BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 1/22/15**
SECTION: DRUGS	**LAST REVIEW DATE: 1/18/18**
	LAST CRITERIA REVISION DATE: 1/18/18
	ARCHIVE DATE:

NORTHERA™ (droxidopa) oral capsule

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.

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.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. 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 or forms without the chart notes will be returned.**

NORTHERA™ (droxidopa) oral capsule (cont.)

Description:

Northera (droxidopa) 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 (MSA), and pure autonomic failure (PAF)], dopamine beta-hydroxylase deficiency, and non-diabetic autonomic neuropathy. The effectiveness of Northera (droxidopa) beyond 2 weeks of treatment has not been established, continued effectiveness of Northera (droxidopa) should be assessed periodically.

Northera (droxidopa) is a synthetic amino acid analog that is directly metabolized to norepinephrine by dopa-decarboxylase, which is extensively distributed throughout the body. It is believed to exert its effects through norepinephrine and not through the parent molecule. Norepinephrine increases blood pressure by inducing peripheral arterial and venous vasoconstriction.

Use of Northera (droxidopa) is associated with a risk of increased blood pressure while lying down (supine hypertension), individuals must sleep with their head and upper body elevated. In addition, it may exacerbate existing ischemic heart disease, arrhythmias, and congestive heart failure.

Orthostatic hypotension

- Orthostatic hypotension may be categorized as neurogenic or non-neurogenic in origin
- Non-neurogenic causes include disorders that result in cardiac impairment, reduced intravascular volume and electrolyte loss, venous pooling/vasodilation, and iatrogenic from use of numerous medications
    - Age related orthostatic hypotension is considered a non-neurogenic cause of orthostatic hypotension
- Neurogenic causes include Parkinson's disease (PD), pure autonomic failure (PAF), and multiple system atrophy (MSA)
- Orthostatic hypotension is a physical finding and is defined as a documented decrease of $\geq$ 20 millimeters of mercury (mmHg) in systolic blood pressure (SBP) or a $\geq$ 10 mmHg decrease in diastolic blood pressure (DBP) within 3 minutes upon standing or a head-up tilt on a tilt table
- Symptoms of orthostatic hypotension include dizziness, lightheadedness, blurred vision, fatigue and fainting when a person stands
- There are known predisposing factors that cause or contribute to orthostatic hypotension such as dehydration, deconditioning, poor nutrition, aging, and others, as well as numerous drugs such as diuretics, antihypertensive agents, anti-anginal agents, antidepressants, alpha-blockers, and others
- Management of orthostatic hypotension involves liberalizing and maximizing fluid and sodium intake (where appropriate), elevation of head of the bed, a comprehensive review of medications used to reduce the doses or discontinue agents that contribute to orthostatic hypotension (if safe to do so), patient education on how to change position from supine to standing in gradual stages, and use of fitted elastic stockings

NORTHERA™ (droxidopa) oral capsule (cont.)

- Pharmacologic agents used to treat orthostatic hypotension include fludocortisone and midodrine

- Midodrine is the only other FDA-approved medication for symptomatic orthostatic hypotension
  - Midodrine is a direct acting agonist for peripheral alpha-1 adrenoreceptors
  - It is a pro-drug that is activated to desglymidodrine, the active receptor agonist
    - Desglymidodrine is 15 times more potent than the parent compound and is primarily responsible for the therapeutic effect
  - The pressor effect is due to both arterial and venous constriction
  - The dose should be titrated from 2.5 mg to 10 mg three times a day

- Fludrocortisone is commonly used off-label to treat orthostatic hypotension
  - Fludrocortisone, is a synthetic mineralocorticoid, is considered agent of first choice for orthostatic hypotension and is used in individuals who are not are unable to increase plasma volume effectively with liberalized fluid and salt intake
  - It has a long duration of action and is well-tolerated by most individuals
  - Fludrocortisone increases blood volume and enhances the sensitivity of blood vessels to circulating catecholamines
  - Other potential actions include enhancing norepinephrine release from sympathetic neurons and increasing vascular fluid content
  - Treatment is initiated with a 0.1 mg tablet and can be increased to 1 mg daily although little benefit is obtained by increasing beyond 0.5 mg daily

- Other off-label treatments that are less commonly used include ephedrine, desmopressin, dihydroergotamine, erythropoietin, indomethacin, octreotide, pyridostigmine, and yohimbine

Northera (droxidopa)

Medication class:
Alpha-Beta agonist

FDA-approved indication(s):
- Treatment of orthostatic dizziness, light-headedness, or the "feeling that you are about to black out" in adults with symptomatic neurogenic orthostatic hypotension (NOH) caused by primary autonomic failure (Parkinson disease, multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, and nondiabetic autonomic neuropathy

Recommended Dose:
- Initial dose: 100 mg three time daily, titrate using 100 mg three times daily increments every 24-48 hours, the last dose of the day should be given at least 3 hours before bedtime

Maximum dosage
- 600 mg three times daily

NORTHERA™ (droxidopa) oral capsule (cont.)

