Clinical Policy: Dextromethorphan/Quinidine (Nuedexta)

Reference Number: PA.CP.PMN.93
Effective Date: 12/2017
Last Review Date: 01/2026

Description

Dextromethorphan and quinidine (Nuedexta®) are a fixed-dose combination of dextromethorphan hydrobromide, an N-methyl-D-aspartate (NMDA) receptor antagonist and sigma-1 agonist, and quinidine sulfate, a CYP450 2D6 inhibitor.

FDA Approved Indication(s)

Nuedexta is indicated for the treatment of pseudobulbar affect (PBA).

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of PA Health & Wellness that Nuedexta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pseudobulbar Affect (must meet all)**:**

1. Diagnosis of PBA;
2. Prescribed by or in consultation with a neurologist, neuropsychologist, or psychiatrist;
3. Age ≥ 18 years;
4. Baseline Center for Neurologic Study-Lability Scale (CNS-LS) score ≥ 13 (*see Appendix D*);
5. Dose does not exceed 40 mg dextromethorphan and 20 mg quinidine per day (2 capsules per day).

Approval duration: 12 weeks

B. Other diagnoses/indications

1. Refer to PA.CP.PMN.53.

II. Continued Therapy

A. Pseudobulbar Affect (must meet all)**:**

1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, a decreased frequency of PBA episodes or a decrease in the CNS-LS score of ≥ 3 points from baseline (*see Appendix D*);
3. If request is for a dose increase, new dose does not exceed 40 mg dextromethorphan and 20 mg quinidine (2 capsules) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies; **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to PA.CP.PMN.53.

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 policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALS: amyotrophic lateral sclerosis
FDA: Food and Drug Administration
MS: multiple sclerosis
NMDA: N-methyl-D-aspartate
PBA: pseudobulbar affect

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): concomitant use with quinidine, quinine, or mefloquine; history of quinidine, quinine or mefloquine-induced thrombocytopenia, hepatitis, or other hypersensitivity reactions; known hypersensitivity to dextromethorphan; use with an MAOI or within 14 days of stopping an MAOI; prolonged QT interval, congenital long QT syndrome, history suggestive of torsades de pointes, or heart failure; complete atrioventricular (AV) block without implanted pacemaker, or patients at high risk of complete AV block; concomitant use with drugs that both prolong QT interval and are metabolized by CYP2D6 (e.g., thioridazine or pimozide).
- Boxed warning(s): none reported.

Appendix D: General Information

- Nuedexta was studied in 367 patients with PBA secondary to dementia, stroke, or traumatic brain injury. Although use of Nuedexta resulted in statistically significant improvement from baseline in CNS-LS scores, applicability of this data in clinical practice is limited as the study was open-label and not compared to placebo[7].
- There is one randomized, double-blind, placebo-controlled phase 2 trial[8] evaluating the use of Nuedexta in 220 patients with aggression or agitation secondary to Alzheimer's disease over 10 weeks. Nuedexta showed that the treatment difference in Neuropsychiatric Inventory (NPI) Agitation/Aggressive scores was -1.8 (95% CI, -2.8 to -0.7, p = 0.003) compared to placebo. Although this outcome was statistically significant, it did not meet the prespecified difference of 2.5 points. Also, unlike the total NPI score, use of the single NPI domain of agitation/aggression is not well validated as an endpoint. Additional long-term data is needed to confirm evidence of benefit and safety.
- The CNS-LS is a short (seven-item), self-administered questionnaire, designed to be completed by the patient, that provides a quantitative measure of the perceived frequency

of PBA episodes. Each question is scored from 1 (applies never) to 5 (applies most of the time). A CNS-LS score of 13 or higher may suggest PBA. A complete list of included questions is available at: https://www.nuedextahcp.com/documents/CNS-LS-English.pdf

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pseudobulbar affect (PBA)	1 capsule PO QD for the initial 7 days, then 1 capsule PO BID for maintenance	Dextromethorphan 40 mg/quinidine 20 mg/day

VI. Product Availability

Capsules: dextromethorphan hydrobromide 20 mg and quinidine sulfate 10 mg

VII. References

1. Nuedexta Prescribing Information. Aliso Viejo, CA: Avanir Pharmaceuticals, Inc.: December 2022. Available at: https://www.nuedextahcp.com/. Accessed October 23, 2025.
2. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review). American Academy of Neurology. 2009;73:1227-1233.
3. Minden SL, Feinstein A, Kalb RC, et al. Evidence-based guideline: assessment and management of psychiatric disorders in individuals with MS. American Academy of Neurology. 2014;82:174-181.
4. Pioro EP, Brooks BR, Cummings J, et al. Dextromethorphan plus ultra low-dose quinidine reduces pseudobulbar affect. Ann Neurol. November 2010; 68(5):693-702.
5. Brooks BR, Thisted RA, Appel SH, et al. Treatment of pseudobulbar affect in ALS with dextromethorphan/quinidine: a randomized trial. Neurology. October 26, 2004; 63(8):1364-1370.
6. Panitch HS, Thisted RA, Smith RA, et al. Randomized, controlled trial of dextromethorphan/quinidine for pseudobulbar affect in multiple sclerosis. Ann Neurol. May 2006; 59:780-787.
7. Hammond FM, Alexander DN, Cutler AJ, et al. PRISM II: an open-label study to assess effectiveness of dextromethorphan/quinidine for pseudobulbar affect in patients with dementia, stroke, or traumatic brain injury. BMC Neurology. 2016; 16:89. doi: 10.1186/s12883-016-0609-0.
8. Cummings JL, Lyketsos CG, Peskind ER, et al. Effect of dextromethorphan-quinidine on agitation in patients with Alzheimer disease dementia: a randomized clinical trial. JAMA. 2015;314(12):1242-1254.
9. Hammong FM, Sauve W, Ledon F, et. al. Safety, Tolerability, and Effectiveness of Dextromethorphan/Quinidine for Pseudobulbar Affect Among Study Participants With Traumatic Brain Injury: Results From the PRISM-II Open Label Study. PM&R 2018 Oct;10(10):993-1003.

Reviews, Revisions, and Approvals	Date
1Q 2019 annual review: references reviewed and updated.	01/2019

Reviews, Revisions, and Approvals	Date
1Q 2020 annual review: addition of Age ≥ 18 years for treatment; references reviewed and updated.	01/2020
1Q 2021 annual review: no significant changes; references reviewed and updated.	01/2021
1Q 2022 annual review: references reviewed and updated.	01/2022
1Q 2023 annual review: for continuation of therapy request, added the following as an option to identify positive response: decreased frequency of PBA episodes; references reviewed and updated.	01/2023
1Q 2024 annual review: added neuropsychologist and psychiatrist as optional specialist prescribers; in Appendix C updated link to CNS-LS questionnaire; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; corrected reference to Appendix D for additional information on CNS-LS questionnaire; references reviewed and updated.	01/2025
1Q 2026 annual review: no significant changes; references reviewed and updated.	01/2026