Clinical Policy: Dextromethorphan/Quinidine (Nuedexta)

Reference Number: PA.CP.PMN.93
Effective Date: 12.05.17
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Revision Log

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 health plans affiliated with 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;
3. Baseline Center for Neurologic Study-Lability Scale (CNS-LS) score ≥ 13;
4. Dose does not exceed 40 mg dextromethorphan and 20 mg quinidine per day (2 capsules/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.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy, as evidenced by decrease in CNS-LS score by 3 points or greater from baseline;
3. If request is for a dose increase, new dose does not exceed 40 mg dextromethorphan and 20 mg quinidine per day (2 capsules/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.LTSS.PHAR.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
PBA: pseudobulbar affect

Appendix B: Therapeutic Alternatives

Not applicable

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[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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pseudobulbar affect	1 capsule PO QD for the initial 7 days, then 1 capsule PO BID for maintenance	Dextromethorphan 40 mg/quinidine 20 mg (2 capsules) per 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.: January 2015. Available at www.nuedexta.com. Accessed October 27, 2016.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date