BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.60.24

Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	March 1, 2002
Subject:	Amphetamines	**Page:**	1 of 7

Last Review Date: June 16, 2022

Amphetamines

Description

Adderall, Adderall XR, Mydayis (mixed salts of a single entity amphetamine)
Adzenys XR–ODT*****, Adzenys ER, Dyanavel XR*****, Evekeo, Evekeo ODT***** (amphetamine)
Desoxyn***** (methamphetamine)
Dexedrine, Procentra, Xelstrym**, Zenzedi (dextroamphetamine)
Vyvanse (lisdexamfetamine)

*Prior authorization for the brand formulation applies only to formulary exceptions due to being a non-covered medication.

**This medication is included in this policy but not available on the market as of yet.

Background
Amphetamine is a CNS stimulant and DEA schedule II drug, which is FDA approved for attention deficit hyperactivity disorder (ADHD) and narcolepsy. The exact mechanism by which amphetamines exert their action is unknown; however, amphetamines are thought to block the reuptake of norepinephrine and dopamine by the presynaptic neuron. This causes an increase in the release of these monoamines into the extra-neuronal space and increases their levels in the brain (1-13).

Attention deficit disorder (ADD) is no longer a medical diagnosis; however, it is often used to refer to predominantly inattentive type ADHD and associated symptoms. The terms ADD and ADHD will be used throughout this policy (14).

For patients 22 years of age and older prior authorization and review is required for both diagnosis and quantity requested. For patients 21 years of age and younger review is required if the total daily dose exceeds the FDA recommended daily limit.

Regulatory Status
FDA-approved indications: The products addressed by this policy are approved for use in the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy (1-13). Vyvanse is also indicated for moderate to severe binge eating disorder (6).

Limitations of Use:
Vyvanse is not indicated for weight loss. Use of other sympathomimetic drugs for weight loss has been associated with serious cardiovascular adverse events. The safety and effectiveness of Vyvanse for treatment of obesity have not been established (6).

Vyvanse and other stimulants are not indicated for weight loss (1-13).

Off-Label Uses:
Amphetamines can be used as adjunctive therapy in the treatment of resistant depression (14).
Amphetamines have a boxed warning for high abuse and addiction potential. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events.
Other safety issues associated with amphetamines include sudden death in patients who have heart defects. Strokes, myocardial infarction, seizures, visual disturbances, adverse psychiatric reactions, and hypertension have been reported (1-13).

Related policies

Methylphenidates, Provigil-Nuvigil

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Amphetamines may be considered **medically necessary** in patients 22 years of age or older for the treatment of narcolepsy, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD) or depressive disorder, and if the conditions indicated below are met.

Vyvanse may also be considered **medically necessary** in patients 22 years of age or older for the treatment of moderate to severe binge eating disorder (BED), and if the conditions indicated below are met.

Amphetamines may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 22 years of age or older*

*For patients 21 years of age and younger review is required if the total daily dose exceeds the FDA recommended daily limit.

Diagnoses

Patient must have **ONE** of the following:

1. Narcolepsy
2. Attention deficit disorder (ADD)
3. Attention deficit hyperactivity disorder (ADHD)
4. Depressive disorder **AND ONE** of the following:
    a. Used in combination with antidepressants
    b. Inadequate treatment response, intolerance, or contraindication to antidepressants
5. **Vyvanse ONLY**: Moderate to severe binge eating disorder (BED)

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

Age 22 years of age or older - **NONE**
Age 21 years of age or younger

Pre - PA Quantity

Medication / Strength	Quantity Limit	Daily Dosing Limits
Methamphetamine 5mg	5 units per day	25 mg per day
Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg Adderall XR 5 mg, 10 mg, 15mg Dextroamphetamine 2.5 mg, 5 mg, 7.5 mg,10 mg, 15 mg Dexedrine Spansule 5 mg, 10 mg, 15mg Evekeo 5 mg, 10 mg Zenzedi 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg	4 units per day	60 mg per day
Adderall 20 mg	3 units per day	

Adderall XR 20 mg Dextroamphetamine 20 mg Zenzedi 20 mg		
Adderall 30 mg Adderall XR 25 mg, 30 mg Dextroamphetamine 30 mg Zenzedi 30 mg	2 units per day	
Procentra oral solution 5mg/5mL	60 mL per day	
Adzenys ER solution	15 mL per day	18.8 mg per day
Mydayis 12.5 mg, 25 mg Mydayis 37.5 mg, 50 mg (for age 18-21 **ONLY**)	1 unit per day	**Age 17 and younger:** 25 mg per day **Age 18-21:** 50 mg per day
Xelstrym 4.5 mg/9 hours, 9 mg/9 hours, 13.5 mg/9 hours, 18 mg/9 hours	1 unit per day	18 mg per day
Vyvanse 10 mg, 20 mg, 30 mg	2 units per day	70 mg per day
Vyvanse 40 mg, 50 mg, 60 mg, 70 mg	1 unit per day	

