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New Drug Evaluation: Dextromethorphan/Quinidine (NUEDEXTA), capsules

Date of Review: June 2025
Generic Name: dextromethorphan Hbr/quinidine

End Date of Literature Search: 02/14/2025
Brand Name (Manufacturer): NUEDEXTA (Avanir Pharmaceuticals, Inc)

Dossier Received: no

Plain Language Summary:

- This review looks at the evidence for the use of NUEDEXTA (dextromethorphan/quinidine) for management of pseudobulbar affect.
- People with pseudobulbar affect have uncontrollable emotional outbursts such as laughing or crying that do not match the person's mood or situation. This condition often happens after damage to the brain from a stroke, multiple sclerosis, amyotrophic lateral sclerosis, dementia, or traumatic brain injury.
- Only one medicine, the combination of dextromethorphan 20 mg and quinidine 10 mg, is Food and Drug Administration approved to treat pseudobulbar affect. A study in people with multiple sclerosis and amyotrophic lateral sclerosis showed that those taking the medication had less laughing and crying episodes than those taking the placebo.
- Side effects reported with dextromethorphan/quinidine include diarrhea, vomiting, flu-like symptoms, dizziness, cough, and gas.
- Providers must explain to the Oregon Health Authority why someone needs the combination product dextromethorphan/quinidine. This process is called prior authorization.

Research Questions:

1. What is the evidence for efficacy of the combination product dextromethorphan/quinidine for the treatment of pseudobulbar affect (PBA)?
2. What is the evidence for the safety of dextromethorphan/quinidine in the treatment of PBA?
3. Are there subpopulations of adults (i.e., age, gender, ethnicity, disease duration or severity) for whom dextromethorphan/quinidine is more effective or associated with more harms?

Conclusions:

- A 12-week, double-blind randomized controlled trial (RCT) conducted at 60 centers in the United States and South America evaluated the efficacy and safety of dextromethorphan 20 mg/quinidine 10 mg compared with placebo in people with PBA and multiple sclerosis (MS) or amyotrophic lateral sclerosis (ALS).[1] The primary efficacy outcome was a patient's change from baseline in the number of PBA episodes (laughing and/or crying) per day, as recorded in the patient's daily diary.[1] The 12-week mean change in daily episode rate was −3.9 for dextromethorphan/quinidine versus −3.0 for placebo (difference = 0.9 points; 95% confidence interval not reported; p=0.0048; low-quality evidence).[1] A minimal clinically effective difference has not been established for this outcome. Additional study details are presented in **Table 2**.

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- The most frequently reported adverse events reported in this 12-week RCT included diarrhea, dizziness, cough, vomiting, asthenia, and peripheral edema (moderate-quality evidence). See **Table 1** for adverse event rates compared to placebo.[2] There were no proarrhythmic events reported and changes from baseline in QT interval were mild (no greater than 60 msec) in patients who received dextromethorphan/quinidine.[1] Of note, patients with any clinically significant abnormality on the electrocardiogram or with a family history of a congenital prolonged QT interval syndrome were excluded from the study.
- The study was only conducted in adults aged 18 to 80 years of age with PBA attributed to ALS or MS. There is insufficient evidence to assess the efficacy of dextromethorphan/quinidine in people with PBA due to other neurologic conditions.

Recommendations:
- Implement prior authorization (PA) criteria for dextromethorphan/quinidine to define medical necessity under Early Periodic Screening Diagnostic and Treatment (EPSDT) Benefit.
- Maintain designation of dextromethorphan 20 mg/quinidine 10 mg as nonpreferred on the Prioritized Drug List (PDL).

Background:
Pseudobulbar affect is a neurologic condition characterized by involuntary outbursts of laughing or crying that is incongruous or disproportionate for the patient's emotional state.[3] This condition is associated with underlying neurodegenerative diseases, including stroke, traumatic brain injury, Parkinson's disease, Alzheimer's disease, ALS, and MS.[1] Pseudobulbar affect is thought to occur as a result of injury or disease that disrupts pathways regulating emotional expression, or affect, including the corticobulbar tracts and basal ganglia.[4] Prevalence studies have reported that PBA affects 11% of patients 1 year after a stroke,[5] 11% of patients during the first year after traumatic brain injury,[6] 18% of patients with Alzheimer disease,[7] 10% of patients with MS,[8] and 49% of patients with ALS.[9] In addition to the effects of the underlying disorder, PBA can have a severe impact on well-being and social functioning and can be highly disabling, in part due to the stigma attached to loss of emotional control.[1] Differentiating PBA from other common mood disorders, such as depression, anxiety, and bipolar disorder, can be challenging for clinicians, contributing to its high rate of misdiagnosis and leading to ineffective and insufficient treatment.[10] Researchers found that 41% of individuals with PBA symptoms who discussed their inability to control emotional responses during clinical visits were diagnosed and only 52% of those received treatment.[11] Pseudobulbar affect (ICD-10 code F48.2) is not currently funded on the 2025 Health Evidence Review Commission (HERC) Prioritized List.[12] In 2024, approximately 65 people enrolled in the Oregon Health Plan (OHP) Fee-for-Service (FFS) program had a diagnosis of PBA.

