Original Effective Date: 07/01/2018
Current Effective Date: 04/06/2024
Last P&T Approval/Version: 01/31/2024
Next Review Due By: 01/2025
Policy Number: C13402-A

Northera (droxidopa)

PRODUCTS AFFECTED

Northera (droxidopa), droxidopa

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Symptomatic neurogenic orthostatic hypotension (NOH)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. NEUROGENIC ORTHOSTATIC HYPOTENSION (NOH)

1. Documented diagnosis of symptomatic neurogenic orthostatic hypotension (NOH) due to primary autonomic failure (Parkinson’s disease [PD], multiple system atrophy [MSA], pure autonomic failure

[PAF]), dopamine beta-hydroxylase deficiency, or nondiabetic autonomic neuropathy
AND
2. Prescriber attests the member has initiated non-pharmacological measures including, but not limited to: elevation of the head of the bed, orthostatic compression garments, and appropriate physical training
AND
3. Documentation member has tried midodrine AND ONE of the following other medications: fludrocortisone, desmopressin, dihydroergotamine, indomethacin, pyridostigmine, erythropoietin OR member has a labeled contraindication or serious side effects to ALL of the following: midodrine, fludrocortisone, desmopressin, dihydroergotamine, indomethacin, pyridostigmine, and erythropoietin

CONTINUATION OF THERAPY:
A. NEUROGENIC ORTHOSTATIC HYPOTENSION (NOH)
1. Documentation of recent re-assessment and medical necessity for the use beyond 2 weeks of treatment [DOCUMENTATION REQUIRED]
AND
2. Prescriber attests to improvement in the symptoms of neurogenic orthostatic hypotension, such as decreased dizziness, decreased lightheadedness, decreased fainting
AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial: 2 weeks (14 days), Continuation of therapy: 2 weeks (14 days)
Per label, effectiveness for use beyond 2 weeks of treatment has not been established and continued effectiveness should be assessed periodically.

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified cardiologist, neurologist, or nephrologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
600 mg three times daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Neurogenic Orthostatic Hypotension (NOH) - Agents

FDA-APPROVED USES:
NORTHERA is indicated for the treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic neurogenic orthostatic hypotension (nOH)

caused by primary autonomic failure (Parkinson's disease [PD], multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy.

Effectiveness beyond 2 weeks of treatment has not been established. The continued effectiveness of NORTHERA should be assessed periodically.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

NON-PHARMACOLOGIC MEASURES FOR TREATMENT OF OH *Discontinuation of medications that may cause or exacerbate OH*
Alpha blockers (e.g., terazosin)
Antidepressants (e.g., SSRIs, trazodone, MAOIs, tricyclic antidepressants)
Antihypertensive drugs (e.g., sympathetic blockers)
Antiparkinsonism drugs (e.g., levodopa, pramipexole, ropinirole)
Antipsychotic drugs (e.g., olanzapine, risperidone)
Beta-blocker drugs (e.g., propranolol)
Diuretics (e.g., hydrochlorothiazide, furosemide)
Skeletal muscle relaxants (e.g., tizanidine)
Narcotic analgesics (e.g., morphine)
Phosphodiesterase inhibitors (e.g., sildenafil, tadalafil)
Sedatives/hynotics (e.g., temazepam)
Vasodilators (e.g., hydralazine, nitroglycerin, calcium channel blockers)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
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 adult patients with symptomatic neurogenic orthostatic hypotension (NOH) caused by primary autonomic failure (Parkinson’s disease [PD], multiple system atrophy [MSA], pure autonomic failure [PAF]), dopamine beta- hydroxylase deficiency, and non-diabetic autonomic neuropathy. The effectiveness beyond 2 weeks of treatment has not been established. The effectiveness of Northera should be evaluated periodically. The mechanism of action of Northera is unknown. Northera is a synthetic amino acid analog that is metabolized to norepinephrine by dopa decarboxylase, which is found throughout the body. Northera is thought to exert its effects through norepinephrine, which increases blood pressure (BP) by inducing peripheral arterial and venous vasoconstriction.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Northera (droxidopa) are considered experimental/investigational and therefore, will follow Molina’s Off- Label policy. Contraindications to Northera (droxidopa) include: history of hypersensitivity to the drug or its ingredients.

