Clinical Policy: Centanafadine (Simtriyo)

Reference Number: CP.PMN.312
Effective Date: 12.01.26
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

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

Description

Centanafadine (Simtriyo®) is a norepinephrine-dopamine-serotonin reuptake inhibitor and central nervous system stimulant.

FDA Approved Indication(s)

Simtriyo is indicated for the treatment of attention-deficit/hyperactivity disorder (ADHD) in adults and pediatric patients 6 years of age and older weighing at least 20 kg.

Limitation(s) of use: The use of Simtriyo is not recommended in pediatric patients:

- Younger than 6 years of age because this pediatric subpopulation had a higher incidence of weight loss than pediatric patients 6 years of age and older
- Weighing less than 20 kg because of a lack of data for this subpopulation and the risk of weight loss

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 Simtriyo is **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. Age ≥ 6 years;
3. Both of the following (a and b):
   a. Documentation of current weight in kg;
   b. Weight ≥ 20 kg;
4. Member meets one of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   a. Failure of atomoxetine at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Documentation supports inability to swallow capsules;
5. Member meets both of the following (a and b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*

a. Failure of an amphetamine-based stimulant at up to maximally indicated doses, unless clinically significant adverse effects are experienced to any amphetamine product or all are contraindicated;
b. Failure of a methylphenidate-based stimulant at up to maximally indicated doses, unless clinically significant adverse effects are experienced to any methylphenidate product or all are contraindicated;

6. Dose does not exceed one of the following (a or b):
   a. For pediatric members age 6 to 12 years, both of the following (i and ii):
      i. One of the following (1, 2, or 3):
         1) Weight 20 kg to < 35 kg: 140 mg per day;
         2) Weight 35 kg to 50 kg: 210 mg per day;
         3) Weight > 50 kg: 280 mg per day;
      ii. 1 capsule per day;
   b. For adults and pediatric members aged 13 to 17 years, both of the following (i and ii):
      i. 280 mg per day;
      ii. 1 capsule per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;

3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. For pediatric members age 6 to 12 years, both of the following (i and ii):
      i. One of the following (1, 2, or 3):
         1) Weight 20 kg to < 35 kg: 140 mg per day;
         2) Weight 35 kg to 50 kg: 210 mg per day;
         3) Weight > 50 kg: 280 mg per day;
      ii. 1 capsule per day;
   b. For adults and pediatric members aged 13 to 17 years, both of the following (i and ii):
      i. 280 mg per day;
      ii. 1 capsule per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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/ICHRA, 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
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
atomoxetine (Strattera®)	≤ 70 kg: 1.2 mg/kg/day PO > 70 kg: 80 mg/day PO	≤ 70 kg: 1.4 mg/kg/day > 70 kg: 100 mg/day
Short-Acting Amphetamines		
Evekeo® (amphetamine)	Refer to prescribing information	60 mg/day
amphetamine/dextroamphetamine salts (Adderall®)		60 mg/day
dextroamphetamine (Dexedrine®, Procentra®, Zenzedi®)		40 mg/day
methamphetamine (Desoxyn®)		25 mg/day
Long-Acting Amphetamines		
Adzenys XR ODT™ (amphetamine ER)	Refer to prescribing information	6 to 12 years: 18.8 mg/day 13 to 17 years, Adults: 12.5 mg/day
Dyanavel® XR (amphetamine ER)		20 mg/day
amphetamine/ dextroamphetamine salts ER (Adderall® XR)		20 mg/day (20-30 mg/day if ≥ 6 years)
dextroamphetamine ER (Dexedrine Spansule®)		40 mg/day
Short-Acting Methylphenidates		
dexmethylphenidate (Focalin®)	Refer to prescribing information	20 mg/day
methylphenidate (Methylin®, Ritalin®)		60 mg/day
Long-Acting Methylphenidates		
dexmethylphenidate ER (Focalin XR®)	Refer to prescribing information	40 mg/day (30 mg/day if 6-17 years)
methylphenidate ER (Aptensio XR™, Metadate CD®, QuilliChew ER®, Quillivant XR®, Ritalin LA®)		60 mg/day
methylphenidate ER (Concerta®)		72 mg/day
Daytrana® (methylphenidate transdermal)		One 30 mg/9-hour patch/day
Cotempla XR-ODT® (methylphenidate ER)		51.8 mg/day
Adhansia XR® (methylphenidate)		6 to 17 years: 70 mg Adults: 85 mg

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):
  - Known hypersensitivity to centanafadine or any of the excipients of Simtriyo
  - Taking or within 14 days of stopping a monoamine oxidase inhibitor
  - Pheochromocytoma or a history of pheochromocytoma
- Boxed warning(s):
  - Suicidal ideation and behaviors in pediatric patients aged ≥ 6 years
  - Abuse, misuse and addiction

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ADHD	Age 6 to 12 years by body weight: • 20 kg to < 35 kg: 140 mg PO QD • 35 kg to 50 kg: 210 mg PO QD • > 50 kg: 280 mg PO QD Age 13 to 17 years: 280 mg PO QD Adults: Starting dose of 210 mg PO QD. May be increased to the maximum recommended dosage of 280 mg PO QD based on clinical response and tolerability Capsules may be swallowed whole or opened and entire contents sprinkled on applesauce or yogurt, or in orange juice	Pediatric members age ≤ 12 years: see Dosing Regimen Adults and pediatric members age ≥ 13 years: 280 mg/day

VI. Product Availability

Extended-release capsules: 140 mg, 210 mg, 280 mg

VII. References

1. Simtriyo Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc.; July 2026. Available at: https://otsuka-us.com/media/static/Simtriyo-PI.pdf. Accessed July 29, 2026.
2. Ward CL, Childress AC, Jin N, Turkoglu O, Skubiak T, Wilens TE. Centanafadine for attention-deficit/hyperactivity disorder in adolescents: a randomized clinical trial. J Am Acad Child Adolesc Psychiatry. 2026;65(6):805-817.
3. Adler LA, Adams J, Madera-McDonough J, et al. Efficacy, safety, and tolerability of centanafadine sustained-release tablets in adults with attention-deficit/hyperactivity disorder: results of 2 phase 3, randomized, double-blind, multicenter, placebo-controlled trials. J Clin Psychopharmacol. 2022;42(5):429-439.
4. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier, Inc. Updated periodically. Available at: http://www.clinicalkey.com/pharmacology. Accessed July 29, 2026.

5. Wolraich LM, Hagan Jr 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
Policy created	07.29.26	11.26

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.

©2026 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.