PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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NOCDURNA® (desmopressin acetate) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

NOCDURNA® (desmopressin acetate) oral

Criteria:

- **Criteria for initial therapy:** Nocdurna (desmopressin acetate) oral sublingual tablet is considered ***medically necessary*** and will be approved when **ALL** of 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. A confirmed diagnosis of nocturia due to nocturnal polyuria in an individual who awakens at least 2 times per night to void

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

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

  6. Individual has failure, contraindication per FDA label, intolerance to **oral desmopressin acetate**

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

  8. 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

  9. There is no history of urinary retention

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

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

Initial approval duration:

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

NOCDURNA® (desmopressin acetate) oral

- **Criteria for continuation of coverage (renewal request):** Nocdurna (desmopressin acetate) oral sublingual tablet is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  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 responded while on therapy
     a. Response is defined as **ONE** of the following:
        i. Achieved and maintains at least a 50% reduction in nocturia episodes per night
        ii. Achieves 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. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
     a. Contraindications as listed in the criteria for initial therapy section
     b. Significant adverse effect such as:
        i. Hyponatremia

  5. There are no significant interacting drugs

  Renewal duration:
  Nocdurna: 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 a Non-Cancer Medications**

  2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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

NOCDURNA® (desmopressin acetate) oral

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:

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

NOCDURNA® (desmopressin acetate) oral

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

Resources:

Desmopressin acetate tablet product information, revised by Apotex Corp. 03-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 13, 2021.

Nocdurna (desmopressin acetate) sublingual tablet product information, revised by Ferring Pharmaceuticals, Inc. 06-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on April 12, 2021.

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. Accessed on April 12, 2021.

Johnson TM. Nocturia: Clinical presentation, evaluation, and management of adults. In: UpToDate, O'Leary MP, Givens J (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on April 12, 2021.

Han J, Jung JH, Bakker CJ, et al. Desmopressin for treating nocturia in men. Cochrane Database Syst Rev 2017; 10:CD012059. Accessed on April 13, 2021.

Bergman AM, Sih AM, Weiss JP. Nocturia: An overview of evaluation and treatment. Bladder 2015; 2(2):1-5. Accessed on May 17, 2018. Re-reviewed on April 13, 2021.

Ebell MH, Radke T, Gardner J. A systematic review of the efficacy and safety of desmopressin for nocturia in adults. J Urol 2014; 192:829-835. Accessed on May 13, 2018. Re-reviewed on April 13, 2021.

Weiss JP, Blaivas JG, Blanker MH, et al.: The New England research Institutes, Inc (NERI) Nocturia Advisory Conference 2012: Focus on outcomes of therapy. BJU International 2013; 111:700-716. Accessed on May 17, 2018. Re-reviewed on April 13, 2021.

Cornu JN, Abrams P, Chapple CR, et al.: A contemporary assessment of nocturia: Definition, epidemiology, pathophysiology, and management – a systematic review and meta-analysis. Eur Urol 2012; 62: 877-890. . Accessed on March 22, 2017. Re-reviewed on April 13, 2021.

van Kerrebroeck P,Rezapour M, Cortesse A, et al.: Desmopressin in the Treatment of Nocturia: A double-blinded, placebo controlled study. Eur Urol 2007; 52:221-229. Accessed on March 20, 2017. Re-reviewed on April 13, 2021.