OTHER SPECIAL CONSIDERATIONS:
Northera has a black box warning for supine hypertension. Monitor supine blood pressure prior to and during treatment and more frequently when increasing doses. Elevating the head of the bed lessens the risk of

supine hypertension, and blood pressure should be measured in this position. If supine hypertension cannot be managed by elevation of the head of the bed, reduce or discontinue Northera.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Northera CAPS 100MG, 200MG, 300MG
Droxidopa CAPS 100MG, 200MG, 300MG

REFERENCES

1. Northera (droxidopa) [prescribing information]. Deerfield, IL: Lundbeck NA Ltd; July 2019.
2. FDA Briefing Document: Cardiovascular and Renal Drug Advisory Committee Meeting. Accessed March 2018. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/CardiovascularandRenalDrugsAdvisoryCommittee/UCM381154.pdf
3. Berger, MJ, Kimpinski. K. A practical guide to the treatment of neurogenic orthostatic hypotension. Can J Neurol Sci 2014; 41:156.
4. Chisholm P, Anpalahan M. Orthostatic hypotension - pathophysiology, assessment, treatment, and the paradox of supine hypertension - a review. Available at: Intern Med J2017 Apr;47(4):370 Accessed March 2018
5. Biaggioni et al. Randomized withdrawal study of patients with symptomatic neurogenic orthostatic hypotension responsive to droxidopa. Hypertension 2015; 65:101.
6. Isaacson S, Skettini J. Neurogenic orthostatic hypotension in Parkinson's disease: evaluation, management, and emerging role of droxidopa. Vasc Health Risk Manag2014;10:169-76.
7. Kaufmann H et al. (2014): Droxidopa for neurogenic orthostatic hypotension; A randomized, placebo-controlled, phase 3 trial. Neurology 83:328-335.
8. Metzler M, Granata R, Robertson D. Neurogenic orthostatic hypotension: pathophysiology, evaluation, and management. J Neurol 2013;260:2212-9.
9. RA Hauser et al. Droxidopa for the short-term treatment of symptomatic neurogenic orthostatic hypotension in Parkinson's disease (nOH306B). Mov Disord 2015; 30:646.
10. Shill H, Vernino S, Hutchman R, Adkins L, Isaacson S. A multicenter, open-label study to assess the long-term safety of droxidopa in patients with symptomatic neurogenic orthostatic hypotension (NOH 304) [abstract]. Mov Disord. 2012;27(suppl 1):S428.
11. Abramowicz, M. ed. Droxidopa (Northera) for Neurogenic Orthostatic Hypotension. The Medical Letter on Drugs and Therapeutics. Med Lett Drugs Ther. 2015 Jun 22;57(1471):92-3
12. Jankovic J, Gilden JL, Hiner BC, et al. Neurogenic orthostatic hypotension: a double-blind, placebo-controlled study with midodrine. Am J Med 1993;95:38-48.
13. Low PA, Gilden JL, Freeman R, Sheng KN, McElligott MA. Efficacy of midodrine vs placebo in neurogenic orthostatic hypotension. A randomized, double-blind multicenter study. Midodrine Study Group. JAMA 1997;277:1046-51.
14. Low PA, Wolfgang S. Update on management of neurogenic orthostatic hypotension. Lancet Neurol 2008;7:451-8.
15. Wright RA, Kaufmann HC, Perera R, et al. A double-blind, dose-response study of midodrine in

neurogenic orthostatic hypotension. Neurology 1998;51:120-4.
16. Task Force for the Diagnosis and Management of Syncope, European Society of Cardiology (ESC), European Heart Rhythm Association (EHRA), Heart Failure Association (HFA), Heart Rhythm Society (HRS). Moya A, Sutton R, Ammirati F, et al. Guidelines for the diagnosis and management of syncope (version 2009). Eur Heart J. 2009 Nov;30(21):2631-71. Accessed March 2018
17. Freeman R, Wieling W, Axelrod FB, Benditt DG, Benarroch E, Biaggioni I, et al. Consensus statement on the definition of orthostatic hypotension, neutrally mediated syncope and the postural tachycardia syndrome. Clin Auton Res. 2011;21:69-72.
18. Lahrmann H, Cortelli P, Hilz M, Mathias CJ, Struhal W,Tassinari M. Orthostatic hypotension. In:Gilhus NE, Barnes MP, Brainin M, eds. European Handbook of Neurological Management, 2nded, vol. 1. Oxford, UK: Wiley-Blackwell. 2011:469-475.
19. Gibbons, C. H., Schmidt, P., Biaggioni, I., Frazier-Mills, C., Freeman, R., Isaacson, S., Karabin, B., Kuritzky, L., Lew, M., Low, P., Mehdirad, A., Raj, S. R., Vernino, S., & Kaufmann, H. (2017). The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. Journal of neurology, 264(8), 1567– 1582. https://doi.org/10.1007/s00415-016-8375-x
20. Eschlböck, S., Wenning, G., & Fanciulli, A. (2017). Evidence-based treatment of neurogenic orthostatic hypotension and related symptoms. Journal of Neural Transmission (Vienna, Austria: 1996), 124(12), 1567–1605. https://doi.org/10.1007/s00702-017-1791-y

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Quantity Background Other Special Considerations Available Dosage Forms References	Q1 2024
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Prescriber Requirements Quantity Contraindications/Exclusions/Discontinuation References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file