dextromethorphan/quinidine (Nuedexta®)

Policy # 00628
Original Effective Date: 01/01/2019
Current Effective Date: 01/01/2019

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider dextromethorphan/quinidine (Nuedexta®)‡ in patients when pseudobulbar affect to be **eligible for coverage** when the patient selection criteria are met**.**

Patient Selection Criteria
Coverage eligibility for dextromethorphan/quinidine (Nuedexta) will be considered when the following criterion is met:

- The patient has a diagnosis of Pseudobulbar Affect (PBA) associated with a chronic neurological condition (e.g. amyotrophic lateral sclerosis, multiple sclerosis, stroke, dementia, traumatic brain injury)

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers dextromethorphan/quinidine (Nuedexta) when the patient selection criterion is not met to be **investigational.***

Background/Overview

Nuedexta is a combination product containing 20 milligrams (mg) of dextromethorphan hydrobromide and 10 mg quinidine sulfate per capsule. Dextromethorphan is a sigma-1 receptor agonist and an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist. Quinidine increases plasma levels of dextromethorphan by competitively inhibiting the enzyme (CYP2D6) that primarily metabolizes it. Nuedexta is indicated for the treatment of PBA and should be dosed as one capsule by mouth daily for the first seven days then one capsule twice daily thereafter. It is contraindicated in combination with other drugs containing quinidine, quinine, or mefloquine; in patients with a history of Nuedexta, quinine, mefloquine, or quinidine-induced thrombocytopenia, hepatitis, bone marrow depression or lupus-like syndrome; in patients taking monoamine oxidase inhibitors; in patients with prolonged QT interval, congenital long QT syndrome, or a history suggestive of torsades de pointes; in patients with heart failure; and in patients with complete atrioventricular block without implanted pacemakers.

PBA occurs secondary to a variety of otherwise unrelated neurologic conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. PBA episodes typically occur out of

proportion or incongruent to the underlying emotional state. PBA is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury. Other terms for PBA include pathological laughing and crying, affective lability, emotional incontinence, emotionalism, and involuntary emotional expression disorder. The need for continued treatment should be reassessed periodically as spontaneous improvement of PBA occurs in some patients.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Nuedexta was approved in 2010 for the treatment of pseudobulbar affect.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Nuedexta was demonstrated in one trial in patients with PBA and underlying amyotrophic lateral sclerosis (ALS) or multiple sclerosis (MS). Patients were randomized 1:1:1 to receive dextromethorphan 2 mg/quinidine 10mg, dextromethorphan 30 mg/quinidine 10 mg, or placebo. The primary outcome measure, laughing and crying episodes, was statistically significantly lower in each dextromethorphan/quinidine arm compared to placebo. There were no clinically important differences between doses of dextromethorphan/quinidine.

There is limited published data on the use of dextromethorphan/quinidine for indications other than PBA. One available study was conducted in patients undergoing heroin detoxification and found no differences between dextromethorphan/quinidine and placebo in reducing opioid withdrawal symptoms. Evidence for use in the treatment of neuropathic pain includes a small (n=36) open-label tolerability study and one phase III, randomized, placebo-controlled study in 379 patients. In both of these studies, the dextromethorphan/quinidine treatment groups had significant reductions in mean daily pain scores vs. placebo. However, all of these studies were conducted with a formulation containing 30mg of dextromethorphan and 30 mg of quinidine. Doses studied cannot be obtained with Nuedexta. More data are needed to define the place in therapy of Nuedexta in the treatment of neuropathic pain.

References

1. Nuedexta [package insert]. Avanir Pharmaceuticals, Inc. Aliso Viejo, CA. January 2016
2. Nuedexta PA policy. Express Scripts. July 2017.

Policy History

Original Effective Date: 01/01/2019
Current Effective Date: 01/01/2019
09/06/2018 Medical Policy Committee review

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09/19/2018 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 09/2019

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.