A 2022 systematic review evaluated the benefits and harms of pharmaceutical treatment in people with unpredictable crying or laughing after a stroke.[13] Five RCTs involving 213 people met inclusion criteria.[13] Low-quality evidence showed off-label use of antidepressants may reduce the frequency and severity of crying or laughing episodes when compared to placebo.[13] Despite lack of substantial clinical evidence supporting their use for PBA, the serotonergic actions of selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) seem to reduce the frequency of PBA episodes by increasing serotonin activity.[10]

In the randomized controlled trial (RCT) evaluating the efficacy of dextromethorphan 20 mg/quinidine 10 mg, 3 patient-reported assessments were used as secondary endpoints.[1] The Center for Neurologic Study-Lability Scale (CNS-LS) is a patient-reported measure of affective lability that was first used in people with ALS.[14] The reliability of this tool was evaluated in a total of 99 patients with ALS[14] and 90 patients with MS.[15] The 7-item questionnaire is composed of two subscales measuring labile laughter (4 items) and labile tearfulness (3 items).[14] Each item is rated on a scale from 1 (applies never) to 5 (applies most of the time).[16] The total score is calculated as the sum of the item values that resulted in a score ranging from 7 (no symptoms) to 35 (maximum symptom severity and frequency).[16] The American Academy of Neurology (AAN) considers this assessment as possibly effective and may be considered for screening in people with MS (weak recommendation; moderate-quality evidence).[16] The Beck Depression Inventory-II (BDI-II) is a 21-item self-assessment of symptoms of depression.[16] A

total score of 14–19 is considered mild, 20–28 is moderate, and 29–63 is severe.[1] The Neuropsychiatric Inventory (NPI) is a caregiver questionnaire covering 12 neuropsychiatric symptom domains; it provides a brief, informant-based assessment of neuropsychiatric symptoms and caregiver distress.[17] This tool was validated in 60 patients with Alzheimer's Disease.[17] The NPI severity score is based on a 4-point scale (0=absent, 1=mild to 3 = severe).[1] Minimal clinically important differences have not been determined for any of the 3 assessments used in this trial.

A 2009 guideline issued by the AAN stated that dextromethorphan 20 mg/quinidine 10 mg is probably effective for treatment of PBA in people with ALS, although side effects may limit its usefulness (moderate recommendation; high-quality evidence).[18] No other pharmacologic agents were addressed in the guideline. Guidance issued by the AAN in 2014 provided recommendations for management of psychiatric disorders in people with MS.[16] This guidance suggests that dextromethorphan/quinidine is possibly effective and safe and may be considered for treating individuals with MS and PBA (weak recommendation; moderate-quality evidence)[16]

Several studies have evaluated the efficacy of dextromethorphan 30 mg in combination with quinidine 10 mg (this combination is not commercially available) in patients with agitation due to Alzheimer's disease.[19] A 10-week, phase 2 RCT showed a decrease in agitation as measured by a neuropsychiatric inventory-agitation and aggression scale, compared to placebo (127 subjects).[20] Based on these results, two phase 3 trials (NCT02442765 and NCT02442778) were conducted using a modified formulation of dextromethorphan with contradictory findings.[19] The full dataset from both studies is not published in any peer-reviewed journals.[19] The FDA[2] has not approved an expanded indication for use of dextromethorphan/quinidine in agitation associated with Alzheimer's disease and this indication is not listed as compendial, off-label use for dextromethorphan/qunidine in Micromedex.[21]

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations.

