



# Louisiana

## desmopressin acetate (Noctiva™, Nocdurna®)

Policy # 00619

Original Effective Date: 05/16/2018

Current Effective Date: 04/12/2021

*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 desmopressin acetate (Noctiva™, Nocdurna®)‡ for the treatment of nocturia due to nocturnal polyuria to be **eligible for coverage**.\*\*

#### Patient Selection Criteria

Coverage eligibility for desmopressin acetate (Noctiva, Nocdurna) will be considered when the following criteria are met:

- For Noctiva requests
  - Patient is greater than or equal to 50 years old; AND
  - Patient has been diagnosed with nocturnal polyuria as confirmed by a 24-hour urine collection which notes the presence of greater than one-third of 24-hour urine production occurring at night; AND
  - Patient awakens at least 2 times per night to void; AND
  - Patient has a documented normal serum sodium level based on laboratory reference range within the previous 60 days; AND
  - Patient is NOT currently taking ANY of the following agents:
    - Loop diuretics (bumetanide, furosemide, torsemide)
    - Inhaled or systemic glucocorticoids (beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone, or any combination); AND
  - Patient does NOT have a disease state that increases risk for hyponatremia or would be worsened with fluid retention (e.g., Heart Failure Class II-IV, primary nocturnal enuresis, renal impairment, syndrome of inappropriate antidiuretic hormone secretion [SIADH]); AND

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- Patient has tried and failed (e.g., intolerance or inadequate response) generic oral desmopressin acetate tablets unless there is clinical evidence or patient history that suggests generic desmopressin acetate tablets will be ineffective or cause an adverse reaction to the patient; AND  
*(Note: This specific patient criterion is an additional Company requirement and will be denied as not medically necessary\*\* if not met).*
- Patient has tried non-pharmacologic techniques or lifestyle interventions to manage the nocturia (e.g., nighttime fluid restriction, avoidance of caffeine and alcohol, or earlier timing of medications).  
*(Note: This specific patient criterion is an additional Company requirement and will be denied as not medically necessary\*\* if not met).*
- For Nocdurna requests
  - Patient is greater than or equal to 18 years old; AND
  - Patient has been diagnosed with nocturnal polyuria as confirmed by a 24-hour urine collection which notes the presence of greater than one-third of 24-hour urine production occurring at night; AND
  - Patient awakens at least 2 times per night to void; AND
  - Patient has a documented normal serum sodium level based on laboratory reference range within the previous 60 days; AND
  - Patient is NOT currently taking ANY of the following agents:
    - Loop diuretics (bumetanide, furosemide, torsemide)
    - Inhaled or systemic glucocorticoids (beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone, or any combination); AND
  - Patient does NOT have a disease state that increases risk for hyponatremia or would be worsened with fluid retention (e.g., Heart Failure Class II-IV, primary nocturnal enuresis, renal impairment, syndrome of inappropriate antidiuretic hormone secretion [SIADH]); AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) generic oral desmopressin acetate tablets unless there is clinical evidence or patient history that suggests generic desmopressin acetate tablets will be ineffective or cause an adverse reaction to the patient; AND  
*(Note: This specific patient criterion is an additional Company requirement and will be denied as not medically necessary\*\* if not met).*

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- Patient has tried non-pharmacologic techniques or lifestyle interventions to manage the nocturia (e.g., nighttime fluid restriction, avoidance of caffeine and alcohol, or earlier timing of medications).

*(Note: This specific patient criterion is an additional Company requirement and will be denied as not medically necessary\*\* if not met).*

## When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of desmopressin acetate (Noctiva, Nocdurna) when the patient has not tried and failed generic oral desmopressin acetate tablets AND non-pharmacologic techniques or lifestyle interventions for a clinically sufficient duration to be **not medically necessary.\*\***

## 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 desmopressin acetate (Noctiva, Nocdurna) when patient selection criteria are not met (other than those denoted as not medically necessary\*\*) to be **investigational.\***

## Background/Overview

Desmopressin is a selective agonist at vasopressin receptors on the collecting ducts which increases water reabsorption and therefore decreases urine production. It is also known as ddAVP and is available as a generic oral tablet that has been used to treat nocturia. Noctiva and Nocdurna are new formulations of desmopressin acetate and are both indicated to prevent nocturia in adults with nocturnal polyuria who awaken at least 2 times per night to void. Noctiva is a nasal spray available in two strengths: 0.83 microgram (mcg) per 0.1 milliliter (mL) and 1.66 mcg per 0.1mL, but two sprays of the 0.83 mcg strength are not interchangeable for 1 spray of the 1.66 mcg strength. The recommended dose for patients who are not at increased risk for hyponatremia is 1 spray of Noctiva 1.66 mcg in either the left or right nostril approximately 30 minutes before going to bed. Nocdurna is a sublingual tablet formulation available in two strengths: 27.7 mcg and 55.3 mcg. The

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recommended dose of Nocdurna for women is 27.7 mcg once daily, one hour before bedtime, and the recommended dose for men is 55.3 mcg once daily, one hour before bedtime.

