NOCTIVA™ (desmopressin acetate) nasal spray

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.

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Description:

Noctiva (desmopressin acetate) nasal spray is a vasopressin analog indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least two times per night to void. It has not been studied in individuals younger than 50 years of age.

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 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) > 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.

Noctiva (desmopressin acetate) nasal spray is available as a 0.83 mcg and 1.66 mcg nasal spray. The package label for Noctiva (desmopressin acetate) nasal spray indicates that the 0.83 mcg dose did not meet all pre-specified efficacy endpoints in clinical trials but may have a lower risk of hyponatremia. It also states that two sprays of 0.83 mcg are not interchangeable with one spray of 1.66 mcg. The labeling further states that the efficacy and safety of Noctiva (desmopressin acetate) nasal spray have not been established for all causes of nocturia. Noctiva (desmopressin acetate) nasal spray is indicated only for patients who have nocturia due to nocturnal polyuria.

**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 nocturnal urine production
NOCTIVA™ (desmopressin acetate) nasal spray (cont.)

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

Drug related events:
Ineffective / failure
Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

Adverse Drug Event: Allergic reaction / Hypersensitivity / Intolerance
Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

Allergic reaction / hypersensitivity – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

Intolerance – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

Contraindication
Use of a drug that is not recommended by the manufacturer or FDA labelling

Use of any drug in the face of a contraindication is outside of the FDA and manufacturer's labelled recommendation and is considered investigational or experimental
NOCTIVA™ (desmopressin acetate) nasal spray (cont.)

Non-adherence
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record

Precertification:

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

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.

Criteria:

See “Resources” section for FDA-approved dosage.

- Precertification for Noctiva (desmopressin acetate) nasal spray requires completion of the specific request form in its entirety. 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 will be returned.

- **Initial therapy:** FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Noctiva (desmopressin acetate) nasal spray is considered medically necessary when ALL of the following criteria are met:

  1. Individual is 50 years of age or older

  2. Medical record documentation of a confirmed diagnosis of nocturia due to nocturnal polyuria in an individual who awakens at least 2 times per night to void

  3. **ALL** of the following baseline tests have been completed before initiation of treatment:

     - Comprehensive metabolic panel
     - 24-hour urine collection
     - Nocturnal Polyuria Index (NPI) is > 33%

  4. Medical record documentation that the individual is unable to use **ALL** of the following due to failure, adverse drug event, or contraindication:
NOCTIVA™ (desmopressin acetate) nasal spray (cont.)

- Oral desmopressin acetate

5. Absence of ALL of the following contraindications:
   - Hyponatremia or a history of hyponatremia
   - Polydipsia
   - Primary nocturnal enuresis
   - Simultaneous use with loop diuretics
   - Simultaneous use with glucocorticoids, systemic or inhaled
   - Estimated glomerular filtration rate < 50 mL/min/1.73 m²
   - Known or suspected syndrome of inappropriate antidiuretic hormone secretion (SIADH) secretion
   - Use during an illness that can cause fluid or electrolyte imbalance such as gastroenteritis, systemic infection, or salt-wasting nephropathies
   - New York Heart Association (NYHA) Class II-IV congestive heart failure
   - Uncontrolled hypertension

6. Absence of ALL of the following exclusions:
   - History of urinary retention
   - Individual at risk for increased intracranial pressure
   - Use in individual who requires another drug that is administered via the nasal route
   - Use in individual with atrophy of nasal mucosa
   - Use in individual with chronic rhinitis
   - Use in individual with acute rhinitis, unless the condition has resolved
   - Woman of child bearing age who is pregnant, unless uses appropriate contraception

➢ Continuation of coverage (renewal request): Noctiva (desmopressin acetate) nasal spray is considered medically necessary with documentation of ALL of the following:
   1. The individual has benefited from therapy but remains at high risk
   2. The condition has not progressed or worsened while on therapy
   3. Individual has not developed any contraindications or other exclusions to its continued use

➢ Noctiva (desmopressin acetate) nasal spray for all other indications not previously listed is considered experimental or investigational based upon:
   1. Lack of final approval from the Food and Drug Administration, and
   2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
   3. Insufficient evidence to support improvement of the net health outcome, and
   4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
   5. Insufficient evidence to support improvement outside the investigational setting.
NOCTIVA™ (desmopressin acetate) nasal spray (cont.)

Resources:


Barkin J. Nocturia: Diagnosis and management for the primary care physicians. Can J Urol 2016; 23 (Suppl 1)16-19

FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<tr>
<td>NOCTIVA (desmopressin acetate) nasal spray 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.</td>
<td>• For patients younger than 65 years of age who are not at increased risk for hyponatremia: The recommended dose is one spray of NOCTIVA 1.66 mcg in either the left or right nostril approximately 30 minutes before going to bed</td>
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<td>It has not been studied in individuals younger than 50 years of age.</td>
<td>• For patients ≥65 years of age, or younger patients at increased risk for hyponatremia: The recommended starting dose is one spray of NOCTIVA 0.83 mcg in either the left or right nostril approximately 30 minutes before going to bed</td>
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<td>After at least 7 days of treatment, the dose can be increased to 1.66 mcg, if needed, provided the serum sodium is within the normal range during treatment with the 0.83 mcg dose</td>
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