Clinical Efficacy:
NUEDEXTA, a combination drug containing dextromethorphan and quinidine, received FDA-approval for the treatment of PBA in 2010.[2] Quinidine is FDA-approved as an antiarrhythmic administered at doses ranging from 200 to 400 mg every 6 hours.[21] Dextromethorphan is available over the counter for use as a cough suppressant at a dose of 10 to 20 mg every 4 hours.[21] Dextromethorphan is an N-methyl-D-aspartate (NDMA) receptor antagonist and high affinity sigma-1 receptor agonist, but the mechanism of action of dextromethorphan in treating PBA is not known.[2] The addition of quinidine, an antiarrhythmic agent at therapeutic doses, is provided at subtherapeutic dosing to inhibit the rapid hepatic CYP2D6 metabolism of dextromethorphan, thereby increasing the bioavailability of dextromethorphan.[10] The starting dose of dextromethorphan 20 mg/quinidine 10 mg is one capsule once daily for 7 days.[2] After 7 days, the dose is increased to one capsule every 12 hours.[2] The clinical trial which contributes to the efficacy data for this indication is described and evaluated below in **Table 2**. Specific drug information for dextromethorphan combined with quinidine is presented in **Appendix 2** including pharmacokinetics and pharmacodynamics.

A 12-week, randomized, double-blind, placebo-controlled, 3-arm, parallel-group study conducted at 60 centers in the United States and South America evaluated the efficacy and safety of dextromethorphan/quinidine in PBA.[1] For entry, men or women 18 to 80 years old were required to have clinically significant PBA, with a score ≥13 on the CNS-LS, and a diagnosis either of ALS or MS.[1] Patients with a history of major psychiatric disorder were excluded from the trial. The authors did not report on the use of concomitant drugs that may interact with dextromethorphan or quinidine. Patients were randomized (1:1:1) to

receive placebo, dextromethorphan 30 mg/quinidine 10 mg or dextromethorphan 20 mg/quinidine 10 mg.[1] For the first treatment week, patients took a single capsule of study drug in the morning. During weeks 2 through 12, they took study drug once in the morning and once in the evening. Follow-up visits occurred at 2, 4, 8, and 12 weeks. In addition, for 1 week prior to baseline and throughout the trial, patients were required to maintain a diary recording the daily number of laughing and/or crying episodes experienced, the medications they took, and any adverse experiences.[1] The primary efficacy endpoint was the change from baseline in the number of PBA episodes (laughing and/or crying) per day, as recorded in the patient's daily diary.[1] The mean baseline was 5 PBA episodes per day. The 12-week mean change in daily episode rate was −4.1 for dextromethorphan 30 mg/quinidine 10 mg and −3.9 for dextromethorphan 20 mg/quinidine 10 mg, versus −3.0 for placebo (95% confidence interval [CI] not reported; p=0.0099 and p=0.0048, respectively).[1]

Secondary endpoints included change from baseline on CNS-LS, which was administered at baseline and at each follow-up visit, the BDI-II and the NPI, which were administered at baseline and at 12 weeks.[1] Among secondary endpoints, the 12-week mean reduction from baseline CNS-LS score was statistically significantly greater at both dextromethorphan/quinidine dosage levels than for placebo.[1] On BDI-II, mean improvement was statistically significantly greater for dextromethorphan 30 mg/quinidine 10 mg than for placebo, but not for the 20 mg/10 mg dose. On the caregiver NPI assessment, total scores showed no significant change for either dosage versus placebo (see **Table 2** for results).[1]

Trial Limitations:
This study required a baseline CNS-LS of 13 or greater in people PBA due to underlying ALS or MS.[1] Because its subjects were carefully screened, the findings should be cautiously generalized to a broader spectrum of patients with PBA due to other neurologic conditions or those with a CNS-LS score less than 12.[1] There was a substantial placebo effect on reduction of PBA episodes per day. Although the results were statistically significant, the clinical relevance of a decrease of 1 PBA episode per day is not clear. Compared with the dextromethorphan 30 mg/quinidine 10 mg group, there were higher attrition rates in the dextromethorphan 20 mg/quinidine 10mg group and placebo group due to AEs due to withdrawal of consent. The intention to treat analysis was used for outcome assessment; it is not clear how missing data were handled.

Clinical Safety:
The most frequently reported adverse events reported over 12 weeks in the RCT included diarrhea, dizziness, cough, vomiting, asthenia, and peripheral edema.[2] There were no proarrhythmic events reported and changes from baseline in QT interval were mild (no greater than 60 msec) in patients who received dextromethorphan/quinidine.[1] Of note, patients with any clinically significant abnormality on the electrocardiogram or with a family history of a congenital prolonged QT interval syndrome were excluded from the study. Seven deaths were reported, all in ALS patients.[1] All deaths were classified by an independent mortality adjudication committee as having a respiratory cause likely to be the result of progression of the underlying neurologic disease.[1] Discontinuation rates attributable to adverse events were 9.3% (10 patients) with dextromethorphan 20 mg/quinidine 10 mg, and 1.8% (2 patients) with placebo.[1] **Table 1** provides a summary of all the reported adverse events with dextromethorphan 20 mg/quinidine 10 mg in comparison with placebo.

