

STEP THERAPY POLICY

- POLICY:** Attention Deficit Hyperactivity Disorder Stimulant Step Therapy Policy
- Adderall XR[®] (mixed amphetamine salts [dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine sulfate, amphetamine aspartate] extended-release capsules – Shire US, generics)
 - Adhansia XR[™] (methylphenidate extended-release capsule – Purdue)
 - Adzenys ER[™] (amphetamine extended-release oral suspension – Neos Therapeutics)
 - Adzenys XR-ODT[™] (amphetamine extended-release orally disintegrating tablets – Neos Therapeutics)
 - Aptensio XR[™] (methylphenidate extended-release capsules – Rhodes, generics)
 - Concerta[®] (methylphenidate extended-release tablets – McNeil Pediatrics, generics)
 - Cotempla XR-ODT[™] (methylphenidate extended-release orally disintegrating tablets – Neos Therapeutics)
 - Daytrana[®] (methylphenidate transdermal system – Noven Pharmaceuticals)
 - Dexedrine[®] Spansules[®] (dextroamphetamine sustained-release capsules – Amedra Pharmaceuticals, generics)
 - Dyanavel[™] XR (amphetamine extended-release oral suspension – Tris)
 - Focalin[®] XR (dexmethylphenidate extended-release capsules – Novartis, generics)
 - Jornay PM[™] (methylphenidate hydrochloride extended-release capsules – Ironshore)
 - Metadate[®] CD (methylphenidate extended-release capsules – UCB, Inc., generics)
 - Metadate[®] ER (methylphenidate sustained-release tablets – UCB, Inc., generic only)
 - methylphenidate extended-release capsules (generics to discontinued Methylin[™] ER)
 - methylphenidate 72 mg extended-release tablets (branded product – Trigen)
 - Mydayis[™] (mixed salts of a single-entity amphetamine product extended-release capsules – Shire)
 - QuilliChew ER[™] (methylphenidate extended-release chewable tablets – Pfizer)
 - Quillivant[™] XR (methylphenidate extended-release oral suspension – NextWave)
 - Relexxii[®] (methylphenidate extended-release tablets – Vertical [branded generic])
 - Ritalin[®] LA (methylphenidate extended-release capsules – Novartis, generics)
 - Ritalin-SR[®] (methylphenidate sustained-release tablets – Novartis, generics)
 - Vyvanse[®] (lisdexamfetamine dimesylate capsules and chewable tablets – Shire)

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OVERVIEW

All of the long-acting stimulants are indicated for the treatment of **attention-deficit hyperactivity disorder (ADHD)**.¹⁻²² Some products are also indicated for the treatment of **narcolepsy**. Vyvanse is the only stimulant medication indicated for the treatment of **binge eating disorder**.¹¹ Refer to Table 1 for a summary of indications. All of these products have abuse potential and are Schedule II controlled substances.

Table 1. FDA-Approved Indications for Long-Acting Stimulants.¹⁻²²

Product	FDA-Approved Indication(s)
Adderall XR [®] (generics)	• ADHD in children 6 to 12 years, adolescents 13 to 17 years, and adults
Adhansia XR [™]	• ADHD in patients > 6 years
Adzenys ER [™]	• ADHD in patients > 6 years
Adzenys XR-ODT [™]	• ADHD in patients ≥ 6 years
Aptensio XR [™] (generics)	• ADHD in patients ≥ 6 years old
Concerta [®] (generics)	• ADHD in children ≥ 6 years, adolescents (13 to 17 years), and adults ≤ 65 years
Cotempla XR-ODT [™]	• ADHD in patients 6 to 17 years
Daytrana [®]	• ADHD in children 6 to 12 years, and adolescents (13 to 17 years)
Dexedrine [®] Spansule [®] (generics)	• ADHD in children ≥ 6 years & adolescents up to 16 years • Narcolepsy
Dyanavel [™] XR	• ADHD in children ≥ 6 years & adults
Focalin [®] XR (generics)	• ADHD in patients ≥ 6 years
Jornay PM [™]	• ADHD in patients ≥ 6 years
Metadate [®] CD (generics)	• ADHD in children 6 to 15 years
Metadate [®] ER (generics, brand product considered generic per FDB)	• ADHD in children ≥ 6 years & adults • Narcolepsy
Methylin [™] ER (generics, brand discontinued)	• ADHD in children ≥ 6 years & adults • Narcolepsy
Mydayis [™]	• ADHD in patients ≥ 13 years & adults
QuilliChew ER [™]	• ADHD in children ≥ 6 years & adults
Quillivant [™] XR	• ADHD in patients ≥ 6 years
Relexxii [®] (branded generic)	• ADHD in children and adolescents ≥ 6 years & adults up to 65 years of age
Ritalin [®] LA (generics)	• ADHD in children 6 to 12 years
Ritalin-SR [®] (generics)	• ADHD in children ≥ 6 years & adults • Narcolepsy
Vyvanse [®]	• ADHD in children 6 to 12 years, adolescents (13 to 17 years), and adults • Bing eating disorder in adults

ADHD – Attention-deficit hyperactivity disorder.

