 2022. Accessed March 01, 2022.

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