Table 1. Adverse Drug Reactions that Occurred with Dextromethorphan/Quinidine-Treated Patients versus Placebo-Treated Patients[2]

Adverse Drug Reaction	Dextromethorphan 20 mg /Quinidine 10 mg (n=107)	Placebo (n=109)
Diarrhea	13%	6%
Dizziness	10%	5%
Cough	5%	2%

Vomiting	5%	1%
Asthenia	5%	2%
Peripheral Edema	5%	1%
Urinary Tract Infection	4%	1%
Influenza	4%	1%
Increased gamma-glutamyltransferease	3%	0%
Flatulence	3%	1%

Contraindications

Avoid concomitant use of dextromethorphan/quinidine with quinidine, quinine, or mefloquine.[2] Avoid use in patients with atrioventricular (AV) block, prolonged QT interval, congenital long QT syndrome, history suggestive of torsades de pointes, or heart failure.[2] Dextromethorphan/quinidine should not be used with monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping an MAOI due to the risk of serotonin syndrome.[2] Drugs that both prolong the QT interval and are metabolized by CYP2D6 (e.g., thioridazine or pimozide) should not be administered concomitantly with dextromethorphan/quinidine.[2]

Drug Interactions

Use of SSRIs or TCAs with dextromethorphan/quinidine increases the risk of serotonin syndrome.[2] Dextromethorphan/quinidine inhibits CYP2D6 and may decrease the safety or efficacy of concomitant CYP2D6 metabolized drugs.[2]

Look-alike / Sound-alike Error Risk Potential: Neulasta

Comparative Endpoints:

Clinically Meaningful Endpoints:
1) Number of laughing and crying episodes
2) Serious adverse events
4) Study withdrawal due to an adverse event

Primary Study Endpoint:
1) Reduction in PBA episodes (laughing/crying episodes) from baseline

Table 2. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. Piro et al. 2010.[1] DB, PC, MC RCT	1. Dextromethorphan 30 mg + Quinidine 10 mg one capsule PO daily x 7 days, then BID weeks 2-12. 2. Dextromethorphan 20 mg + Quinidine 10 mg one capsule PO daily x 7 days, then BID weeks 2-12. 3. Matched placebo at same dosing as active comparator Duration: 12 weeks	Demographics: -Mean age: 51 y -Female: 54% -Race/Ethnicity: White: 75% Hispanic: 19% Black: 3% Other: 2% -ALS: 61% -MS: 39% -PBA episodes per day: ~5 -Mean baseline CNS-LS score: 20 Key Inclusion Criteria: -Age 18 to 80 y with PBA -CNS-LS score ≥ 13 -Diagnosis of ALS or MS Key Exclusion Criteria: -Abnormality on ECG -FH of congenital QT syndrome -History of major psychiatric disturbance -Diagnosis of myasthenia gravis	ITT: 1. 110 2. 107 3. 109 PP: 1. 101 2. 88 3. 94 Attrition: 1. 9 (8%) 2. 19 (18%) 3. 15 (14%)	Primary Endpoint: Change from baseline in number of PBA episodes per day (ITT analysis) 1. -4.1 2. -3.9 3. -3.0 1 vs. 3: difference = 1.1; 95% CI NR; p=0.0099 2 vs. 3: difference = 0.9; 95% CI NR; p=0.0048 Secondary Endpoints: Change from baseline in CNS-LS score (range 1-35) (ITT analysis) 1. -8.2 2. -8.2 3. -5.7 1 vs. 3: difference = -2.5; 95% CI NR: p=0.0002 2 vs. 3: difference = -2.5; 95% CI NR; p=0.0113 -Change from baseline in BDI-II score (ITT analysis) 1. -1.6 2. -1.0 3. 0.02 1 vs. 3: difference = -1.58; 95% CI NR; p=0.0368 2 vs. 3: difference = -0.98; NS -Change from baseline in 4-point NPI score (ITT analysis) 1. -1.6 2. -2.6 3. -1.3 1 vs. 3: difference: 0.3; NS	NA NA NA NS NS NS	Any AE: 1.90 (82.7%) 2.84 (79.4%) 3.90 (82.6%) Serious AE: 1.8 (7.3%) 2.9 (8.4%) 3.10 (9.2%) Discontinuation due AE: 1. 6 (5.5%) 2. 10 (9.3%) 3. 2 (1.8%) 95% CI and p-values NR	NA NA NA	**Risk of Bias (low/high/unclear)**: Selection Bias: Low. Randomized 1:1:1 via computer generated process. Baseline demographics were well matched between groups. Performance Bias: Unclear. Patients and investigators blinded to treatment assignment. Method of blinding not described. Study drug and placebo supplied in blister packs of identical-looking capsules. Detection Bias: Unclear. Patients maintained a diary recording daily PBA episodes. Subjective outcome reporting increases the risk of bias. Attrition Bias: High. Higher attrition rates in 20 mg/10mg group and placebo group due to AEs and due to withdrawal of consent. ITT analysis used for outcome assessment; not clear how missing data were handled. Reporting Bias: High. Protocol available online. All outcomes reported as stated in the protocol. Statistical analysis does not include confidence interval reporting. Other Bias: High. Manufacturer funded study. Several authors reported conflicts of interest due to financial support from the manufacturer. **Applicability**: Patient: Enrolled patients had PBA and either MS or ALS, which limits PBA due to other causes (stroke, traumatic brain injury). Intervention: 20/10 mg dosing approved by FDA and available in US. Comparator: Since no medications are approved for treatment of PBA, placebo is an appropriate comparator to establish efficacy. Outcomes: Change in frequency of PBA episodes is an appropriate metric. Quality of life would be a better outcome assessment. Secondary endpoints do not have defined MCIDs and were validated in small populations of patients with MS or ALS. Setting: 60 sites in the United States and South America

