droxidopa (Northera ®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: UMP122

Description

Droxidopa (Northera ®) is a synthetic amino acid analog that is metabolized to a norepinephrine by the enzyme aromatic L-amino acid decarboxylase (dopa-decarboxylase). Norepinephrine increases blood pressure by inducing peripheral arterial and venous vasoconstriction.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
droxidopa (Northera)	100 mg capsules	neurogenic orthostatic hypotension (nOH)	90 capsules /30 days
	200 mg capsules		180 capsules /30 days
	300 mg capsules		180 capsules/30 days

Initial Evaluation

I. Droxidopa (Northera) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a neurologist or cardiologist; **AND**
   C. A diagnosis of **neurogenic orthostatic hypotension (nOH)** when the following are met:
      1. Member is experiencing one of the following symptoms: orthostatic dizziness, light-headedness, or syncope; **AND**
      2. Member has an additional diagnosis of:
         i. Primary autonomic failure (Parkinson disease, multiple system atrophy, or pure autonomic failure); **OR**
         ii. dopamine beta-hydroxylase deficiency; **OR**
         iii. non-diabetic autonomic neuropathy; **AND**
      3. Member has attempted at least one non-pharmacologic intervention (e.g., use of compression stockings/abdominal binder, increasing salt and fluid intake, regular exercise, or discontinuation or reduction of antihypertensive medications); **AND**
      4. Treatment with at least one standard therapy (e.g., dihydroergotamine, ephedrine, fludrocortisone, midodrine) for symptomatic nOH has been ineffective, contraindicated, or not tolerated.

II. Droxidopa (Northera) is considered investigational when used for all other conditions.

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms (orthostatic dizziness, light-headedness, or syncope).

Supporting Evidence

I. There is a lack of scientific evidence from clinical trials to show safety and efficacy for the use of droxidopa (Nothera) in pediatric patients.
II. Neurogenic orthostatic hypotension (nOH) is a fall in blood pressure upon standing as a result of reduced norepinephrine release from sympathetic nerve terminals. nOH is a feature of several neurological disorders that affect the autonomic nervous system, most notably Parkinson disease (PD), multiple system atrophy, pure autonomic failure, and other autonomic neuropathies. Droxidopa (Northera) is a prodrug, which is converted to norepinephrine, increases BP, and improves symptoms of nOH. Due to the complexity and association with progressive neurodegenerative disorders, droxidopa (Nothera) needs to be prescribed by or in consultation with a neurologist or cardiologist.
III. Orthostatic hypotension (OH), a fall in blood pressure (BP) upon standing not due to reduced norepinephrine release, is a very common problem, particularly in the frail elderly. It is the result of a variety of medical conditions, such as intravascular volume depletion, severe anemia, use of antihypertensive therapies, and physical deconditioning. It usually resolves after the underlying cause is treated. nOH, in contrast, is a much less common and chronic condition. nOH is the result of a failure to increase sympathetic vasomotor nerve outflow and an inability to raise peripheral vascular resistance on standing. nOH is a feature of several neurological disorders that affect autonomic neurons. These include neurodegenerative diseases associated with the abnormal deposition of the protein α-synuclein (i.e., synucleinopathies such as Parkinson disease), other peripheral neuropathies, high spinal cord injury and a handful of rare genetic diseases.
IV. Droxidopa (Nothera) is indicated for the treatment of orthostatic dizziness, lightheadedness, or syncope in adult patients with symptomatic 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.
V. Consensus guidelines for the treatment of nOH are lacking, although there are expert reviews, there are currently no long-term studies showing the impact of treatment on survival, falls or quality of life. Up to 70% patients with nOH also have supine hypertension, which poses a therapeutic challenge as increasing BP in the upright position can worsen hypertension when supine. Therefore, treatment of nOH requires careful consideration of the potential risks and benefits. The goal of treatment is to reduce symptom burden, prolong standing time, and

improve physical capabilities. The steps in management include a) removing aggravating factors (drug-induced hypotension, anemia, dehydration, prolonged bed rest and physical deconditioning), b) implementing non-pharmacological measures (physical counter maneuvers, life-style changes, volume expansion, acute drinking of water, sleep with the head of the bed raised, compression stockings, small frequent meals), and c) pharmacological approaches; while the other methods are effective, many patients with nOH still require pharmacological treatment to raise BP. This is achieved with two strategies: a) Expanding intravascular volume and b) Increasing peripheral vascular resistance. Medications used for the treatment of nOH consist of the following: dihydroergotamine, ephedrine, fludrocortisone, midodrine, erythropoetin, atomoxetine, pyridostigmine, and droxidopa (Northera®).

VI. No sufficient evidence was found to show superiority of one agent over the other.

VII. Classic symptoms of nOH include lightheadedness, dizziness or feeling close to fainting, and when the fall in BP is severe enough: loss of consciousness. In contrast to vasovagal (neurally-mediated) syncope, syncope in nOH occurs without signs of autonomic activation such as sweating, tachycardia, nausea or abdominal discomfort. After syncope, patients with nOH recover quickly and may be unaware of the event. Patients report that symptom severity varies day-to-day and fluctuates throughout the day. Mornings tend to be most difficult as symptoms are aggravated by intravascular volume loss overnight. Meals, particularly carbohydrate-rich, produce splanchnic vasodilatation and post-prandial hypotension (i.e., fall in BP within 2 hours of eating). Physical inactivity and cardiovascular deconditioning are common in patients with nOH, and, as a result, worsens the symptom severity creating a vicious cycle.

Investigational or Not Medically Necessary Uses

There is limited or no evidence to support the use of droxidopa (Nothera) in conditions other than nOH.

References

1. Northera (droxidopa) [prescribing information]. Lundbeck NA Ltd. Deerfield (IL) February 2017.
2. droxidopa. In: Lexi-Drugs Online. Hudson (OH):Lexi-Comp; 1978-2014 [cited 2014 October]. Available from http://online.lexi.com/ with subscription
3. Horacio Kaufmann, MD, Lucy Norcliffe-Kaufmann, PhD, and Jose-Alberto Palma, MD PhD (2015). Droxidopa in neurogenic orthostatic hypotension. Expert Review of Cardiovascular Therapy, 13(8), 875–891. doi: 10.1586/14779072.2015.1057504. PMID: 26092297 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4509799/
4. Shibao C, Lipsitz LA, Biaggioni I. ASH position paper: evaluation and treatment of orthostatic hypotension. J. Clin. Hypertens. (Greenwich) 2013;15(3):147–153. PMID: 23458585

Policy Implementation/Update:

Date Created	November 2014
Date Effective	November 2014
Last Updated	November 2019
Last Reviewed	11/2019

Action and Summary of Changes	**Date**
Updated criteria to policy format; Added age limit, added attempted at least one non-pharmacologic intervention criteria	11/2019