



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 09/08/11
LAST REVIEW DATE: 05/18/17
LAST CRITERIA REVISION DATE: 05/01/17
ARCHIVE DATE:

NUEDEXTA™ (dextromethorphan and quinidine) oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Nuedexa 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.

Nuedexa 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 Nuedexa, its purpose is to inhibit metabolism of Dextromethorphan via CYP2D6, leading to higher levels plasma levels of Dextromethorphan.

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

Definitions:

Drug related events:

Ineffective / failure

Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

Adverse Drug Event: Allergic reaction / Hypersensitivity / Intolerance

Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

Allergic reaction / hypersensitivity – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

Intolerance – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

Contraindication

Use of a drug that is not recommended by the manufacturer or FDA labelling

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Use of any drug in the face of a contraindication is outside of the FDA and manufacturer's labelled recommendation and is considered investigational or experimental

Non-adherence

Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record

Precertification:

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Criteria:

See "Resources" section for FDA-approved dosage.

- Precertification for Nuedexta requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms will be returned.
- **Initial therapy:** FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Nuedexta is considered **medically necessary** when **ALL** of the following criteria are met:
 1. Individual is 18 years of age or older
 2. Medical record documentation of a confirmed diagnosis of pseudobulbar affect (PBA) characterized by involuntary, sudden, and frequent episodes of laughing and/or crying that are out of proportion or incongruent to the underlying emotional state
 3. Absence of **ALL** the following contraindications:
 - Concurrent use with Quinidine, Quinine, or Mefloquine
 - History of Quinidine, Quinine, or Mefloquine induced thrombocytopenia, hepatitis, or other hypersensitivity reaction

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- Known hypersensitivity to Dextromethorphan
- Use with a mono-amine oxidase inhibitor (MAOI) or within 14 days of stopping a MAOI
- Prolonged QT interval, congenital long QT syndrome, history of torsades de pointes, or heart failure
- Complete atrioventricular (AV) node block without an implanted pacemaker, or individual at high risk of complete AV block
- Use with drugs that both prolong QT interval and are metabolized by cytochrome P450 2D6 (such as thioridazine or pimozide)

4. Absence of **ALL** of the following exclusions:

- Concurrent use with Dextromethorphan for other medical conditions

➤ **Continuation of coverage (renewal request):** Nuedexta is considered *medically necessary* with documentation of **ALL** of the following:

1. The individual has benefited from therapy but remains at high risk
2. The condition has not progressed or worsened while on therapy
3. Individual has not developed any contraindications or other exclusions to its continued use

➤ Nuedexta for all other indications not previously listed is considered *experimental or investigational* based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

Resources:

Nuedexta. Package Insert. Revised 01/2016. Accessed 03-28-2017.

Nuedexta. Package Insert. Revised 01/2015. Accessed 05-06-2015.

Nuedexta. Package Insert, 10/2010, NUE-0279-WEB-0912/ Rev. Date 08/2011; viewed on 08-25-2012.

King RR and Reiss JP: The epidemiology and pathophysiology of pseudobulbar affect and its association with neurodegeneration. Degen Neurolog Neuromusc Dis 2013;3:23-31

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FDA-approved indication and dosage:

Indication	Recommended Dose
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).	<ul style="list-style-type: none">• Starting dose: One capsule daily by mouth for 7 days.• Maintenance dose: After 7 days, 1 capsule every 12 hours.
