Clinical Policy: CNS Stimulants

Reference Number: CP.PMN.92
Effective Date: 03.01.18
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are central nervous system (CNS) stimulants requiring prior authorization: methylphenidate extended-release (Adhansia XR™, Aptensio XR™, Jornay PM™), methylphenidate transdermal system (Daytrana®), methylphenidate extended-release chewable tablets (Quillichew ER®), methylphenidate extended-release oral suspension (Quillivant XR®), methylphenidate extended-release orally disintegrating tablets (Cotempla XR-ODT®), amphetamine orally disintegrating tablets (Evekeo ODT™), amphetamine extended-release orally disintegrating tablets (Adzenys XR-ODT™), amphetamine extended-release oral suspension (Adzenys ER™, Dyanavel XR®), amphetamine-dextroamphetamine extended-release (Mydayis®), dexmethylphenidate hydrochloride (Focalin XR®), dextroamphetamine patches (Xelstrym™), and serdexmethylphenidate –dexmethylphenidate capsules (Azstarys™).

FDA Approved Indication(s)

Extended release methylphenidate and amphetamine products are indicated for attention-deficit/hyperactivity disorder (ADHD).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Adhansia XR, Adzenys ER, Adzenys XR-ODT, Aptensio XR, Azstarys, Cotempla XR-ODT, Daytrana, Dyanavel XR, Evekeo ODT, Focalin XR, Jornay PM, Mydayis, Quillichew ER, Quillivant XR, and Xelstrym are medically **necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Attention Deficit Hyperactivity Disorder (must meet all)**:**

1. Diagnosis of ADHD;
2. One of the following (a, b, or c):
   a. Evekeo ODT: Age ≥ 3 years;
   b. Mydayis: Age ≥ 13 years;
   c. All other requests: Age ≥ 6 years;
3. Member meets one of the following (a or b):
   a. Failure of two formulary extended release products at maximally indicated doses from the same therapeutic class of the requested product (i.e., amphetamine or methylphenidate), unless clinically significant adverse effects are experienced or all are contraindicated;

b. Request is for Adzenys ER, Adzenys XR-ODT, Cotempla XR-ODT, Daytrana, Dyanavel XR, Evekeo ODT, Quillichew ER, Quillivant XR, or Xelstrym, and documentation supports inability to use dosage forms available on the formulary (e.g., inability to swallow tablets or capsules);

4. Dose does not exceed the following:
   a. Adhansia XR: 85 mg per day (1 tablet per day);
   b. Adzenys ER: 15 mL per day;
   c. Adzenys XR-ODT: 12.5-18.8 mg per day (1 tablet per day);
   d. Azstarys: 52.3 mg/10.4 mg per day;
   e. Cotempla XR-ODT: 51.8 mg per day (2 tablets per day);
   f. Daytrana: 30 mg per day (1 patch per day);
   g. Dyanavel XR: 20 mg per day;
   h. Evekeo ODT: 40 mg per day (2 tablets per day);
   i. Focalin XR: 30 mg per day (pediatric patients), 40 mg per day (adults);
   j. Jornay PM: 100 mg per day (1 tablet per day);
   k. Mydayis: 50 mg per day;
   l. Quillichew ER, Quillivant XR, Aptensio XR: 60 mg per day (1 tablet or capsule per day);
   m. Xelstrym: 18 mg per day (1 patch per day).

Approval duration:
Medicaid/HIM: 12 months
Commercial: 12 months or duration of request, whichever is less

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Attention Deficit Hyperactivity Disorder (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the following:
   a. Adhansia XR: 85 mg per day (1 tablet per day);
   b. Adzenys ER: 15 mL per day;
   c. Adzenys XR-ODT: 12.5-18.8 mg per day (1 tablet per day);
   d. Azstarys: 52.3 mg/10.4 mg per day;
   e. Cotempla XR-ODT: 51.8 mg per day (2 tablets per day);
   f. Daytrana: 30 mg per day (1 patch per day);
   g. Dyanavel XR: 20 mg per day;
   h. Evekeo ODT: 40 mg per day (2 tablets per day);
   i. Focalin XR: 30 mg per day (pediatric patients), 40 mg per day (adults);
   j. Jornay PM: 100 mg per day (1 tablet per day);
   k. Mydayis: 50 mg per day;

l. Quillichew ER, Quillivant XR, Aptensio XR: 60 mg per day (1 tablet or capsule per day);
m. Xelstrym: 18 mg per day (1 patch per day).

