

## PRIOR AUTHORIZATION WITH STEP THERAPY POLICY

- POLICY:** Desmopressin Products – Noctiva Prior Authorization with Step Therapy Policy
- Noctiva™ (desmopressin acetate nasal spray for intranasal use [0.83 mcg/0.1 mL and 1.66 mcg/0.1 mL] – Avadel)

**REVIEW DATE:** 10/07/2020

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### OVERVIEW

Noctiva, a vasopressin analog, is indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least two times per night to void.<sup>1</sup> A limitation of use is that the agent has not been studied in patients < 50 years of age.

### Disease Overview

Nocturnal polyuria is defined as nocturnal urine volume exceeding 33% of the total 24-hour urine volume in patients ≥ 65 years of age or exceeding 20% of 24-hour urine volume in younger patients.<sup>2</sup> Nocturnal polyuria may improve via lifestyle and behavior modifications, which should be implemented prior to pharmacotherapy.<sup>3</sup> Such modifications include minimizing fluid intake before bed (particularly caffeine and alcohol), restriction of total fluid consumption, emptying the bladder before bed, increasing exercise and fitness levels, earlier dosing of medications such as diuretics, and elevating the legs above heart level for a few hours before going to bed (for patients with peripheral edema).

### Safety

Noctiva has a Boxed Warning regarding hyponatremia.<sup>1</sup> Noctiva is contraindicated in patients with hyponatremia or among those with a history of hyponatremia. Also, patients with polydipsia or primary nocturnal enuresis should not use Noctiva. Do not administer Noctiva concomitantly with loop diuretics or with systemic or inhaled glucocorticoids. Patients with renal impairment with an estimated glomerular filtration rate below 50 mL/min/1.73 m<sup>2</sup> should not use Noctiva. Those with known or suspected syndrome of inappropriate antidiuretic hormone secretion should not use Noctiva. Do not utilize Noctiva during illnesses that may cause fluid or electrolyte imbalance, such as gastroenteritis, salt-wasting nephropathies, or systemic infection. Noctiva is contraindicated in patients with congestive heart failure (CHF) [New York Heart Association {NYHA} class II to IV] or among those with uncontrolled hypertension because the fluid retention in these conditions increases the risk of worsening the underlying condition. Also, Noctiva is not recommended in patients at risk for increased intracranial pressure or those with a history of urinary retention, and should be used with caution (e.g., monitoring of volume status) in patients with NYHA class I CHF. Noctiva is contraindicated for the treatment of primary nocturnal enuresis because of reports of hyponatremic-related seizures in pediatric patients treated with other intranasal formulations of desmopressin. Trials involving Noctiva have not been performed in pediatric patients.

### Guidelines

A consensus statement on the diagnosis and treatment of nocturia was published by the International Continence Society in 2019.<sup>2</sup> There was consensus that fluid restriction should be advised for all desmopressin-treated patients. Newer desmopressin formulations, including Nocurna® (desmopressin acetate sublingual tablets [27.7 mcg and 55.3 mcg]) and Noctiva, are generally regarded as low-dose desmopressin. Low-dose formulations are appropriate in the absence of contraindications to desmopressin therapy. Oral desmopressin tablets are cited as another formulation in the consensus statement (available as 100 mcg and 200 mcg tablets in the US). This is noted to be an option for certain patients, although lower-dose formulations should be used when concomitant hyponatremia risk factors are present. Of note,

it is uncertain how the pharmacokinetic profile of Noctiva aligns with the other FDA-approved nasal desmopressin products because there are no comparative bioavailability studies and Noctiva contains a novel excipient, cyclopentadecanolide, which enhances absorption.<sup>1</sup> The consensus statement suggests that pharmacodynamic and pharmacokinetic studies in nocturia patients during an overnight evaluation would be ideal to characterize plasma desmopressin levels and rationale for dose differentiation.<sup>2</sup>

### **POLICY STATEMENT**

Prior authorization is recommended for prescription benefit coverage of Noctiva. All approvals are provided for the duration noted below. Due to the specialized skills required for evaluation and diagnosis of patients treated with Noctiva well as the monitoring required for adverse events and long-term efficacy, approval requires Noctiva to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

### **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of Noctiva is recommended in those who meet the following criteria:

#### **FDA-Approved Indications**

- 1. Nocturia due to Nocturnal Polyuria.** Approve for 1 year if the patient meets all of the following criteria (A, B, C, D, E, F, G and H):
  - A)** Patient is  $\geq 50$  years of age; AND
  - B)** The diagnosis of nocturnal polyuria has been confirmed with a 24-hour urine collection before treatment initiation and the patient meets one of the following (i or ii):
    - i.** The nocturnal urine volume exceeds 20% of the total 24-hour urine volume in patients  $< 65$  years of age; OR
    - ii.** The nocturnal urine volume exceeds 33% of the total 24-hour urine volume in patients  $\geq 65$  years of age; AND
  - C)** Prior to desmopressin therapy, patient awakens at least two times per night to void; AND
  - D)** Patient has serum sodium concentrations within the normal range (135 to 145 mmol/L); AND
  - E)** Prescriber has verified that the patient does not have the following conditions/circumstances in which use of Noctiva is not recommended (i, ii, iii, iv, v, or vi):
    - i.** Currently receiving loop diuretics (e.g., furosemide, torsemide, bumetanide); OR
    - ii.** Currently receiving systemic or inhaled glucocorticoids; OR
    - iii.** Renal impairment with an estimated glomerular filtration rate  $< 50$  mL/min/1.73 m<sup>2</sup>; OR
    - iv.** New York Heart Association class II to IV congestive heart failure; OR
    - v.** Polydipsia; OR
    - vi.** Known or suspected syndrome of inappropriate antidiuretic hormone secretion; AND
  - F)** Patient has tried non-pharmacologic techniques or lifestyle interventions to manage the nocturia; AND  
Note: Examples of non-pharmacologic techniques include nighttime fluid restriction, avoidance of caffeine and alcohol, earlier timing of medications, leg elevation, or use of compression stockings.
  - G)** Patient tried one of Nocturna (desmopressin acetate sublingual tablets) or oral desmopressin acetate tablets (DDAVP tablets, generics); AND
  - H)** Noctiva is prescribed by or in consultation with a urologist, geriatrician, or endocrinologist.

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Coverage of Noctiva is not recommended in the following situations:

1. **Primary Nocturnal Enuresis.** Use of Noctiva is contraindicated for the treatment of patients with primary nocturnal enuresis.<sup>1</sup> Reports of hyponatremia-related seizures have occurred in pediatric patients treated with other intranasal formulations of desmopressin.
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

**REFERENCES**

1. Noctiva™ nasal spray [prescribing information]. Chesterfield, MO: Avadel; December 2017.
2. Everaert K, Hervé F, Bosch R, et al. International Continence Society consensus on the diagnosis and treatment of nocturia. *Neurourol Urodyn*. 2019 Feb;38(2):478-498.
3. Weiss JP, Everaert K. Management of nocturia and nocturnal polyuria. *Urology*. 2019;133S:24-33.