PHARMACY COVERAGE GUIDELINE

NOCDURNA® (desmopressin acetate) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Nocdurna (desmopressin acetate) oral sublingual tablet and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist, Urologist, or Endocrinologist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of nocturia due to nocturnal polyuria in an individual who awakens at least 2 times per night to void

ORIGINAL EFFECTIVE DATE: 05/18/2017 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 05/18/2023

4. Confirmation was made with a 24-hour frequency/volume chart that showed nighttime urine production of greater than 33% of the total 24-hour urine production

5. Individual awakens at least 2 times per night to void

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **oral desmopressin acetate tablet**

8. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Basic metabolic panel
    b. Serum sodium is within the normal range
    c. 24-hour urine collection

9. There are **NO** FDA-label contraindications such as:
    a. Hyponatremia or a history of hyponatremia
    b. Polydipsia
    c. Simultaneous use with loop diuretics
    d. Simultaneous use with glucocorticoids, systemic or inhaled
    e. Estimated glomerular filtration rate less than 50 mL/min/1.73 m^2
    f. Known or suspected syndrome of inappropriate antidiuretic hormone (SIADH) secretion
    g. Use during an illness that can cause fluid or electrolyte imbalance such as gastroenteritis, systemic infection, or salt-wasting nephropathies
    h. Heart failure
    i. Uncontrolled hypertension

10. There is no history of urinary retention

11. The individual is not at risk for increased intracranial pressure

12. It is not being used for the treatment of nocturia of pregnancy

Initial approval duration: 1 carton of 30 sublingual tabs (3 blister cards of 10 tablets each) for 6 months

- **Criteria for continuation of coverage (renewal request):** Nocdurna (desmopressin acetate) oral sublingual tablet and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist, Urologist, or Endocrinologist

2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
    a. Achieved and maintains at least a 33% reduction in nocturia episodes per night

b. Achieved and maintains an increase in number of nights with no or at most 1-epsode of nocturia per night

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant or severe hyponatremia
   c. Severe fluid overload
   d. Seizures
   e. Respiratory arrest

Renewal duration: 1 carton of 30 sublingual tabs (3 blister cards of 10 tablets each) for 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Nocdurna (desmopressin acetate) oral sublingual tablet is a vasopressin analog indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void.

The International Continence Society (ICS) defines the symptom of nocturia as the complaint of awakening at night one or more times to void urine. Nocturia results from production of nocturnal urine that exceeds the capacity of the bladder to store it comfortably. Evidence suggests that nocturia becomes bothersome when an individual needs to void two or more times a night. It is important to note that nocturia is distinct from nocturnal enuresis which is voiding that occurs during sleep.

Many conditions cause or contribute to the symptom of nocturia. These include polyuria, sleep disorders, bladder storage disorders (BPH, OAB, or interstitial cystitis), diabetes mellitus, diabetes insipidus, heart failure, nephrotic syndrome, drugs, advancing age, and many others. Excessive fluid consumption of water, alcohol, and caffeine are also factors to consider when evaluating nocturia. With causes related to urine storage issues and with implementation of therapy for overactive bladder (OAB) or benign prostatic hypertrophy (BPH), the individual may still have nocturnal polyuria (NP). A cornerstone for the evaluation of nocturia is use of frequency-volume chart (FVC) to help characterize and identify the etiology of the symptom of nocturia. FVC quantifies the timing and volume of 24-hour and nocturnal urine output and can be used to calculate the nocturnal polyuria index (NPI). The

efficacy and safety of Nocdurna (desmopressin acetate) oral sublingual tablet have not been established for the treatment of all causes of nocturia; it is indicated only for patients who have nocturia due to nocturnal polyuria.

The normal physiologic pattern of urination is a decrease in nighttime urine output relative to daytime urine output. Overproduction of urine at night, with a normal 24-hour urine output, is called nocturnal polyuria. The ICS definition of NPI is nocturnal urine volume divided by the 24-hour urine volume. NP may be defined as voiding an abnormal nocturnal urine volume from the time of first sleep until the time of first void after arising in the morning. Younger adults with a NPI of greater than 20% and adults > 65 years of age with a NPI of greater than 33% have an abnormal NPI. However, the definition of NP and what is considered normal urine production are not universally agreed upon. Other definitions of NP include nocturnal urine volume > 6.4 mL/kg, nocturnal urine output > 0.9 mL/min, or nocturnal urine production (NUP) of > 90 mL/hour regardless of age.

Treatment of NP involves life-style modification to decrease the amount of urine produced at night. These life-style behaviors include void immediately before going to bed, avoid fluids (such as caffeine and alcohol) especially in the evening, take diuretic agent earlier (mid-afternoon), and elevate the legs in the evening to mobilize fluids. Pharmacologic treatment of nocturia due to NP includes use of desmopressin.

The anti-diuretic hormone (ADH), also known as arginine vasopressin (AVP) stimulates the reabsorption of fluid from renal tubules. Under normal conditions secretion of AVP follows a circadian rhythm and is released at night which would prevent nocturnal polyuria. Individuals with severe nocturia have been found to lack the normal nocturnal increase in AVP levels. Desmopressin is a synthetic analogue of AVP that acts on the distal renal tubule and collecting duct to reabsorb water during the night to reduce amount of urine and nocturia. Desmopressin can be administered by intranasal spray, oral tablets, or by injection. Oral desmopressin has demonstrated efficacy using doses ranging from 0.1-0.4 mg at bedtime. The dosage depends on the pharmaceutical formulation of the drug.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Polyuria:
Production of more than 2.8 L of urine in 24-hours for a 70 kg adult or 40 mL/kg of body weight

Nocturia:
Complaint of having to wake at night one or more times to void

Nocturnal polyuria:
A nocturnal polyuria index that exceeds 1/3 (33%) of the 24-hour urine production

Nocturnal Polyuria Index (NPI):
Nocturnal urine volume divided by the 24-hour urine volume
NPI of >33% for all ages indicates presence of nocturnal polyuria

Frequency volume chart (FVC):
Volumes voided and times of each void, throughout the day and night, for at least 24-hours

Some examples of concomitant medications that can increase the risk of hyponatremia, such as:

- Carbamazepine
- Chlorpromazine
- Chlorpropamide
- Lamotrigine
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Opiate analgesics
- Selective serotonin reuptake inhibitors
- Thiazide diuretics
- Tricyclic antidepressants

Resources:

Nocdurna (desmopressin acetate) sublingual tablet product information, revised by Antares Pharma, Inc. 11-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Bichet DG. Evaluation of patients with polyuria. In: UpToDate, Sterns RH, Emmett M, Forman JP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated February 13, 2024. Accessed March 05, 2025.

Johnson TM. Nocturia: Clinical presentation, evaluation, and management in adults. In: UpToDate, O'Leary MP, Law K (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through February 2025. Topic last updated February 15, 2023. Accessed March 05, 2025.

Suvada K, Plantinga L, Vaughan C, et al.: Comorbidities, Age, and Polypharmacy Limit the Use by US Older Adults with Nocturia of the Only FDA-approved Drugs for the Symptom. Clin Ther 2020 Dec; 42 (12):e259-e274. Doi: 10.1016/j.clinthera.2020.11.003. Accessed May 08, 2022. Re-evaluated March 05, 2025.