				2 vs. 3: difference: 1.3; NS				

Abbreviations: AE = adverse events; ALS = amyotrophic lateral sclerosis; ARR = absolute risk reduction; BDI-II = Beck Depression Inventory; CI = confidence interval; CNS-LS = Center for Neurologic Study-Lability Scale; DB = double blind; ECG = electrocardiogram; FH = family history; ITT = intention to treat; MC = multi-center; mITT = modified intention to treat; MMSE = Mini-Mental State Examination; MS = multiple sclerosis; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NPI = Neuropsychiatric Inventory; NR = not reported; NS = not statistically significant; OL = open label; PBA = pseudobulbar affect; PC = placebo controlled; PO = oral; PP = per protocol; TBI = traumatic brain injury; y = years.

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Appendix 1: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NUEDEXTA safely and effectively. See full prescribing information for NUEDEXTA.

NUEDEXTA (dextromethorphan hydrobromide and quinidine sulfate) capsules, for oral use
Initial U.S. Approval: 2010

----------INDICATIONS AND USAGE----------
NUEDEXTA is a combination product containing dextromethorphan hydrobromide (an uncompetitive NMDA receptor antagonist and sigma-1 agonist) and quinidine sulfate (a CYP450 2D6 inhibitor) indicated for the treatment of pseudobulbar affect (PBA). (1)

----------DOSAGE AND ADMINISTRATION----------
- Starting dose: one capsule daily by mouth for 7 days. (2.1)
- Maintenance dose: After 7 days, 1 capsule every 12 hours. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
Capsules: Dextromethorphan hydrobromide 20 mg/quinidine sulfate 10 mg. (3)

----------CONTRAINDICATIONS----------
- Concomitant use with quinidine, quinine, or mefloquine. (4.1)
- Patients with a history of quinidine, quinine or mefloquine-induced thrombocytopenia, hepatitis, or other hypersensitivity reactions. (4.2)
- Patients with known hypersensitivity to dextromethorphan. (4.2)
- Use with an MAOI or within 14 days of stopping an MAOI. Allow 14 days after stopping NUEDEXTA before starting an MAOI. (4.3)
- Prolonged QT interval, congenital long QT syndrome, history suggestive of torsades de pointes, or heart failure. (4.4)
- Complete atrioventricular (AV) block without implanted pacemaker, or patients at high risk of complete AV block. (4.4)
- Concomitant use with drugs that both prolong QT interval and are metabolized by CYP2D6 (e.g., thioridazine or pimozide). (4.4)

