PHARMACY COVERAGE GUIDELINE

NUEDEXTA™ (dextromethorphan and quinidine) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Nuedexta (dextromethorphan and quinidine) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Individual is 18 years of age or older

  2. Individual has a confirmed diagnosis of pseudobulbar affect (PBA)

  3. The diagnosis of PBA is associated with a chronic neurological condition (e.g., amyotrophic lateral sclerosis, multiple sclerosis, stroke, dementia, or traumatic brain injury)

  4. Individual has symptoms characterized by involuntary, sudden, and frequent episodes of laughing and/or crying that are out of proportion or incongruent to the underlying emotional state

5. Individual has a Center for Neurologic Studies Lability Scale (CNS-LS) of 13 or more

6. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Serum potassium and magnesium, if abnormal must be corrected prior to use
    b. Electrocardiogram in individuals at risk for QT prolongation and torsade de pointes such as individuals with bradycardia, family history of QT abnormality, left ventricular hypertrophy or left ventricular dysfunction

7. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

8. Individual has documented failure after 3-month of use, contraindication per FDA label, intolerance, or is not a candidate for **TWO** of the following:
    a. Either amitriptyline or nortriptyline
    b. Fluoxetine
    c. Fluvoxamine
    d. Sertraline

9. There are **NO** FDA-label contraindications such as:
    a. Concurrent use with Quinidine, Quinine, or Mefloquine
    b. History of Quinidine, Quinine, or Mefloquine induced thrombocytopenia, hepatitis, bone marrow depression or lupus-like syndrome or other hypersensitivity reaction
    c. Known hypersensitivity to Dextromethorphan such as rash or hives
    d. Use with a mono-amine oxidase inhibitor (MAOI) or within 14 days of starting and stopping a MAOI
    e. Prolonged QT interval, congenital long QT syndrome, history of torsades de pointes, or heart failure
    f. Complete atrioventricular (AV) node block without an implanted pacemaker, or individual at high risk of complete AV block
    g. Use with drugs that both prolong QT interval and are metabolized by cytochrome P450 2D6 (such as thioridazine or pimozide)

10. Will not be used with another Dextromethorphan containing product for other medical condition

11. Individual does not have severe renal impairment

12. Individual does not have severe hepatic impairment

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Nuedexta (dextromethorphan and quinidine) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual's condition has responded while on therapy with response defined as **ONE** of the following:

a. Achieved and maintains at least a 30% reduction in Center for Neurologic Studies Lability Scale (CNS-LS) over baseline
b. Achieved and maintains at least a 30% reduction in the frequency of laughing and crying episodes that are out of proportion or incongruent to the underlying emotional state

2. Individual has been adherent with the medication

3. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant adverse effect such as:
      i. Immune mediated drug induced thrombocytopenia
      ii. Hepatitis
      iii. Serotonin syndrome
      iv. Torsades de point-type ventricular arrhythmia

5. Will not be used with another Dextromethorphan containing product for other medical condition

6. Individual does not have severe renal impairment

7. Individual does not have severe hepatic impairment

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Nuedexta (dextromethorphan and quinidine) is the first and only FDA-approved treatment for pseudobulbar affect (PBA). PBA is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying that are out of proportion or incongruent to the underlying emotional state. PBA occurs as a secondary presentation to a variety of unrelated neurological conditions. It is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury.

Nuedexta capsules contain 20mg of dextromethorphan hydrobromide and 10mg of quinidine sulfate. Dextromethorphan, found in many cough medicines, is a sigma-1 receptor agonist and an uncompetitive NMDA

receptor antagonist. Its mechanism of action as an antitussive agent occurs through depression of the medullary cough center, interruption of cough impulse transmission, and a reduction of the sensitivity of cough reflex. The mechanism by which dextromethorphan exerts therapeutic effects in PBA is unknown. Quinidine is a class 1A anti-arrhythmic used in individuals with atrial fibrillation. In Nuedexta (dextromethorphan and quinidine), its purpose is to inhibit metabolism of dextromethorphan via CYP2D6, leading to higher levels plasma levels of dextromethorphan.

Nuedexta (dextromethorphan and quinidine) is contraindicated in individuals with a history of Nuedexta (dextromethorphan and quinidine), quinine, mefloquine or quinidine-induced thrombocytopenia, hepatitis, bone marrow depression or lupus-like syndrome. Nuedexta (dextromethorphan and quinidine) is also contraindicated in individuals with a known hypersensitivity to dextromethorphan (e.g., rash, hives). The safety and effectiveness of Nuedexta (dextromethorphan and quinidine) in pediatric individuals below the age of 18 have not been established.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Center for Neurologic Studies Lability Scale (CNS-LS):

- A seven-item self-report questionnaire with 3 items assessing crying and 4 assessing laughter
- A score of 13 or more may suggest PBA
- The CNS-LS has been validated in ALS and MS patients

Center for Neurologic Studies Lability Scale (CNS-LS)					
Using the scale below, write the number that describes the degree to which each item applies to you during the past week. Write only one number for each item					
Never applies	Rarely applies	Occasionally applies	Frequently applies	Applies most of the time	
1	2	2	4	4	
					Degree
There are times when I feel fine one minute, and then I'll become tearful the next over something small or for no reason at all					
Others have told me that I seem to become amused very easily or that I seem to become amused about things that are not funny					
I find myself crying very easily					
I find that even when I try to control my laughter, I am often unable to do so					
There are times when I won't be thinking of anything happy or funny at all, but then I'll suddenly be overcome by funny or happy thoughts					
I find that even when I try to control my crying, I am often unable to do so					
I find that I am easily overcome by laughter					
				Total	

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Resources:

Nuedexta (dextromethorphan and quinidine) product information, revised by Otsuka America Pharmaceuticals, Inc. 12-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Galvez-Jimenez N. Quinn C. Symptom-based management of amyotrophic lateral sclerosis. In: UpToDate, Shefner JM, Morrison S, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated September 05, 2024. Accessed March 06, 2025.

Press D. Management of neuropsychiatric symptoms of dementia. In: UpToDate, DeKosky ST, Schmader KE, Mendez, MF, Wilterdink JL (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated April 07,2022. Accessed March 06, 2025.