Approval duration:
Medicaid/HIM: 12 months
Commercial: 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ADHD: attention-deficit and hyperactivity disorder
CNS: central nervous system
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
methylphenidate extended release (Ritalin LA®, Concerta®, Metadate CD®)	Concerta: 18 - 36 mg PO QD Ritalin LA, Metadate CD: 20 mg PO QD	Concerta: 72 mg/day Ritalin LA, Metadate CD: 60 mg/day
amphetamine (Adderall XR®)	Patients 6-17 years: 10 mg PO QD Adults: 20 mg PO QD	30 mg/day
dextroamphetamine (Dexedrine SR®)	5 mg PO QD/BID	60 mg/day
Vyvanse® (lisdexamfetamine)	30 mg PO QD	70 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity; use with monoamine oxidase (MAO) inhibitor, or within 14 days of last MAO inhibitor dose
  - Azstarys: Known hypersensitivity to serdexmethylphenidate, methylphenidate, or product components
  - Daytrana: marked anxiety, tension, or agitation; glaucoma; tics or family history of Tourette's syndrome
- Boxed warning(s): abuse and dependence

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Adhansia XR (methylphenidate extended-release capsule)	25 mg PO QD	6 to 17 years: 70 mg Adults: 85 mg
Adzenys ER (amphetamine ER oral suspension)	Patients 6 to 17 years: 6.3 mg PO QD Adults: 12.5 mg PO QD	6 to 12 years: 15 ml/day 13 year and older: 10 ml/day
Adzenys XR-ODT (amphetamine ER orally disintegrating tablet)	Patients 6 to 17 years: 6.3 mg PO QD Adults: 12.5 mg PO QD	6 to 12 years: 18.8 mg/day 13 to 17 years: 12.5 mg/day
Azstarys (serdexmethylphenidate-dexmethylphenidate capsule)	Patients 6 to 12 years: 39.2 mg/7.8 mg PO in the morning. Dosage may be increased to 52.3 mg/10.4 mg daily or decreased to 26.1 mg/5.2 mg daily after one week Adults and pediatric patients 13-17 years: 39.2 mg/7.8 mg PO in the morning. Increase the dosage after one week to 52.3 mg/10.4 mg once daily	52.3 mg/10.4 mg/day
Evekeo ODT (amphetamine orally disintegrating tablet)	Patients age 3 to 5 years: 2.5 mg PO QD. Titrate dosage in increments of 2.5 mg at weekly intervals. Patients 6 to 17 years: 5 mg PO QD or BID. Titrate daily dose in increments of 2.5 or 5 mg at weekly intervals.	40 mg/day
Methylphenidate ER (Adhansia XR)	Patients 6 and older: 25 mg PO QD. Dose may be increased in increments of 10 to 15 mg at intervals of at least 5 days.	85 mg/day
Methylphenidate ER (Aptensio XR)	10 mg PO QD	60 mg/day

Drug Name	Dosing Regimen	Maximum Dose
Methylphenidate ER (Jornay PM)	Starting dose 20 mg PO QHS, dose may be increased weekly in increments of 20 mg/day	100 mg/day
Cotempla XR-ODT (methylphenidate ER orally disintegrating tablet)	Patients 6 to 17 years: 17.3 mg PO QD	51.8 mg/day
Dexmethylphenidate (Focalin XR)	Pediatric patients: 5 mg PO QD, dose may be titrated weekly in increments of 5 mg Adult patients: 10 mg PO QD, dose may be titrated weekly in increments of 10 mg	Pediatric: 30 mg per day Adults: 40 mg per day
Methylphenidate Transdermal System (Daytrana)	10 mg applied to the hip area (using alternating sites) 2 hours before an effect is needed and should be removed 9 hours after application	30 mg/9-hour patch per day
Dyanavel XR (amphetamine oral suspension/tablet)	2.5 - 5 mg PO QD	20 mg/day
amphetamine-dextroamphetamine extended-release (Mydayis)	12.5 mg PO QD	Adults: 50 mg/day Pediatrics (13 to 17 years): 25 mg/day
Quillichew ER (methylphenidate chewable tablet)	20 mg PO QD	60 mg/day
Quillivant XR (methylphenidate oral suspension)	20 mg PO QD	60 mg/day
Xelstrym (dextroamphetamine transdermal patch)	• Patients 6-17 years: Recommended starting dose is 4.5 mg/9 hours, dose may be titrated in weekly increments of 4.5 mg • Adults: Recommended starting dose is 9 mg/9 hours Apply one patch at a time for not more than 9 hours. Use only one patch per 24 hours.	18 mg/9-hour patch per day

