Lundbeck Medical Education: Request for Independent Medical Education Grant Proposals	
Therapeutic Area	Orthostatic hypotension (OH) due to dysautonomia, otherwise known as neurogenic orthostatic hypotension (nOH).
	The objective of this RFP is to support activities that improve healthcare provider (HCP) education on topics related to autonomic dysfunction and understanding of orthostatic hypotension due to dysautonomia. Preference will be given to programs that provide practical guidance, demonstrate new initiatives, or otherwise showcase "best practices" on the early presentation and identification of autonomic dysfunction, including nOH, as the prodromal stages of movement disorders, as well as the identification of nOH as the most consequential condition associated with autonomic dysfunction. As nOH is a condition seen by a variety of healthcare providers (i.e. physicians, nurse practitioners, physician assistances) from diverse specialties (i.e. neurologists, cardiologists, internal medicine), preference will also be given to programs designed to educate on the identification and diagnosis of movement disorders and symptomatic progression of NOH as a medical condition. We are seeking to support an online, interactive and dynamic education program that can address the needs of a variety of learners. In the cardiology setting, there is a gap in nOH awareness as most HCPs do not distinguish between OH and nOH. An important education objective for this specialty is to increase healthcare provider recognition of the term nOH and their understanding of the association between orthostatic hypotension and dysautonomia. In the neurology setting, healthcare providers are fairly aware of nOH, but may require additional education to ensure patients are properly screened and diagnosed when working in a busy clinic. Furthermore, education on appropriate therapy selection and long-term management is necessary as well.
Intended Audience	Enduring Online Programs/Materials • Primary audiences: Electrophysiologists, Movement Disorder Specialists, Cardiologists, Neurologists • Secondary audiences: PCPs, NPs, PAs
Date Issued:	September 17, 2018
Submission Timeframe:	September 17st 2018 – October 31, 2018
Program Format:	Online learning destination that offers a curricular approach to HCP education. Preference given to proposals that offer various learning formats and ability to effectively target various audiences involved in the diagnosis and treatment of nOH patients. Providers should detail ability to attract the greatest number of potential learners and demonstrate good financial stewardship. Programs should ideally employ experiential or inquiry-based learning strategies. These may include case based discussions, HCP office simulations or other engaging and interactive

	educational formats to best facilitate understanding, retention, and application of content.
Maximum Lundbeck Contribution	$1,000,000
Deadline for Application:	All proposals to this RFP must be received on or before 8 PM Eastern/5 PM Pacific Time on October 31, 2018. Proposals received after the deadline will not be considered. Notification regarding the status of all submitted RFP responses will be made by December 7, 2018.
Applicant Eligibility	Eligible program sponsors are third-party providers of medical or scientific educational programs and include, but are not limited to, accredited CME/CE providers, not-for-profit charities, associations, patient advocacy groups, foundations and societies, institutions, hospitals and managed care organizations. Ineligible program sponsors include, but are not limited to, non-accredited CME/CE providers, individual healthcare providers, group practices, physician practice management companies, provider medical groups, or commercial publishers, any of which is not accredited as a CME provider.
Disease Summary/Burden	Orthostatic hypotension is defined as a reduction in systolic blood pressure of at least 20 mm Hg or a reduction of diastolic blood pressure of at least 10 mm Hg within the first 3 minutes of standing.[1] The drop in blood pressure is associated with an inadequate increase in heart rate of typically less than 15 beats per minute.[2] Neurogenic OH, or OH with dysautonomia, is triggered by the failure of the autonomic nervous system's ability to appropriately release norepinephrine and modulate blood pressure in response to postural changes.[4,5] Neurogenic OH, and is associated with loss of the baroreceptor reflex that normally buffers changes in blood pressure in both directions.[2] The appropriate diagnosis and management of nOH is a challenge due to many factors. Patients may present with a variety of non-specific signs and symptoms such as dizziness, lightheadedness, pre-syncope, syncope, orthostatic dyspnea, orthostatic angina, neck and shoulder pain, generalized weakness, falls, leg buckling, fatigue, and lethargy.[4,9,26-28] Patients with nOH often experience a sudden increase of blood pressure upon postural changes, an effect called supine hypertension. Supine hypertension is present in up to 70% of patients with nOH.[5,7] Supine hypertension is most prevalent during sleep but it may occur anytime the patient is in a recumbent or semi-recumbent position.[7,8] The diagnostic lack of heart rate increase on standing may result in the misdiagnosis of chronotropic incompetence and inappropriate installation of a pacemaker.

