Effective Date **6/1/2023**
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Coverage Policy Number **IP0110**

Droxidopa

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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 droxidopa (**Northera**®).

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

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

Medical Necessity Criteria

Droxidopa (Northera) is considered medically necessary when the following are met:

Neurogenic Orthostatic Hypotension (NOH). Individual meets **ALL** of the following criteria:

A. 18 years of age or older
B. Symptomatic neurogenic orthostatic hypotension (NOH) caused by **ONE** of the following:

i. Primary autonomic failure (Parkinson's disease [PD], multiple system atrophy, and pure autonomic failure)
ii. Dopamine beta-hydroxylase deficiency
iii. Non-diabetic autonomic neuropathy

C. Documented diagnosis of Neurogenic Orthostatic Hypotension (NOH) is confirmed by a sustained decrease in systolic blood pressure of at least 20 mmHg or diastolic blood pressure of at least 10 mmHg within 3 minutes of standing **OR** during a head-up tilt-table test
D. Non-pharmacological measures including, but not limited to, elevation of the head of the bed, orthostatic compression garments, and appropriate physical training have been initiated
E. Documentation of failure, contraindication, or intolerance to **TWO** of the following:
i. atomoxetine
ii. dihydroergotamine
iii. fludrocortisone
iv. indomethacin
v. midodrine
vi. pyridostigmine
F. Medication is prescribed by, or in consultation with, a cardiologist, nephrologist, or neurologist
G. Non-Covered Product Criteria is met, refer to below table(s)

Employer Group Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Northera (droxidopa)	Documentation of trial of **droxidopa capsule** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

Individual and Family Plan Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Northera (droxidopa)	Documentation of trial of **droxidopa capsule** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

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

Droxidopa (Northera) is considered medically necessary for continued use when initial 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.

Background

OVERVIEW
Northera, a norepinephrine-type product, is indicated for the treatment of orthostatic dizziness, lightheadedness, or the "feeling that one is about to black out" in adults with symptomatic **neurogenic orthostatic hypotension (NOH)** caused by primary autonomic failure (Parkinson's disease, multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy.[1]

Disease Overview
Orthostatic hypotension (OH) is a sustained reduction in systolic blood pressure (SBP) of at least 20 mmHg or diastolic blood pressure (DBP) of 10 mmHg within 3 minutes of standing or head-up tilt to at least 60° on a tilt table.[2] OH may be symptomatic or asymptomatic, with only symptomatic OH requiring treatment. NOH is a specific subset of this condition, in which OH is due to inadequate release of norepinephrine from sympathetic vasomotor neurons leading to vasoconstrictor failure. NOH is a rare, chronic and often debilitating condition that is associated with Parkinson's disease, multiple system atrophy, and pure autonomic failure, and with peripheral neuropathies and ganglionopathies that affect the autonomic nerves.[2-4] Symptoms of NOH include dizziness, lightheadedness, blurred vision, fatigue, and fainting upon standing up. These symptoms can adversely affect patients' quality of life and ability to conduct activities of daily living that involve standing or walking. Treatment of symptomatic NOH is aimed at increasing standing systolic blood pressure into the range of compensatory cerebrovascular autoregulation (approximately 50 to 150 mmHg).[5] Unapproved pharmacologic agents include fludrocortisone, dihydroergotamine (oral), indomethacin (oral or intravenous), pyridostigmine, and atomoxetine.[2-4,6] Midodrine, an alpha$_1$-agonist, is the only other medication approved with a similar indication (treatment of symptomatic orthostatic hypotension) to Northera.[7]

Guidelines
Consensus panel recommendations initiated by the American Autonomic Society and the National Parkinson Foundation for the screening, diagnosis, and treatment of NOH and associated supine hypertension were published in 2017.[8] Once a patient is diagnosed with NOH, the goals of treatment should be to reduce the burden of symptoms (especially falls), prolong standing time, and restore independence in activities of daily living. The recommendations propose a four-step treatment algorithm for NOH: assessing and adjusting preexisting medications that may be causing or exacerbating NOH, utilizing non-pharmacologic approaches (e.g., blood volume repletion, increased salt intake, physical conditioning, compression garments, elevating the head of the bed), implementing single-agent pharmacologic treatment, and with great caution, combining pharmacologic treatments. Recommended treatments include midodrine, Northera, fludrocortisone, and pyridostigmine. The initial choice of NOH treatments should be individualized and should consider severity, comorbid disease (especially cardiac or renal failure), and treatment goals. Based on the experience of the consensus panel, the recommendation is to titrate to maximum tolerable dose of a single medication and then, if symptomatic benefit is not obtained, consider switching to a different medication or adding a second agent and titrate from its lowest starting dose.

References

1. Northera® [prescribing information]. Deerfield, IL: Lundbeck; February 2017.
2. Freeman R, Wieling W, Axelrod FB, et al. Consensus statement on the definition of orthostatic hypotension, neutrally mediated syncope and the postural tachycardia syndrome. *Clin Auton Res.* 2011;21(2):69-72
3. Wieling W, Kaufmann H, Claydon et al. Diagnosis and treatment of orthostatic hypotension. *Lancet Neurol*. 2022; 21(8):735-746.
4. Peixoto AJ. Evaluation and management of orthostatic hypotension: Limited data, limitless opportunity. *Cleve Clin J Med*. 2022; 89(1):36-45.
5. Cipolla MJ. The cerebral circulation. San Rafael (CA): Morgan & Claypool Life Sciences; 2009. Available at: http://www.ncbi.nlm.nih.gov/books/NBK53081/. Accessed on December 5, 2022.
6. Merative Micromedex®. © 2022 Merative. Available at: https://www.micromedexsolutions.com. Accessed on December 12, 2022. Search terms: dihydroergotamine and indomethacin.
7. ProAmatine® tablets [prescribing information]. Lexington, MA: Shire; January 2017.

8. Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. *J Neurol*. 2017; 264(8):1567-1582.