VI. Product Availability

Drug Name	Availability
Adhansia XR (methylphenidate)	Extended-release capsules: 25 mg, 35 mg, 45 mg, 55 mg, 70 mg, 85 mg
Adzenys ER (amphetamine)	Extended-release oral suspension: 1.25 mg/mL
Adzenys XR-ODT (amphetamine)	Extended-release orally disintegrating tablets: 3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg, 18.8 mg

Drug Name	Availability
Azstarys (serdexmethylphenidate-dexmethylphenidate capsule)	Capsules: 26.1 mg/5.2 mg, 39.2 mg/7.8 mg, 52.3 mg/10.4 mg
Evekeo ODT (amphetamine orally disintegrating tablet)	Orally disintegrating tablets: 5 mg, 10 mg, 15 mg, 20 mg
Methylphenidate ER (Adhansia XR)	Extended-release capsules: 25 mg, 35 mg, 45 mg, 55 mg, 70 mg, 85 mg
Methylphenidate ER (Aptensio XR)	Extended-release capsules: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg
Methylphenidate ER (Jornay PM)	Extended-release capsules: 20 mg, 40 mg, 60 mg, 80 mg, 100 mg
Cotempla XR-ODT (methylphenidate ER orally disintegrating tablet)	Extended-release orally disintegrating tablets: 8.6 mg, 17.3 mg, 25.9 mg
Dexmethylphenidate (Focalin XR)	Extended-release capsules: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg
Methylphenidate Transdermal System (Daytrana)	Transdermal patch: 10 mg/9 hours, 15 mg/9 hours, 20 mg/9 hours, and 30 mg/9 hours
Dyanavel XR (amphetamine)	Extended-release oral suspension: 2.5 mg/mL Extended-release tablets: 5 mg, 10 mg, 15 mg, 20 mg
amphetamine-dextroamphetamine extended-release (Mydayis)	Extended-release capsules: 12.5 mg, 25 mg, 37.5 mg, 50 mg
Quillichew ER (methylphenidate chewable)	Extended-release chewable tablets, scored: 20 mg, 30 mg Extended-release chewable tablets, not scored: 40 mg
Quillivant XR (methylphenidate oral suspension)	Extended-release oral suspension: 25 mg/5 mL (5 mg/mL)
Xelstrym (dextroamphetamine)	Transdermal patch: 4.5 mg/9 hours, 9 mg/9 hours, 13.5 mg/9 hours, 18 mg/9 hours

VII. References

1. Adhansia XR Prescribing Information. Wilson, NC: Purdue Pharmaceuticals; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212038s002lbl.pdf . Accessed September 27, 2021September 27, 2021.
2. Adzenys ER Prescribing Information. Grand Prairie, TX: Neos Therapeutics; September 2017. Accessed September 27, 2021.
3. Adzenys XR-ODT Prescribing Information. Grand Prairie, TX: Neos Therapeutics. December 2017. Available at: https://www.adzenysxrodt.com/. September 27, 2021.
4. Aptensio XR Prescribing Information. Greenville, NC: Rhodes Pharmaceuticals: June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/205831s006lbl.pdf. Accessed September 27, 2021