Available Dosage Forms:
- 100 mg, 200 mg, and 300 mg capsules

Warnings, Precautions, and other Clinical Information:
- The effectiveness of Northera beyond 2 weeks of treatment has not been established
- Reduce dose or discontinue Northera if supine hypertension cannot be managed by elevation of the head of the bed
- Dosing recommendations cannot be given for individual with GFR of < 30 mL/min
- A symptom complex of hyperpyrexia and confusion resembling neuroleptic malignant syndrome (NMS) has been reported with use of Northera
- Discontinue Northera if a hypersensitivity reaction occurs
- Northera contains a tartrazine dye which can cause allergic-type reactions, especially in patients who have aspirin hypersensitivity
- Woman who is breast feeding an infant or child should stop breast feeding
- Non-selective MAO inhibitors and linezolid should be avoided
- Northera is not indicated for the treatment of drug induced orthostatic hypotension

Criteria:

- **Criteria for initial therapy:** Northera (droxidopa) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a either a Neurologist or a Cardiologist

2. Individual is 18 years of age or older

3. A confirmed diagnosis of neurogenic orthostatic hypotension (NOH) caused by **ONE** of the following conditions:
   - Parkinson's disease
   - Multiple system atrophy
   - Pure autonomic failure
   - Dopamine beta-hydroxylase deficiency
   - Non-diabetic neuropathy

4. Orthostatic hypotension is documented as a decrease of ≥ 20 millimeters of mercury (mmHg) in systolic blood pressure (SBP) or a ≥ 10 mmHg decrease in diastolic blood pressure (DP) within 3 minutes upon standing or head-up tilt on a tilt table

5. There are symptoms of orthostatic dizziness, lightheadedness, or feelings of about to black out

6. Non-pharmacologic measures have been maximized:
   - Non-pharmacologic factors include:
     - Intake of fluid and salt has been liberalized or maximized, where appropriate
     - Uses fitted elastic/compression stockings or abdominal binder, unless contraindicated
     - Head of the bed has been elevated

NORTHERA™ (droxidopa) oral capsule (cont.)

- Individual instructed on how to change position from supine to standing in gradual stages

7. A comprehensive medication review has been performed to either reduce or discontinue agents that contribute or cause orthostatic hypotension, if clinically safe to do so

8. Individual has failure, contraindication or intolerance to simultaneous use of **fludrocortisone AND midodrine**

Initial approval duration: 1 month, renewal requires documentation of reduction in orthostatic symptoms **and** an increase in blood pressure for approval

- **Criteria for continuation of coverage (renewal request):** Northera (droxidopa) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a Neurologist or a Cardiologist

2. Individual's condition responded while on therapy
   - Response is defined as:
     - There is a sustained reduction in dizziness, lightheadedness, feeling faint, or feeling like the patient my black out **and** an increase 10 SBP within 3 min of standing

3. Individual has been adherent with the medication and all non-pharmacologic measures as deemed appropriate for the individual patient

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
   - Significant adverse effect such as:
     - NMS-like reaction with hyperpyrexia and confusion
       - Signs and symptoms may include: high fever, stiff muscles, muscle rigidity, involuntary movements, confusion, altered consciousness, mental status changes, sweating, changes in pulse, heart rate, and blood pressure
     - Hypersensitivity
       - Signs and symptoms may include: hives over neck and face, itching, nasal congestion, difficulty breathing, swelling of lips, mouth, tongue or throat

5. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

Northera. Package Insert. Revised by manufacturer 08/2014. Accessed 01/08/2015.

Northera. Package Insert. Revised by manufacturer 11/2016. Accessed 12/05/2016.

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Northera. Package Insert. Revised by manufacturer 02/2017. Accessed 12/11/2017.

UpToDate: Mechanisms, causes, and evaluation of orthostatic hypotension. Current through Oct 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/mechanisms-causes-and-evaluation-of-orthostatic-hypotension?source=search_result&search=neurogenic%20orthostatic%20hypotension&selectedTitle=2~150#H5755741

UpToDate: Treatment of orthostatic hypotension and postprandial hypotension. Current through Oct 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-orthostatic-and-postprandial-hypotension?source=search_result&search=neurogenic%20orthostatic%20hypotension&selectedTitle=1~150#H17

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.