Nocturia is defined as any waking at night to void, although 2 or more awakenings are most often considered clinically significant. Nocturnal polyuria is a subset of nocturia defined as the excretion of more than one-third of the 24-hour urine output during the hours of sleep. Because it is theorized that nocturnal polyuria may be caused by inadequate levels of arginine vasopressin (AVP), treatment often includes desmopressin (ddAVP) which is structurally similar to AVP but does not have vasopressor activity. Clinical trials have demonstrated some efficacy of desmopressin compared to placebo in reducing nighttime voids, but there are persistent concerns related to the safety of the therapy due to the occurrence of severe hyponatremia, particularly in older ( $\geq 65$  years) patients. For this reason, the Food and Drug Administration (FDA) has listed a boxed warning for Noctiva and Nocdurna warning that they can cause hyponatremia and are contraindicated in patients at increased risk of severe hyponatremia (e.g., concomitant loop diuretic use, excessive fluid intake, etc.).

## **FDA or Other Governmental Regulatory Approval**

### **U.S. Food and Drug Administration (FDA)**

Noctiva is approved for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void. Nocturnal polyuria was defined in the Noctiva clinical trials as nighttime urine production exceeding one-third of the 24-hour urine production.

Nocdurna is indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void. Nocturnal polyuria was defined in the Nocdurna clinical trials as night-time urine production exceeding one-third of the 24-hour urine production.

## **Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration 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.

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The efficacy of Noctiva in patients with nocturia due to nocturnal polyuria was established in two 12-week randomized, double-blind, placebo-controlled trials in adults at least 50 years of age. At baseline, patients were required to have a 6-month history of at least 2 nocturic episodes per night, on average, and at least 13 documented nocturia episodes over 6 nights during screening. In trial 1, 612 patients were randomized 1:1:1 to receive either Noctiva 1.66 mcg, Noctiva 0.83 mcg, or placebo. In trial 2, 433 patients were randomized 1:1:1 to receive Noctiva 1.66 mcg, Noctiva 0.83 mcg, or placebo. The co-primary endpoints of both trials were the change in mean number of nocturic episodes per night from baseline during the 12-week treatment period and the percentage of patients who achieved at least a 50% reduction from baseline in the mean number of nocturia episodes per night. Noctiva was determined to be efficacious only in those patients whose nocturia was caused by nocturnal polyuria. Of the patients with nocturnal polyuria in study 1, the change in the mean number of nocturia episodes per night from baseline (range, 3.2 to 3.4) was -1.5 for both doses of Noctiva compared with -1.2 with placebo. Of the patients with nocturnal polyuria in study 2, the change in mean number of nocturia episodes per night from baseline (range, 3.3 to 3.4) was -1.5 for Noctiva 1.66 mcg and -1.4 for Noctiva 0.83 mcg compared with -1.1 with placebo. In study 1, the percentage of patients achieving at least a 50% reduction in nocturic episodes per night was 47%, 35%, and 27% for Noctiva 1.66 mcg, Noctiva 0.83 mcg, and placebo, respectively. In study 2, the percentage of patients achieving at least a 50% reduction in nocturic episodes per night was 49%, 41%, and 29% for Noctiva 1.66 mcg, Noctiva 0.83 mcg, and placebo, respectively.

The efficacy of Nocdurna in the treatment of adults with nocturia due to nocturnal polyuria was established in two 12-week, randomized, double-blind, placebo-controlled, multicenter trials in adults over 18 years of age. Study 1 enrolled only women (n=237) and study 2 enrolled only men (n=230). At baseline, patients were required to document at least 2 nocturnal voids per night in a consecutive 3-day diary collected during screening. In both studies, patients were randomized to receive either Nocdurna or placebo every night approximately 1 hour prior to bedtime for 3 months. The co-primary efficacy endpoints in each trial were 1) the change in number of nocturia episodes per night from baseline during the treatment period, and 2) 33% responder status during the months of treatment. A 33% responder was defined as a subject with a decrease of at least 33% in the mean number of nocturnal voids compared to baseline. In study 1, the difference from placebo in number of nocturnal voids was -0.3 (95% CI -0.5 to -0.1) and in study 2 it was -0.4 (95% CI -0.6 to -0.2). In study 1, the probability (adjusted for age stratification, visit, and baseline nocturnal voids) of achieving a 33% decrease in nocturnal voids was 0.62 for placebo and 0.78 for Nocdurna with an

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odds ratio of 2.15 (95% CI 1.36-3.41). In study 2, the probability of achieving a 33% decrease in nocturnal voids was 0.5 for placebo and 0.67 for Nocdurna with an odds ratio of 2.02(1.3-3.14).

## References

1. Noctiva [package insert]. Avadel Specialty Pharmaceuticals, LLC. Chesterfield, MO. Updated January 2018.
2. Nocturia: Clinical presentation, evaluation, and management in adults. UpToDate. Accessed April 2018.
3. Noctiva Drug Evaluation. Express Scripts. Updated June 14, 2017.
4. Nocdurna [package insert]. Ferring Pharmaceuticals Inc. Parsippany, NJ. Updated December 2018.

## Policy History

Original Effective Date: 05/16/2018

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05/03/2018 Medical Policy Committee review

05/16/2018 Medical Policy Implementation Committee approval. New policy.

03/07/2019 Medical Policy Committee review

03/20/2019 Medical Policy Implementation Committee approval. Added new drug, Nocdurna, along with relevant background information. Title change.

03/05/2020 Medical Policy Committee review

03/11/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

03/04/2021 Medical Policy Committee review

03/10/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 03/2022

\*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:

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- 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.

\*\*Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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**NOTICE:** If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**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.

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