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Coverage Policy Number.....IP0324

Dextromethorphan/quinidine (Nuedexta) for Individual and Family Plans

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Related Coverage Resources

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The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for dextromethorphan hydrobromide and quinidine sulfate capsules (**Nuedexta**®).

Medical Necessity Criteria

Dextromethorphan hydrobromide and quinidine sulfate capsules (**Nuedexta**) **is considered medically necessary when the following are met:**

1. **Pseudobulbar Affect.** Individual meets **BOTH** of the following criteria (A and B):
   A. Documented diagnosis of pseudobulbar affect associated with chronic neurological condition (examples of chronic neurological conditions include amyotrophic lateral sclerosis, multiple sclerosis, stroke, dementia, traumatic brain injury)
   B. Medication is prescribed by, or in consultation with, a neurologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of dextromethorphan hydrobromide and quinidine sulfate capsules (Nuedexta) is considered medically necessary for pseudobulbar affect when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

1. **Heroin Detoxification.** Limited published data are available in patients undergoing heroin detoxification.[9] The available study was conducted with the DM 30 mg/quinidine 30 mg formulation, using daily doses of DM 60 mg/quinidine 60 mg (dose cannot be achieved with Nuedexta capsules). There were no differences between DM/quinidine and placebo with regard to reducing opioid withdrawal symptoms.

2. **Levodopa-Induced Dyskinesia in Parkinson's Disease.** A single pilot study demonstrated benefit with dextromethorphan/quinidine for treating levodopa-induced dyskinesia in Parkinson's disease.[12] Larger studies with a longer treatment duration are needed to define the place in therapy for Nuedexta in this condition.

3. **Neuropathic Pain.** Limited published data are available in patients (n = 36) with diabetic peripheral neuropathic (DPN) pain (open-label tolerability study).[10] The available study was conducted with the DM 30 mg/quinidine 30 mg formulation, using daily doses up to DM 120 mg/quinidine 120 mg (dose cannot be achieved with Nuedexta capsules). Higher daily doses of DM and quinidine (60 mg/60 mg and 90 mg/60 mg [doses cannot be achieved with Nuedexta capsules]) have also been evaluated in patients with DPN pain (n = 379) in one Phase III, randomized, placebo-controlled 13-week study.[7] Both DM/quinidine treatment groups had significant reductions in mean daily pain scores vs. placebo. More data are needed to define the place in therapy of Nuedexta in the treatment of neuropathic pain.

4. **Psychosis-Related Aggression**. A case series (n = 4) supports DM/quinidine as a potential alternative to conventional regimens for treating aggression and impulsive behavior in patients with psychotic disorder.[11] More data are needed to define the place in therapy of Nuedexta in the treatment of psychosis-related aggression.

5. **Treatment-Resistant Depression.** A Phase II, open-label, proof-of-concept study (n = 20) demonstrated preliminary efficacy for DM 45 mg/quinidine 10 mg every 12 hours. This dosing could not be achieved with Nuedexta capsules.[13] Additional data are needed to define the place in therapy for Nuedexta in the treatment of treatment-resistant depression.

Background

OVERVIEW

Nuedexta, a combination product containing dextromethorphan hydrobromide (DM) and quinidine sulfate, is indicated for the **treatment of pseudobulbar affect**.[1]

The need for continued treatment should be reassessed periodically, as spontaneous improvement of pseudobulbar affect occurs in some patients.[1]

Disease Overview
Pseudobulbar affect is a neurologic condition characterized by involuntary outbursts of laughing and/or crying incongruous or disproportionate to the patients' emotional state.[2,7] There are many terms that have been used to describe this condition, including pathological laughing and crying, affective lability, emotional incontinence, emotionalism, and involuntary emotional expression disorder.[7] Pseudobulbar affect, hypothesized to arise from disconnection of brainstem structures from cortical inhibition, is associated with underlying central nervous system disorders including stroke, traumatic brain injury, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS).[2] In addition to the effects of the underlying disorder, pseudobulbar affect can have a severe impact on well-being and social functioning and can be highly disabling, owing in part to the stigma attached to loss of emotional control. Episodes of laughing can also lead to respiratory compromise, especially in patients with a neurological disorder that already compromises respiratory function, such as ALS.[7] For these reasons, treatment should be strongly considered in any patient with pseudobulbar affect. The goal of therapy is to reduce the frequency of attacks.

Clinical Efficacy
The efficacy of Nuedexta was established in one trial in patients with pseudobulbar affect with underlying ALS or MS.[1,2] Two additional trials conducted with higher doses (DM 30 mg/quinidine 30 mg) provided supportive evidence.[3,4] PRISM II, an open-label, 90-day, published study, evaluated Nuedexta in patients with pseudobulbar affect and a diagnosis of dementia, stroke, or traumatic brain injury (n = 367).[8] Nuedexta was shown to be an effective treatment for pseudobulbar affect secondary to dementia, stroke, or traumatic brain injury, showing similar improvement to that reported in patients with pseudobulbar affect secondary to ALS or MS.

Guidelines
There are no guidelines specific to the management of pseudobulbar affect. However, the American Academy of Neurology (AAN) published an evidence-based guideline on the assessment and management of psychiatric disorders in individuals with MS (reaffirmed 2019).[5] The guideline found that Nuedexta is possibly effective and may be considered for treating individuals with MS with pseudobulbar affect (Level C, one Class II study). Also, prior to the approval of Nuedexta, the AAN published a practice parameter on the care of the patient with ALS (reaffirmed 2023).[6] With regard to pharmacologic measures to reduce pseudobulbar affect, the AAN concludes that the combination DM/quinidine product is probably effective for pseudobulbar affect in ALS based on one Class I study[3], although side effects may limit its usefulness. Therefore, the AAN recommends that if approved by the FDA, and if side effects are acceptable, the combination DM/quinidine product should be considered for symptoms of pseudobulbar affect in patients with ALS (Level B). No other pharmacologic agents are addressed in the practice parameter for use in the management of pseudobulbar affect.

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Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes, minor format updates only.	12/01/2024

The policy effective date is in force until updated or retired.