GUIDELINES

The American Academy of Pediatrics (AAP) clinical practice guideline for the diagnosis, evaluation, and treatment of ADHD in children and adolescents was updated in 2019, and incorporates many of the findings from the Multimodal Treatment Study of Children With ADHD (MTA).²³ The AAP recommendations for treatment of children and youth with ADHD vary depending on the patient's age. For preschool-aged children (4 to 5 years of age), parent- and/or teacher-administered behavior therapy should be prescribed as first-line treatment; methylphenidate may be prescribed if behavior interventions do not provide significant improvement and disturbance of function continues. For elementary school-aged children (6 to 11 years of age), an FDA-approved medication for ADHD (and/or behavior therapy, but preferably both) should be prescribed. Evidence is particularly strong for stimulant medications, and sufficient but less strong for atomoxetine, guanfacine extended-release (ER) tablets, and clonidine ER tablets (in that order). For adolescents (12 to 18 years of age), an FDA-approved medication for ADHD (and/or behavior therapy, but preferably both) should be prescribed with the assent of the adolescent. The dose of medication should be titrated to achieve maximum benefit with minimum adverse events (AEs). The findings from the MTA study suggested that more than 70% of children and youth with ADHD respond to one of the stimulant medications at an optimal dose when a systematic trial is used. Titration to maximum doses that control symptoms without AEs is recommended instead of titration strictly on a mg-per-kg basis.

Methylphenidate and amphetamine formulations have similar effects and AEs, and remain the first choice of medication treatment.²³ Some patients will respond better to or display more AEs with one compound vs. another; however, these effects cannot be predetermined. Therefore, if a trial with one group is

unsuccessful (poor efficacy or AEs), a trial on a medication from the other group should be undertaken. At least half of the patients whose symptoms fail to respond to one stimulant medication may have a positive response to the alternative medication.

The American Psychiatric Association (APA) guideline on the treatment of patients with eating disorders (2006 with a Guideline Watch in 2012) does not mention the use of stimulants for the treatment of binge eating disorder.^{24,25} The guideline suggests treatment with antidepressant medications, particularly selective serotonin reuptake inhibitor antidepressants, is associated with at least a short-term reduction in binge eating behavior but, in most cases, not with substantial weight loss (recommended with substantial clinical confidence); topiramate is effective for binge reduction and weight loss (recommended with moderate clinical confidence); and zonisamide may produce similar effects regarding weight loss (may be recommended on the basis of individual circumstances).²⁴ The 2012 Guideline Watch referenced a 2011 literature review by a multinational task force on eating disorders which concluded that Grade A evidence supports the use of imipramine (with moderate risk-benefit ratio), sertraline and citalopram/escitalopram (all with good risk-benefit ratios), and topiramate (with moderate risk-benefit ratio), and Grade D evidence for fluvoxamine and fluoxetine (i.e., inconsistent results).²⁵ The usefulness of acamprosate and lamotrigine in binge-eating disorder has not been established.

DOSING AND DOSAGE FORMS

The choice of formulation depends on factors such as the efficacy of each agent for a given child/adolescent, the preferred length of coverage time, whether a child can swallow pills or capsules, and expense.²³ The ER formulations may be preferred over immediate-release (IR) formulations because they provide benefits of consistent and sustained coverage with fewer administrations per day. Long-acting formulations usually preclude the need for school-based administration of ADHD medications. Better coverage with fewer administrations leads to greater convenience for the family and, therefore, might also lead to better adherence to the medication management plan. Some patients, particularly adolescents, might require more than 12 hours of coverage to ensure adequate focus and concentration during evening study time and driving; in these cases, a short-acting (IR) preparation might be used in addition to a long-acting (ER) preparation.

Many of the generic ER stimulant medications for the treatment of ADHD are available as capsules: generic amphetamine/dextroamphetamine extended-release capsules (generics to Adderall XR), generic dexamethylphenidate extended-release capsules (generics to Focalin XR), and generic methylphenidate ER capsules (generics to Metadate CD, Ritalin LA, Adhansia XR, Aptensio XR). According to the prescribing information, the capsules may be taken whole, or the capsule may be opened and the entire contents sprinkled on applesauce.^{1,5,6,9,13,21} Patients should take the applesauce with sprinkled beads in its entirety without chewing.

Long-acting formulations of stimulants are equally efficacious as the IR forms and have been shown to be efficacious in adolescents as well as children.

Additional information on stimulant medications for the treatment of ADHD can be obtained by accessing the *Central Nervous System Stimulants for ADHD Therapy Class Summary*.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a history of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy. **Note:** Adderall XR with DAW 9 (indicating that substitution is allowed by the prescriber but the Plan requests brand) will also count as a Step 1 Product.