5. Azstarys Prescribing Information. North Liberty, IA: KemPharm, Inc.; March 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212994s000lbl.pdf. Accessed September 27, 2021.
6. Cotempla XR-ODT Prescribing Information. Grand Prairie, TX: Neos Therapeutics; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/205489s007lbl.pdf. Accessed September 27, 2021.
7. Daytrana Prescribing Information. Miami, FL: Noven Therapeutics, LLC; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021514s032lbl.pdf. Accessed September 27, 2021.
8. Dyanavel XR Prescribing Information. Monmouth Junction, NJ: Tris Pharma: November 2021. Available at http://dyanavelxr.com/. Accessed December 6, 2021.
9. Evekeo ODT Prescribing Information. Atlanta, GA: Abor Pharmaceuticals, LLC; April 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/209905Orig1s001lbl.pdf. Accessed April 29, 2021.
10. Focalin XR Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021802s039lbl.pdf. Accessed September 27, 2021.
11. Jornay PM Prescribing Information. Cherry Hill, NJ: Ironshore Pharmaceuticals, Inc.; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/209311s008lbl.pdf. Accessed September 27, 2021.
12. Mydayis Prescribing Information. Lexington, MA: Shire US Inc.; September 2019. Available at https://www.mydayis.com/. Accessed September 27, 2021.
13. Quillichew ER Prescribing Information. Monmouth Junction, NJ: Tris Pharma. June 2021. Available at https://www.quillivantxr-quillichewer.com/. Accessed September 27, 2021.
14. Quillivant XR Prescribing Information. Monmouth Junction, NJ: Tris Pharma; June 2021. Available at: https://www.quillivantxr-quillichewer.com/. Accessed September 27, 2021.
15. Xelstrym Prescribing Information. Miami, FL: Noven Pharmaceuticals; March 2022. Available at: https://www.noven.com/wp-content/uploads/2020/02/Xelstrym-Final-FDA-Approved-Label-03222022.pdf. Accessed April 6, 2022.
16. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with Attention-Deficit/Hyperactivity Disorder. J Am Acad Child Adolesc Psychiatry. 2007; 46(7):894-921.
17. Wolraich ML, Hagan JF, 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created	11.14.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
- Policies created from existing Centene Medicaid and Commercial lines of business policies for CNS Stimulants - No significant changes from previous corporate approved policy - Age requirement is new for the Centene Commercial and changed requirement from failure of 2 methylphenidate products to failure of 1 methylphenidate and 1 amphetamine. - References reviewed and updated.		
Added Cotempla XR-ODT and Mydayis to policy	02.13.18	
Medicaid: Revised approval duration to length of benefit	03.08.18	05.18
Per SDC: added Adzenys ER to policy	06.14.18	
1Q 2019 annual review: removed 2 week trial duration requirement for alternatives as effects from amphetamine and methylphenidate are expected to be immediate; added Focalin XR to policy; references reviewed and updated.	10.10.18	02.19
No significant changes; added Adhansia XR to policy.	03.07.19	
Added Jornay PM to policy per SDC and prior clinical guidance.	10.01.19	
1Q 2020 annual review: added HIM line of business as Daytrana requires PA on HIM (all other agents are either generic on formulary (Focalin XR) or NF for HIM); references reviewed and updated. Added Evekeo ODT to policy per SDC and prior clinical guidance.	12.02.19	02.20
1Q 2021 annual review: no significant changes; changed auth duration for Medicaid to 12 months from Length of Benefit to align with customary auth duration for the Medicaid line of business; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	12.01.20	02.21
RT4: Added new agent Azstarys to policy.	03.25.21	
Revised redirection from failure of 1 methylphenidate and 1 amphetamine product to failure of 2 from the same therapeutic class; RT4: for Evekeo ODT added pediatric extension to 3 years of age and 2.5 mg strength per updated prescribing information; for Mydayis added age requirement for 13 years or older per label.	04.29.21	08.21
1Q 2022 annual review: RT4: for Dyanavel XR added new tablet dose form to policy; modified Commercial approval duration from length of benefit to 12 months or duration of request, whichever is less; references reviewed and updated.	09.27.21	02.22
RT4: added new agent Xelstrym to policy.	04.06.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical

policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.