Clinical Policy: Dextromethorphan-Quinidine (Nuedexta)

Reference Number: CP.PMN.93
Effective Date: 12.05.17
Last Review Date: 02.21
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Dextromethorphan and quinidine (Nuedexta®) is 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 (including 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 Nuedexta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of PBA secondary to multiple sclerosis or amyotrophic lateral sclerosis;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Baseline Center for Neurologic Study-Lability Scale (CNS-LS) score ≥ 13;
5. Dose does not exceed 40 mg dextromethorphan and 20 mg quinidine (2 capsules) per day.

Approval duration: 12 weeks

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. Pseudobulbar Affect (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 as evidenced by a decrease in the CNS-LS score of ≥ 3 points from baseline;

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 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

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 C: 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.
- There is one randomized, double-blind, placebo-controlled phase 2 trial 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/sites/default/files/pdf/CNS_LS_Questionnaire.pdf

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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 combined with quinidine sulfate 10 mg

VII. References

1. Nuedexta Prescribing Information. Aliso Viejo, CA: Avanir Pharmaceuticals, Inc.: June 2019. Available at: www.nuedexta.com. Accessed November 12, 2020.
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	P&T Approval Date
Policy created	12.05.17	02.18
Removed HIM line of business (currently on formulary without prior authorization for 2018)	06.14.18	
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.06.18	02.19
No significant changes; added HIM line of business.	02.01.19	
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.26.19	02.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.12.20	02.21

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.