

OVERVIEW

The central nervous system (CNS) stimulant medications in this policy are indicated for the following uses:^{1-24,43,44,48-54}

- **Attention deficit hyperactivity disorder (ADHD)**, treatment. All of the stimulant medications in this policy are indicated for the treatment of ADHD.
- **Binge eating disorder**, treatment. Vyvanse is the only stimulant medication indicated for the treatment of binge eating disorder.
- **Narcolepsy**, treatment. Several methylphenidate and amphetamine-containing products are also indicated for the treatment of narcolepsy.
- **Exogenous obesity**, treatment. Evekeo is indicated as adjunctive therapy for the short-term (i.e., a few weeks) treatment of exogenous obesity.

Dextroamphetamine sulfate tablets, Zenedi, and Adderall (generic) are indicated in patients ≥ 3 years of age; the other products are indicated in patients ≥ 6 years of age, except for Mydayis which is indicated in patients ≥ 13 years of age.^{1,2,6,19,43} Adderall XR (generic), Adzenys ER, Adzenys XR-ODT, Mydayis, Vyvanse, Xelstrym, Concerta (generic), and several methylphenidate products are indicated for use in adults with ADHD.^{2,5,9,24,43,48,54} Jornay PM is the only stimulant taken in the evening.⁴⁹

Other Uses with Supportive Evidence

Idiopathic hypersomnia: A condition similar to narcolepsy, idiopathic hypersomnia is characterized by constant or recurrent daytime sleepiness with no other cause of sleepiness, prolonged nocturnal sleep, difficulty awakening with sleep drunkenness, and long unrefreshing naps with no of cataplexy.²⁹⁻³²

Guidelines

Narcolepsy and other hypersomnias: The practice parameters from the American Academy of Sleep Medicine for the treatment of central disorders of hypersomnolence (2021) state that dextroamphetamine and methylphenidate, in addition to other wakefulness-promoting agents, are effective for treatment of daytime sleepiness due to narcolepsy.²⁵ The parameters also state that methylphenidate, in addition to other agents, may be effective for the treatment of daytime sleepiness due to idiopathic hypersomnia. As there may be underlying causes/behaviors associated with excessive daytime sleepiness, a sleep specialist physician has the training to correctly recognize and diagnose this condition.

Major depressive disorder (MDD): The 2010 American Psychiatric Association practice guidelines for the treatment of patients with MDD state that many clinicians find augmentation of antidepressants with low doses of stimulants such as methylphenidate or dextroamphetamine may help ameliorate otherwise suboptimally responsive depression, although not all clinical trials have shown benefits from this strategy.²⁶ There are no clear guidelines regarding the length of time stimulants should be co-administered. A 16-week randomized, double-blind, placebo-controlled trial in older outpatients with major depression (mean age of 70 years) [n = 143] found that combined treatment with citalopram and methylphenidate demonstrated an enhanced clinical response profile in mood and wellbeing, as well as a higher rate of remission, compared with either drug alone.⁴⁵

Cancer-related fatigue: The National Comprehensive Cancer Network (NCCN) guidelines on cancer-related fatigue (version 2.2022 – February 9, 2022) state to consider use of psychostimulants (i.e., methylphenidate) after other causes of fatigue have been ruled out and/or other management strategies have been attempted.²⁷ The NCCN guidelines on adult cancer pain (version 2.2022 – June 27, 2022) state that sedation may hinder the achievement of dose titration of opioids to levels that provide adequate analgesia.²⁸ If opioid-induced sedation develops and persists for greater than 2 to 3 days, it may be managed by administration of a psychostimulant, such as methylphenidate, dextroamphetamine, modafinil, armodafinil,

or by adding caffeine. A meta-analysis of treatments for fatigue associated with palliative care showed a superior effect for methylphenidate in cancer-related fatigue.⁴⁶ A review of methylphenidate for cancer-related fatigue found a small but significant improvement in fatigue over placebo ($P = 0.005$).⁴⁷

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of ADHD stimulant medications in adults. Only patients ≥ 18 years of age will be required to meet the Prior Authorization criteria below. All approvals are provided for the duration noted below.

Automation: This policy includes an age edit targeting patients ≥ 18 years of age. Therefore, a patient less than 18 years of age will be approved at the point of service. For a patient ≥ 18 years of age, coverage will be determined by Prior Authorization criteria.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of ADHD stimulant medications is recommended in those who meet one of the following criteria:

FDA-Approved Indications

- 1. Attention Deficit Hyperactivity Disorder.** Approve for 1 year.
- 2. Binge Eating Disorder.** Approve only Vyvanse for 1 year if the patient is ≥ 18 years of age.
- 3. Narcolepsy.** Approve for 1 year.

