Analysis of Responder Data from Clinical Trials Evaluating NORTHERA® (droxidopa) for the Treatment of Symptomatic Neurogenic Orthostatic Hypotension

Data presented at the 19th International Congress of Parkinson’s Disease and Movement Disorders

San Diego, Calif., June 15, 2015 – A responder analysis of data from two Phase III clinical trials evaluating NORTHERA® (droxidopa) for patients with symptomatic neurogenic orthostatic hypotension (nOH) was presented today at the 19th International Congress of Parkinson’s Disease and Movement Disorders. NORTHERA, a norepinephrine prodrug, was approved by the U.S. Food and Drug Administration in February 2014, and is available across the United States through a specialty pharmacy.1

The analysis included 359 patients from two placebo-controlled clinical trials: study 301, which enrolled adult patients with autonomic failure and symptomatic nOH, and study 306, which enrolled adult patients with Parkinson’s disease and symptomatic nOH. Symptom improvement was analyzed to determine the point at which there was a clinically meaningful change in dizziness, lightheadedness, feeling faint or “feeling like you might black out.”2

“When evaluated individually, both study 301 and 306 show that the ‘average’ response to NORTHERA is clinically meaningful,” said Horacio Kaufmann, M.D., one of the study’s co-authors. “This meta-analysis is important because it allows us to assess the entire range of responses relative to placebo. The analysis was designed to not only describe patients who had average benefits, but also those who had better than average change in symptoms.”

Clinical meaningfulness was estimated by comparing symptom improvement to the patient-reported Clinical Global Impression-Severity (CGI-S) and Item 1.12 of the Movement Disorder Society-Unified Parkinson’s Disease Rating Sale (UPDRS). The analysis presented evaluated the distribution of symptom improvement relative to the estimated clinically meaningful change in item #1 of the Orthostatic Hypotension Symptom Assessment (dizziness, lightheadedness, feeling faint or “feeling like you might black out”).2

NORTHERA is approved for the treatment of orthostatic dizziness, lightheadedness, or the “feeling that you are about to black out” in adult patients with symptomatic 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 Effectiveness beyond two weeks of treatment has not been demonstrated. The continued effectiveness of NORTHERA should be assessed periodically.

NORTHERA carries a boxed warning for supine hypertension. There are other risks associated with NORTHERA including hyperpyrexia and confusion, cardiovascular risk, and allergic reactions.1 The most commonly observed adverse reactions in NORTHERA-treated patients during the three placebo-controlled trials were headache, dizziness, nausea, and hypertension. For more information, please refer to the Important Safety Information below or visit www.NORTHERA.com.

About Symptomatic Neurogenic Orthostatic Hypotension
Symptomatic nOH is a rare autonomic nervous system disorder associated with failure to produce or release adequate amounts of norepinephrine upon standing.3 It is caused by an underlying autonomic neurologic disorder, such as Parkinson’s disease, multiple system atrophy, or pure autonomic failure.4 The prevalence of nOH increases with age, as many of these underlying conditions affect older adults.5-7 Norepinephrine deficiency may result in an inability for a person to maintain adequate blood pressure and blood flow to the brain upon standing, resulting in dizziness, lightheadedness, and the “feeling that you are about to black out.”4
**Indications and Usage**

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, 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 demonstrated. The continued effectiveness of NORTHERA should be assessed periodically.

**Important Safety Information**

**WARNING: 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.

**CONTRAINDICATIONS**

- None.

**WARNINGS AND PRECAUTIONS**

- **Supine Hypertension:** NORTHERA therapy may cause or exacerbate supine hypertension in patients with NOH, which may increase cardiovascular risk if not well-managed.

- **Hyperpyrexia and Confusion:** Postmarketing cases of a symptom complex resembling neuroleptic malignant syndrome (NMS) have been reported in Japan with NORTHERA use. Observe patients carefully when the dosage of NORTHERA is changed or when concomitant levodopa is reduced abruptly or discontinued, especially if the patient is receiving neuroleptics. NMS is an uncommon but life-threatening syndrome characterized by fever or hyperthermia, muscle rigidity, involuntary movements, altered consciousness, and mental status changes. The early diagnosis of this condition is important for the appropriate management of these patients.

- **Ischemic Heart Disease, Arrhythmias, and Congestive Heart Failure:** NORTHERA therapy may exacerbate symptoms in patients with existing ischemic heart disease, arrhythmias, and congestive heart failure.

- **Allergic Reactions:** This product contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

**ADVERSE REACTIONS**

- The most common adverse reactions (greater than 5%) were headache, dizziness, nausea, hypertension, and fatigue.

**DRUG INTERACTIONS**

- Administering NORTHERA in combination with other agents that increase blood pressure (e.g., norepinephrine, ephedrine, midodrine, and triptans) would be expected to increase the risk for supine hypertension. Dopa-decarboxylase inhibitors may require dose adjustments for NORTHERA.

**USE IN SPECIFIC POPULATIONS**

- Clinical experience with NORTHERA in patients with severe renal function impairment (GFR less than 30 mL/min) is limited. There are no adequate and well-controlled trials of NORTHERA in
pregnant women. Women who are nursing should choose nursing or NORTHERA. The safety and effectiveness of NORTHERA in pediatric patients have not been established. No overall differences in safety or effectiveness were observed between subjects aged 75 years and older and younger subjects in clinical trials, but greater sensitivity of some older individuals cannot be ruled out.

For more information, please see the full Prescribing Information.

About Lundbeck in the U.S.
Based in Deerfield, Ill., Lundbeck U.S. companies are subsidiaries of H. Lundbeck A/S in Denmark. With a singular focus on accelerating advances in brain disorders, employees are engaged in the research, development, production, marketing and sale of innovative therapies that fulfill unmet medical needs among people living with challenging and sometimes rare neurologic and psychiatric disorders. In its late-stage research pipeline, the company has neurology compounds under investigation for Alzheimer’s disease and epilepsy, in addition to therapies in development for mental health disorders. With a special commitment to the lives of patients, families and caregivers, Lundbeck actively engages in hundreds of initiatives each year that support our patient communities. To learn more, visit us at www.LundbeckUS.com and connect with Lundbeck on Twitter at @LundbeckUS.

About Lundbeck
H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is a global pharmaceutical company specialized in brain diseases. For more than 70 years, we have been at the forefront of research within neuroscience. Our key areas of focus are alcohol dependence, Alzheimer’s disease, bipolar disorder, depression/anxiety, epilepsy, Huntington’s disease, Parkinson’s disease, schizophrenia and symptomatic neurogenic orthostatic hypotension (nOH).

An estimated 700 million people worldwide are living with brain disease and far too many suffer due to inadequate treatment, discrimination, a reduced number of working days, early retirement and other unnecessary consequences. Every day, we strive for improved treatment and a better life for people living with brain disease - we call this Progress in Mind.


In 2015, Lundbeck celebrates its 100th anniversary. During the past century, millions of people have been treated with our therapies. It is complex and challenging to develop improved treatments for brain disease, but we keep our focus: There is still so much we need to achieve in the next 100 years to ensure a better life for people living with brain disease.

Our approximately 6,000 employees in 57 countries are engaged in the entire value chain throughout research, development, production, marketing and sales. Our pipeline consists of several late-stage development programmes and our products are available in more than 100 countries. We have research centres in China, Denmark and the United States and production facilities in China, Denmark, France and Italy. Lundbeck generated core revenue of DKK 13.5 billion in 2014 (EUR 1.8 billion; USD 2.4 billion).

For additional information, we encourage you to visit our corporate www.lundbeck.com.

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Sources


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