Clinical Policy Title:	dextromethorphan-quinidine
Policy Number:	RxA.240
Drug(s) Applied:	Nuedexta®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
dextromethorphan-quinidine (Nuedexta®)	PBA	1 capsule PO once daily for the initial 7 days, then 1 capsule PO twice daily for maintenance	dextromethorphan - 40mg/day; quinidine - 20mg/day

Dosage Forms

- Capsules: dextromethorphan hydrobromide 20 mg combined with quinidine sulfate 10 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 per day (2 capsules per day).

Approval Duration

Commercial: 3 months

Medicaid: 3 months

II. Continued Therapy Approval

A. Pseudobulbar Affect (must meet all):

1. Member is currently receiving tobramycin that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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 per day (2 capsules per day).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ALS: amyotrophic lateral sclerosis
NMDA: N-methyl-D-aspartate
FDA: Food and Drug Administration
PBA: pseudobulbar affect
MS: multiple sclerosis

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.

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. 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.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to "dextromethorphan-quinidin". 2. Drug(s) Applied was updated to "Nuedexta®". 3. Line of Business Policy Applies to was updated to "All". 4. Clinical policy was updated: Approval duration was updated for both Initial and Continued Approval Criteria. 5. Continued Approval was rephrased to "Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy". 6. References were updated.	07/08/2020	09/14/2020
Policy was reviewed: 1. Policy title was updated.	04/21/2021	06/10/2021

2. Dosing frequency abbreviations expanded. 3. Clinical policy section standard verbiage was updated to include “The provision of provider samples…”. 4. Continued therapy approval criteria II.A.1 was updated to “Member is currently receiving medication…”. 5. References were updated.		