Other Uses with Supportive Evidence

- 4. Depression, Adjunctive/Augmentation Treatment in an Adult.** Approve for 1 year if the patient is concurrently receiving other medication therapy for depression.
Note: Examples of medications for the treatment of depression include selective serotonin reuptake inhibitors.
- 5. Fatigue associated with Cancer and/or its Treatment.** Approve for 1 year.
- 6. Idiopathic Hypersomnolence.** Approve for 1 year if the diagnosis is confirmed by a sleep specialist physician or at an institution that specializes in sleep disorders (i.e., sleep center).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of ADHD stimulant medications is not recommended in the following situations:

- 1. Fatigue Associated with Multiple Sclerosis.** There are no published studies supporting this use. In addition, neither recent review articles nor the 2021 practice parameters for the treatment of narcolepsy and other hypersomnias of central origin mention stimulants (only modafinil). Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin, updated in 2021, state that modafinil may be effective for the treatment of daytime sleepiness due to multiple sclerosis.²⁵ Agents that have been studied for the treatment of fatigue due to multiple sclerosis include amantadine, modafinil, pemoline, aminopyridines, antidepressants, and aspirin.⁴¹



2. **Long-Term Combination Therapy (i.e., > 2 months) with atomoxetine capsules (Strattera, generic) and Central Nervous System (CNS) Stimulants for the treatment of Attention Deficit/Hyperactivity Disorder (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 Strattera and CNS stimulant medications concomitantly.⁴² Short-term drug therapy (≤ 2 months) with both atomoxetine and CNS stimulant medications is allowed for transitioning the patient to only one drug. Guanfacine extended-release tablets (Intuniv[®], generic) and clonidine extended-release tablets (Kapvay[®], generic) 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.^{33,34}
3. **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.³⁵ A 2013 Ethics, Law, and Humanities Committee position paper, endorsed by the American Academy of Neurology indicates that based on available data and the balance of ethics issues, neuroenhancement in legally and developmentally non-autonomous children and adolescents without a diagnosis of a neurologic disorder is not justifiable. In nearly autonomous adolescents, the fiduciary obligation of the physician may be weaker, but the prescription of neuroenhancements is inadvisable due to numerous social, developmental, and professional integrity issues.
4. **Weight Loss.** Of the CNS stimulants, only amphetamine sulfate tablets (e.g., Evekeo tablets) are indicated for exogenous obesity, as a short-term (i.e., a few weeks) adjunct in a regimen of weight reduction based on caloric restriction, for patients in whom obesity is refractory to alternative therapy (e.g., repeated diets, group programs, and other drugs).²⁰ However, guidelines on the management of obesity do not address or recommend use of amphetamine (or any other CNS stimulants).³⁶⁻⁴⁰
5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Adderall[®] immediate-release tablets [prescribing information]. Sellersville, PA: Teva; January 2017.
2. Adderall XR[®] extended-release capsules [prescribing information]. Wayne, PA: Shire; July 2019.
3. Dexedrine[®] Spansule[®] sustained-release capsules [prescribing information]. Hayward, CA: Impax; January 2019.
4. Desoxyn[®] tablets [prescribing information]. Lebanon, NJ: Recordati; March 2019.
5. Vyvanse[®] capsules [prescribing information]. Wayne, PA; Shire; January 2022.
6. Dextroamphetamine sulfate tablets [prescribing information]. St. Louis, MO: Ethex; January 2017.
7. Metadate[®] CD capsules [prescribing information]. Smyrna, GA: Upstate; January 2017.
8. Focalin[®] tablets [prescribing information]. East Hanover, NJ: Novartis; November 2019.
9. Concerta[®] extended-release tablets [prescribing information]. Titusville, NJ: Janssen; January 2017.
10. Methylin[®], Methylin[™] ER tablets [prescribing information]. Hazelwood, MO: Mallinckrodt; January 2017.
11. Methylin[®] tablet, chewable tablets [prescribing information]. Florham Park, NJ: Shionogi; January 2017.
12. Ritalin[®], Ritalin-SR[®] immediate-release and sustained-release tablets [prescribing information]. East Hanover, NJ: Novartis; November 2019.
13. Metadate[®] ER sustained-release tablets [prescribing information]. Philadelphia, PA: Lannett; April 2018.
14. Ritalin[®] LA extended-release capsules [prescribing information]. East Hanover, NJ: Novartis; November 2019.
15. Focalin[®] XR extended-release capsules [prescribing information]. East Hanover, NJ: Novartis; November 2019.
16. Daytrana[®] transdermal system [prescribing information]. Miami, FL: Noven; June 2021.
17. Methylin[®] oral solution [prescribing information]. Florham Park, NJ: Shionogi; January 2017.
18. Quillivant[™] XR extended-release oral suspension [prescribing information]. New York, NY; Pfizer; January 2017.
19. Zenedi[™] tablets [prescribing information]. Atlanta, GA: Arbor; January 2019.
20. Evekeo[™] tablets [prescribing information]. Atlanta, GA: Arbor; April 2019.
21. Aptensio XR[™] extended-release capsules [prescribing information]. Coventry, RI: Rhodes; June 2019.
22. QuilliChew ER[™] extended-release chewable tablets [prescribing information]. New York, NY: Pfizer; March 2017.

