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Coverage Policy Number **IP0132**

Desmopressin Nasal Spray

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for desmopressin acetate nasal spray (**Noctiva**™) for intranasal use.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Desmopressin acetate nasal spray (Noctiva) is considered medically necessary when the following are met:

1. **Nocturia due to Nocturnal Polyuria.** Individual meets **ALL** of the following criteria:
   A. Age 50 years or older
   B. Documented diagnosis of nocturnal polyuria confirmed by 24-hour urine collection before treatment initiation and the individual meets **ONE** of the following:

i. The nocturnal urine volume exceeds 20% of the total 24-hour urine volume in an individual less than 65 years of age
ii. The nocturnal urine volume exceeds 33% of the total 24-hour urine volume in an individual 65 years of age or older

C. Prior to desmopressin therapy, individual awakens at least 2 times per night to void
D. Has serum sodium concentrations within the normal range (135 to 145 mmol/L)
E. Prescriber has verified that the individual does not have the following conditions/circumstances in which use of Noctiva is not recommended:
i. Currently receiving loop diuretics (for example, furosemide, torsemide, bumetanide)
ii. Currently receiving systemic or inhaled glucocorticoids
iii. Renal impairment with an estimated glomerular filtration rate < 50 mL/min/1.73 m^2
iv. New York Heart Association class II to IV congestive heart failure
v. Polydipsia
vi. Known or suspected syndrome of inappropriate antidiuretic hormone secretion
F. Has tried non-pharmacologic techniques or lifestyle interventions to manage the nocturia (for example, nighttime fluid restriction, avoidance of caffeine and alcohol, earlier timing of medications, leg elevation, or use of compression stockings)
G. Medication is being prescribed by, or in consultation with, a urologist, geriatrician, or endocrinologist

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When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of desmopressin nasal spray (Noctiva) is considered medically necessary for the treatment of nocturia due to nocturnal polyuria when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months.
Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

Primary Nocturnal Enuresis. Use of Noctiva is contraindicated for the treatment of individuals with primary nocturnal enuresis.[1] Reports of hyponatremia-related seizures have occurred in pediatric individuals treated with other intranasal formulations of desmopressin.

Background

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.[1] Before initiating therapy, it is recommended that the diagnosis of nocturnal polyuria has been confirmed with a 24-hour urine collection. 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.[2] Nocturnal polyuria may improve via lifestyle and behavior modifications, which should be implemented prior to pharmacotherapy.[3] 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.[1] Use of Noctiva is contraindicated in patients at increased risk of severe hyponatremia such as patients with excessive fluid intake, illness that may cause fluid or electrolyte imbalances, and in patients using loop diuretics or systemic or inhaled glucocorticoids. It is recommended to check serum sodium concentrations prior to initiating or resuming Noctiva and throughout treatment. If hyponatremia occurs, Noctiva may need to be temporarily or permanently discontinued. Noctiva is contraindicated in patients with hyponatremia and 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^2 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] and 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 hyponatremia-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.[2] There was consensus that fluid restriction should be advised for all desmopressin-treated patients. Newer desmopressin formulations, including Nocdurna® (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).[2] 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.[1] 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.[2]

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;38(2):478-498.
3. Weiss JP, Everaert K. Management of nocturia and nocturnal polyuria. *Urology*. 2019;133S:24-33.