



Louisiana

desmopressin acetate (Noctiva™)

Policy # 00619

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

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™)[†] for the treatment of nocturia due to nocturnal polyuria to be **eligible for coverage**.

Patient Selection Criteria

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

- Patient is greater than or equal to 50 years old; AND
- The 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
- The patient awakens at least 2 times per night to void; AND
- The 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).*
- 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).*

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

desmopressin acetate (Noctiva™)

Policy # 00619

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of desmopressin acetate (Noctiva) 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) when patient selection criteria are not met (other than those denoted as not medically necessary**) to be **investigational**.*

Background/Overview

Noctiva is a nasal spray formulation of desmopressin acetate that is indicated to prevent nocturia in adults with nocturnal polyuria who awaken at least 2 times per night to void. Desmopressin, also known as ddAVP, is also available as a generic oral tablet that has been used to treat nocturia. Desmopressin is a selective agonist at vasopressin receptors on the collecting ducts which increases water reabsorption and therefore decreases urine production. Noctiva is available in two strengths: 0.83 microgram (mcg) per 0.1 milliliter (mL) and 1.66 mcg per 0.1 mL, 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.

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 (≥ 65 years) patients. For this reason, the Food and Drug Administration (FDA) has listed a boxed warning that Noctiva can cause hyponatremia and is 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.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

desmopressin acetate (Noctiva™)

Policy # 00619
Original Effective Date: 05/16/2018
Current Effective Date: 05/16/2018

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 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.

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

Policy History

Original Effective Date: 05/16/2018
Current Effective Date: 05/16/2018
05/03/2018 Medical Policy Committee review
05/16/2018 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 05/2019

*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

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



Louisiana

desmopressin acetate (Noctiva™)

Policy # 00619

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

- 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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.