Prior - Approval Limits

Quantity

Medication	Daily Dosing Limits
Adderall	60 mg per day
Adzenys ER solution	12.5 mg per day (10mL per day)
Dexedrine / Dextroamphetamine / Zenzedi	60 mg per day
Evekeo	60 mg per day
Methamphetamine 5mg	25 mg per day
Mydayis	50 mg per day
Procentra oral solution 5mg/ 5mL	60 mg per day (60 mL per day)
Xelstrym	18 mg per day
Vyvanse	70 mg per day

Medication **with approved Formulary Exception only**	Daily Dosing Limits
Adzenys XR-ODT	**Age 12 and younger:** 18.8 mg per day **Age 13 and older:** 12.5 mg per day
Desoxyn	25 mg per day
Dyanavel XR oral suspension 2.5 mg/mL	60 mg per day (24 mL per day)
Evekeo ODT	60 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Amphetamine is a CNS stimulant and DEA schedule II drug, which is FDA approved for attention deficit hyperactivity disorder (ADHD) and narcolepsy. Amphetamines have a boxed warning for high abuse and addiction potential. Misuse of amphetamines may cause sudden death and serous cardiovascular adverse events (1-13).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of amphetamines while maintaining optimal therapeutic outcomes.

References

1. Adderall [package insert]. Horsham, PA: Teva Pharmaceuticals USA; April 2020.
2. Adderall XR [package insert]. Lexington, MA: Takeda Pharmaceuticals America, Inc.; August 2020.
3. Desoxyn [package insert]. Lebanon, NJ: Recordati Rare Disease Inc.; April 2019.
4. Dexedrine Spansule [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; June 2019.
5. Zenzedi [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC; March 2021.
6. Vyvanse [package insert]. Lexington, MA: Shire US Inc.; August 2020.
7. Evekeo [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC; September 2016.
8. Evekeo ODT [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC; March 2019.
9. Dyanavel XR [package insert]. Monmouth Junction, NJ: Tris Pharma Inc.; February 2019.

10. Adzenys XR-ODT [package insert]. Grand Prairie, TX: Neos Therapeutics Inc.; December 2017.
11. Mydayis [package insert]. Lexington, MA: Shire US Inc.; September 2019.
12. Adzenys ER solution [package insert]. Grand Prairie, TX: Neos Therapeutics Inc.; September 2017.
13. Xelstrym [package insert]. Noven Therapeutics, LLC; March 2022.
14. Lange, Klaus W et al. “The history of attention deficit hyperactivity disorder.” Attention Deficit and Hyperactivity Disorders (Nov 2010) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3000907/
15. Stoltz, Gabriele. MD; PhD, Woggon, Brigitte. MD., & Angst, Jules. (1999). Psychostimulants in the therapy of treatment-resistant depression Review of the literature and findings from a retrospective study in 65 depressed patients. 1. 165-74.

Policy History

Date	Action
March 2002	New to PA
July 2007	Vyvanse is a new form of amphetamine that has less potential for abuse.
October 2008	LiquADD is a new solution of D*extroamphetamine 5mg/5ml.*
September 2012	Annual editorial and reference update
June 2013	Annual editorial review and addition of daily limits.
July 2013	Removal of Dextrostat and LiquiADD and the addition of Zenzedi.
January 2014	Addition of quantity limits
May 2014	Addition of 3 new strengths of Zenzedi
September 2014	Annual reference update Removed non-FDA approved indications
January 2015	Addition of line extension of Vyvanse 10mg
February 2015	Addition of Evekeo and Vyvanse indication for BED
March 2015	Annual editorial review and reference update
June 2015	Annual review and reference update Changed Policy # from 5.07.01 and sub-heading from Endocrine and Metabolic Drugs
December 2015	Addition of Dyanavel XR
January 2016	Addition of Adzenys XR-ODT
March 2016	Annual review Policy number change from 5.06.24 to 5.60.24
September 2016	Annual editorial review and reference update. Addition of limitations of use for Vyvanse. Change in coverage from 21 years of age or younger for Pre-PA limits
July 2017	Addition of Mydayis
September 2017	Annual review

September 2017	Addition of Adzenys ER solution
December 2017	Annual review
November 2018	Annual review and reference update
March 2019	Annual review. Addition of Evekeo ODT and added Pre-PA allowance for Mydayis 37.5 mg and 50 mg for age 18-21
December 2019	Annual review. Moved Desoxyn to MFE with PA only. Addition of statement “Vyvanse and other stimulants are not indicated for weight loss” per SME
December 2020	Annual review and reference update
March 2021	Annual review
September 2021	Annual editorial review and reference update. Revised the Pre-PA chart, grouping Evekeo ODT 20 mg with dextroamphetamine and Zenzedi.
December 2021	Revised Pre-PA chart to group all medications with the same mg/day. Changed quantity limit to quantity per day instead of quantity per 90 days. Moved Adzenys XR-ODT, Dyanavel XR, and Evekeo ODT to FE with PA only. Per FEP: Attention deficit disorder with or without hyperactivity (ADD/ADHD) is now being listed as two separate diagnoses: attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD.
March 2022	Annual review. Per SME, added the requirement “used in combination with antidepressants” OR “inadequate treatment response, intolerance, or contraindication to antidepressants” under depressive disorder
April 2022	Addition of Xelstrym to policy
June 2022	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.