Step 1: Generic amphetamine/dextroamphetamine extended-release capsules (generics to Adderall XR), generic dexamethylphenidate extended-release capsules (generics to Focalin XR), generic dextroamphetamine extended-release capsules (generics to Dexedrine Spansules), generic methylphenidate extended-release capsules (generics to Metadate CD and Ritalin LA), Metadate ER (generic according to FDB), generic methylphenidate sustained-release tablets (generics to Ritalin SR), generic methylphenidate extended-release tablets (generics to Concerta)

Step 2: Adderall XR, Adhansia XR, Adzenys ER, Adzenys XR-ODT, Aptensio XR (brand and generics), Concerta, Cotelpla XR-ODT, Daytrana, Dexedrine Spansules, Dyanavel XR, Focalin XR, Jornay PM, Metadate CD, Methylphenidate 72 mg extended-release tablets (branded product), Mydayis, QuilliChew ER, Quillivant XR, Relexxii, Ritalin LA, Ritalin SR, Vyvanse capsules and chewable tablets

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
2. If the patient cannot swallow or has difficulty swallowing oral dosage forms, approve Daytrana.
3. If the patient is being treated for binge eating disorder, approve Vyvanse.
4. No other exceptions are recommended.

REFERENCES

1. Adderall XR[®] extended-release capsules [prescribing information]. Lexington, MA: Shire US Inc.; July 2019.
2. Concerta[®] extended-release tablets [prescribing information]. Titusville, NJ: McNeil Pediatrics; January 2017.
3. Daytrana[®] transdermal system [prescribing information]. Miami, FL: Noven Pharmaceuticals, Inc.; October 2019.
4. Dexedrine[®] Spansule[®] sustained-release capsule [prescribing information]. Middlesex, NJ: Amedra Pharmaceuticals; May 2017.
5. Focalin XR[®] extended-release capsules [prescribing information]. East Hanover, NJ: Novartis; November 2019.
6. Metadate CD[®] extended-release capsules [prescribing information]. Smyrna, GA: UCB, Inc.; January 2017.
7. Metadate[®] ER extended-release tablet [prescribing information]. Smyrna, GA: Upstate Pharma LLC; January 2017.
8. Methylin[™] tablets and Methylin[™] ER extended-release tablets [prescribing information]. Hazelwood, MO: Mallinckrodt Inc.; January 2017.
9. Ritalin LA[®] extended-release capsules [prescribing information]. East Hanover, NJ: Novartis; November 2019.
10. Ritalin[®] tablets and Ritalin SR[®] sustained-release tablets [prescribing information]. East Hanover, NJ: Novartis; November 2019.
11. Vyvanse[®] capsules [prescribing information]. Wayne, PA: Shire US Inc.; July 2017.
12. Quillivant[™] XR extended-release oral suspension [prescribing information]. Cupertino, CA: NextWave Pharmaceuticals, Inc.; January 2017.
13. Aptensio XR[™] extended-release capsules [prescribing information]. Coventry, RI: Rhodes Pharmaceuticals L.P.; June 2019.
14. QuilliChew ER[™] extended-release chewable tablets [prescribing information]. New York, NY: Pfizer Inc.; March 2017.
15. Dyanavel[™] XR extended-release oral suspension [prescribing information]. Monmouth Junction, NJ: Tris Pharma, Inc.; February 2019.
16. Adzenys XR-ODT[™] extended-release orally disintegrating tablets [prescribing information]. Grand Prairie, TX: Neos Therapeutics, LP; January 2017.
17. Mydayis[™] extended-release capsules [prescribing information]. Lexington, MA: Shire US Inc.; September 2019.

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18. Cotempla XR-ODT™ orally disintegrating tablets [prescribing information]. Grand Prairie, TX: Neos Therapeutics Brands, LLC.; June 2017.
19. Adzenys ER™ extended-release oral solution [prescribing information]. Grand Prairie, TX: Neos Therapeutics Brands, LLC.; September 2017.
20. Jornay PM™ extended-release capsules [prescribing information]. Austin, TX: Ironshore Pharmaceuticals & Development, Inc.; April 2019.
21. Adhansia XR™ extended-release capsules [prescribing information]. Stamford, CT: Adlon Therapeutics L.P.; July 2019.
22. Relexxii® extended-release tablets [prescribing information]. Bridgewater, NJ: Vertical Pharmaceuticals, LLC; November 2019.
23. Wolraich ML, Hagan JF Jr, Allan C, et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2019;144(4):e20192528.
24. Yager J, Devlin MJ, Halmi KA, et al. American Psychiatric Association work group on eating disorders. Treatment of patients with eating disorders, 3rd edition. *Am J Psychiatry*. 2006;163(7 Suppl):4-54. Available at: <http://psychiatryonline.org/guidelines>. Accessed on April 24, 2020.
25. Yager J, Devlin MJ, Halmi KA, et al. Guideline watch (August 2012): practice guideline for the treatment of patients with eating disorders, 3rd edition. Available at: <http://psychiatryonline.org/guidelines>. Accessed on April 24, 2020.