PRIOR AUTHORIZATION POLICY

POLICY: Nuedexta Prior Authorization Policy
- Nuedexta® (dextromethorphan hydrobromide and quinidine sulfate capsules – Avanir)

REVIEW DATE: 09/13/2023

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Nuedexta. Because of the specialized skills required for evaluation and diagnosis of patients treated with Nuedexta as well as the monitoring required for adverse events and long-term efficacy, approval requires Nuedexta to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Nuedexta is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Treatment of Pseudobulbar Affect.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** Patient has pseudobulbar affect associated with a chronic neurological condition; AND
     Note: Examples of chronic neurological conditions include amyotrophic lateral sclerosis, multiple sclerosis, stroke, dementia, traumatic brain injury.
   - **B)** Nuedexta is prescribed by or in consultation with a neurologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Nuedexta is not recommended in the following situations:

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.

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Nuedexta® capsules [prescribing information]. Aliso Viejo, CA: Avanir; December 2022.
2. Pioro EP, Brooks BR, Cummings J, et al. Dextromethorphan plus ultra low-dose quinidine reduces pseudobulbar affect. *Ann Neurol.* 2010;68:693-702.
3. Brooks BR, Thisted RA, Appel SH. Treatment of pseudobulbar affect in ALS with dextromethorphan/quinidine. *Neurology.* 2004;63:1364-1370.
4. Panitch HS, Thisted RA, Smith RA. Randomized, controlled trial of dextromethorphan/quinidine for pseudobulbar affect in multiple sclerosis. *Ann Neurol*. 2006;59:780-787.
5. Minden SL, Feinstein A, Kalb RC, et al. Evidence-based guideline: Assessment and management of psychiatric disorders in individuals with MS: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2014;82:174-181.
6. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2009;73:1227-1233.
7. Shaibani AI, Pope LE, Thisted R, Hepner A. Efficacy and safety of dextromethorphan/quinidine at two dosage levels for diabetic neuropathic pain: a double-blind, placebo-controlled, multicenter study. *Pain Med.* 2012;13:243-254.
8. Hammond FM, Alexander DN, Cutler AJ, et al. PRISM II: an open-label study to assess effectiveness of dextromethorphan/quinidine for pseudobulbar affect in patients with dementia, stroke or traumatic brain injury. *BMC Neurology*. 2016;16:89.
9. Akerele E, Bisaga A, Sullivan MA, et al. Dextromethorphan and quinidine combination for heroin detoxification. Am J Addict. 2008;17:176-180.
10. Thisted RA, Klaff L, Schwartz SL, et al. Dextromethorphan and quinidine in adult patients with uncontrolled painful diabetic peripheral neuropathy: a 29-day, multicenter, open-label, dose-escalation study. *Clin Ther.* 2006;28:1607-1618.
11. Chen Q, Calcagno HE, Shad M. Efficacy of dextromethorphan/quinidine for patients with psychosis-related aggression: a retrospective case series. *Prim Care Companion CNS Disord*. 2018;20(3).
12. Fox SH, Metman LV, Nutt JG, et al. Trial of dextromethorphan/quinidine to treat levodopa-induced dyskinesia in Parkinson's disease. *Mov Disord*. 2017;32(6):893-903.
13. Murrough JW, Wade E, Sayed S, et al. Dextromethorphan/quinidine pharmacotherapy in patients with treatment resistant depression: A proof of concept clinical trial. *J Affect Disord*. 2017;218:277-283.