----------WARNINGS AND PRECAUTIONS----------
- Thrombocytopenia or other hypersensitivity reactions: Discontinue if occurs. (5.1)
- Hepatitis: Discontinue if occurs. (5.2)
- QT Prolongation: Monitor ECG if concomitant use of drugs that prolong QT interval cannot be avoided or if concomitant CYP3A4 inhibitors used. (5.3)
- Left ventricular hypertrophy (LVH) or left ventricular dysfunction (LVD): Monitor ECG in patients with LVH or LVD. (5.3)
- CYP2D6 substrate: Nuedexta inhibits CYP2D6. Accumulation of parent drug and/or failure of metabolite formation may decrease safety and/or efficacy of concomitant CYP2D6 metabolized drugs. Adjust dose of CYP2D6 substrate or use alternative treatment when clinically indicated. (5.4, 12.4)
- Dizziness: Take precautions to reduce falls. (5.5)
- Serotonin syndrome: Use of NUEDEXTA with selective serotonin reuptake inhibitor (SSRIs) or tricyclic antidepressants increases the risk. Discontinue if occurs. (5.6, 7.4)
- Anticholinergic effects of quinidine: Monitor for worsening in myasthenia gravis and other sensitive conditions. (5.7)

----------ADVERSE REACTIONS----------
The most common adverse reactions (incidence of ≥ 3% and two-fold greater than placebo) in patients taking NUEDEXTA are diarrhea, dizziness, cough, vomiting, asthenia, peripheral edema, urinary tract infection, influenza, increased gamma-glutamyltransferase, and flatulence. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Avanir Pharmaceuticals, Inc. at 1-855-4NUEDEX (468-3339) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------DRUG INTERACTIONS----------
- Desipramine: Exposure increases 8-fold. Reduce desipramine dose and adjust based on clinical response. (7.5, 12.4)
- Paroxetine: Exposure increases 2-fold. Reduce paroxetine dose and adjust based on clinical response. (7.5, 12.4)
- Digoxin: Increased digoxin substrate plasma concentration may occur. (7.6)

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 6/2019

Appendix 2: Specific Drug Information

Table 3. Pharmacology and Pharmacokinetic Properties of Combination Dextromethorphan/Quinidine.[21,22]

Parameter	
Mechanism of Action	• Dextromethorphan: NMDA receptor antagonist and Sigma-1 receptor agonist: mechanism of action in PBA is unknown • Quinidine: Competitively inhibits CYP2D6 metabolism of dextromethorphan, which increases and prolongs plasma levels of dextromethorphan
Oral Bioavailability	• Bioavailability of dextromethorphan is increased ~20 fold when administered with quinidine
Distribution and Protein Binding	• Dextromethorphan: 60% to 70% protein bound • Quinidine: 80% to 89% protein bound • Volume of distribution not reported
Elimination	• Quinidine: 5 to 20% renally excreted - pH affects extent of clearance, more acidic urine increases extent of excretion
Half-Life	• Dextromethorphan: 13 hours in extensive metabolizers • Quinidine: 7 hours in extensive metabolizers
Metabolism	• Dextromethorphan: Extensive hepatic metabolism via CYP2D6 • Quinidine: Extensive hepatic metabolism via CYP3A4

Abbreviations: NMDA = N-methyl-D-aspartate; PBA = pseudobulbar affect

Dextromethorphan/Quinidine (NUEDEXTA)

Goal(s):
- To ensure appropriate drug use and restrict to indications supported by medical literature.
- Allow case-by-case review for members covered under the EPSDT program.

Length of Authorization:
- Up to 12 months

Requires PA:
- NUEDEXTA (Combination of dextromethorphan 20 mg and quinidine 10 mg capsule)

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is this for a patient with pseudobulbar affect (involuntary outbursts of laughing or crying that are inappropriate to the patient's emotional state) associated with a chronic neurological condition (e.g., amyotrophic lateral sclerosis, multiple sclerosis, stroke, dementia, Parkinson's disease, traumatic brain injury)?	**Yes**: Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
3. Is the patient eligible for EPSDT review?	**Yes:** Go to #4	**No:** Pass to RPh. Deny; not funded by the OHP

Approval Criteria		
4. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc.)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical necessity.
5. Is the medication prescribed by or in consultation with a neurologist?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness
6. Is there documentation of the number of baseline laughing or crying episodes?	**Yes:** Approve for 6 months. Document results here: Number of crying or laughing episodes per day_____ Date:_____	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
1. Is there documentation of improvement in frequency of laughing or crying episodes from baseline as assessed by the prescribing provider?	**Yes**: Approve for 60 months.	**No:** Pass to RPh. Deny; medical appropriateness

P&T/DUR Review: 6/25 (DM)
Implementation: 8/1/25