23. Dyanavel[®] XR extended-release tablets and oral suspension [prescribing information]. Monmouth Junction, NJ: Tris; November 2021.
24. Adzenys XR-ODT[™] extended-release orally disintegrating tablets [prescribing information]. Grand Prairie, TX: Neos; January 2017.
25. Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2021;17(9):1881-1893.
26. Gelenberg A, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder, third edition. American Psychiatric Association, November 2010. Available at: http://www.psychiatryonline.com/pracGuide/pracGuideTopic_7.aspx. Accessed on July 18, 2022.
27. The NCCN Cancer-Related Fatigue Clinical Practice Guidelines in Oncology (version 2.2022 – February 9, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 18, 2022.
28. The NCCN Adult Cancer Pain Clinical Practice Guidelines in Oncology (version 2.2022 – June 27, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on July 18, 2022.
29. Bassetti C, Aldrich MS. Idiopathic hypersomnia. A series of 42 patients. *Brain*. 1997;120:1423-1435.
30. Billiard M, Merle C, Barlander B, et al. Idiopathic hypersomnia. *Psychiatry Clin Neurosci*. 1998;52(2):125-129.
31. Bastuji H, Jouvet M. Successful treatment of idiopathic hypersomnia and narcolepsy with modafinil. *Prog Neuropsychopharmacol Biol Psychiatry*. 1988;12(5):695-700.
32. Laffont F, Mayer G, Minz M. Modafinil in diurnal sleepiness. A study of 123 patients. *Sleep*. 1994;17:S113-S115.
33. Intuniv[®] extended-release tablets [prescribing information]. Wayne, PA: Shire; December 2019.
34. Kapvay[®] extended-release tablets, oral [prescribing information]. Overland Park, KS: Concordia; February 2020.
35. Graf WD, Nagel SK, Epstein LG, et al. Pediatric neuroenhancement: ethical, legal, social, and neurodevelopmental implications. *Neurology*. 2013;80:1251-1260.
36. Snow V, Barry P, Fitterman N, et al; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Pharmacologic and surgical management of obesity in primary care: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2005;142:525-531. Available at: <http://annals.org/article.aspx?articleid=718309>. Accessed on July 18, 2022.
37. Moyer VA, on behalf of the U.S. Preventive Services Task Force. Screening for and management of obesity in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2012;157:373-378. Available at: <http://annals.org/article.aspx?articleid=1355696>. Accessed on July 18, 2022.
38. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association task force on practice guidelines and the Obesity Society. *J Am Coll Cardiol*. 2014; 63(25 pt B): 2985-3023.
39. 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 July 18, 2022.
40. 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 July 18, 2022.
41. Amato MP, Portaccio E. Management options in multiple sclerosis-associated fatigue. *Expert Opin Pharmacother*. 2012;13:207-216.
42. Treuer T, Gau SS-F, Mendez L, et al. A systematic review of combination therapy with stimulants and atomoxetine for attention-deficit/hyperactivity disorder, including patient characteristics, treatment strategies, effectiveness, and tolerability. *J Child Adolesc Psychopharmacol*. 2013;23(3):179-193.
43. Mydayis[™] extended-release capsules [prescribing information]. Lexington, MA: Shire; September 2019.
44. Cotempla XR-ODT[™] orally disintegrating tablets [prescribing information]. Grand Prairie, TX: Neos; June 2017.
45. Lavretsky H, Reinlieb M, St Cyr N, et al. Citalopram, methylphenidate, or their combination in geriatric depression: a randomized, double-blind, placebo-controlled trial. *Am J Psychiatry*. 2015;172(6):561-569.
46. Mücke M; Mochamat, Cuhls H, et al. Pharmacological treatments for fatigue associated with palliative care. *Cochrane Database Syst Rev*. 2015;(5):CD006788.
47. Minton O, Richardson A, Sharpe M, et al. Drug therapy for the management of cancer-related fatigue. *Cochrane Database Syst Rev*. 2010;(7):CD006704.
48. Adzenys ER[™] extended-release oral solution [prescribing information]. Grand Prairie, TX: Neos; September 2017.
49. Jornay PM[®] extended-release capsules [prescribing information]. Austin, TX: Ironshore; April 2019.
50. Adhansia XR[®] extended-release capsules [prescribing information]. Stamford, CT: Adlon; July 2019.
51. Evekeo ODT[®] orally disintegrating tablet [prescribing information]. Atlanta, GA: Arbor; April 2021.
52. Relexxii[®] extended-release tablets [prescribing information]. Alpharetta, GA: Vertical; June 2022.
53. Azstarys[™] capsules [prescribing information]. Grand Rapids, MI: Corium; March 2021.
54. Xelstrym[™] transdermal system [prescribing information]. Miami, FL: Noven; March 2022.