

Clinical Policy: SSRI/SNRI Duplicate Therapy

Reference Number: CP.PMN.60

Effective Date: 05.01.14

Last Review Date: 08.25

Line of Business: Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Due to similarities in mechanism of action, concurrent use of selective serotonin reuptake inhibitor (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) may lead to additive adverse effects, including serotonin syndrome. Serotonin syndrome is characterized by rapid development of hyperthermia, hypertension, myoclonus, rigidity, autonomic instability, mental status changes (e.g., delirium or coma), and in rare cases, death. In its most severe form, serotonin syndrome can resemble neuroleptic malignant syndrome.

FDA Approved Indication(s)

Many SSRIs and SNRIs are indicated for the treatment of depression. Refer to each product's prescribing information for specific indications.

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 therapeutic duplication of SSRIs and SNRIs is **not medically necessary**.

There are currently no controlled clinical studies to support the use of two SSRIs or the concomitant use of an SSRI and SNRI; members are therefore restricted to the use of only 1 SSRI or 1 SNRI at a time.

I. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

SNRI: serotonin-norepinephrine reuptake inhibitor

SSRI: selective serotonin reuptake inhibitor

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

Refer to each product's prescribing information.

II. References

1. Clinical Pharmacology [database online]. Tampa, FL: Elsevier, Inc.; 2025. URL: <https://www.clinicalkey.com/pharmacology/>. Accessed May 8, 2025.

2. Merative™ Micromedex® Alternative Medicine [Internet database]. Merative, Ann Arbor, Michigan, USA. Available at: <https://www.micromedexsolutions.com>. Accessed May 8, 2025.
3. McQuaid JR, Lin EH, Barber JP, et al. Clinical Practice Guideline for the Treatment of Depression across Three Age Cohorts. American Psychological Association, Adopted as APA Policy Feb. 16, 2019. Available at: <https://www.apa.org/depression-guideline/guideline.pdf>. Accessed May 8, 2025.
4. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder. Third edition. American Psychiatric Association. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed May 8, 2025.
5. Qaseem A, Owens DK, Etzeandia-Ikobaltzeta I, et al. Nonpharmacologic and pharmacologic treatments of adults in the acute phase of major depressive disorder: a living clinical guideline from the American College of Physicians. *Ann Intern Med*. 2023 Feb;176(2):239-252. doi: 10.7326/M22-2056.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: no significant changes; references reviewed and updated.	04.29.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.12.22	08.22
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.27.23	08.23
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.09.24	08.24
3Q 2025 annual review: no significant changes; references reviewed and updated.	05.08.25	08.25

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.

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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.

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