This makes management of this condition therapeutically challenging as treatments that improve nOH may worsen supine hypertension.

Many healthcare professionals may be involved in the management of nOH depending upon the underlying etiology and concomitant medical conditions. Patients with a neurodegenerative disorder such as Parkinson's disease (PD), multiple system atrophy (MSA) and/or peripheral neuropathies typically have autonomic dysfunction and, consequently, nOH.[3] According to a number of studies, nOH was found to precede other motor symptoms which characterize PD. In one retrospective study on 35 patients who developed PD, it was found that 11% of these patients developed nOH symptoms before motor symptoms while 60% of the total patients developed early-onset nOH; including those with symptoms appearing before, simultaneous with, or within 1 year after the onset of motor symptoms. [17] Another recent prospective study assessed the autonomic symptoms in a number of patients who suffered from idiopathic rapid eye movement sleep behavior disorder (RBD) with no diagnosis of PD or dementia. The study concluded that nOH can predict the conversion to a specific neurodegenerative disease with a sensitivity up to 60%, where actually 66% of patients were diagnosed with PD or dementia after three years and no patients were still idiopathic at the end of the study.[18] On the other hand, in large prospective cohort study, 18% of patients who developed PD suffered from nOH before motor symptoms and a similar percentage (17.9%) of patients also had nOH but were not diagnosed with PD eventually. The study concluded that nOH cannot predict PD.[19]

The burden of nOH is significant. The total prevalence of nOH in patients with movement disorders is unknown, however, estimates in patients with PD range from 18-50% while approximately 81% of patients with MSA develop nOH at some point.[2,3] nOH occurs in PD patients due to the impaired baroreceptor reflex vasoconstriction in response to standing. This impaired response is likely caused due to sympathetic denervation of vasculature caused by the disease and results in cerebral hypo-perfusion leading primarily, but not exclusively, to lightheadedness, dizziness and lipothymia.[6] Patients report falls as well as an increase in fractures and head trauma due to falls. In addition, patients tend to proactively limit activities due to their history of previous falls which leads to a loss of independence, anxiety and reduction in physical fitness.[9-13] In addition to nOH's ability to impact patient's mobility and increase anxiety, it is also found to significantly increase all-cause mortality and contribute to cognitive impairment.[10,14,15,16] Dysautonomia, particularly nOH whether symptomatic or asymptomatic, was found to be associated with a massive deterioration in the activities of daily living (ADL) and health-related quality of life (HRQoL). [21,22,23] Keeping that in mind, early treatment of nOH with vasopressors may reduce the long-term disabilities and improve the quality of life for PD patients, However, this theory is still under investigation. Screening for nOH even in the absence of light-headedness may be required since almost 50% of PD-OH don't report any symptoms and clinical questionnaires maybe insufficient to recognize nOH in these patients. [24,25]

	Another neurogenic disease called Pure Autonomic Failure (PAF) is also characterized by symptomatic nOH among other symptoms including syncope, reduced sweating, constipation, erectile dysfunction, as well as RBD and hyposmia is some patients. There is still some controversy around the classification of this disease either as a distinct entity or as a part of the premotor spectrum of some neurodegenerative diseases such as PD since most of its patients develop parkinsonism or dementia on the long term. [20] A prospective cohort study by Fereshtehnejad and his colleagues suggested a new classification for PD based on autonomic symptoms rather than motor symptoms only based on their finding that these non-motor symptoms help in better prediction of the prognosis of the disease. [29] The PD patients were grouped into three suggested clusters. Cluster I, the mainly motor/slow progression cluster, represented patients who had mainly motor symptoms with or without mild cognitive impairment (MCI) and mild depression. This group had the best prognosis among the groups. The Intermediate group, Cluster II, were characterized by nOH with no MCI and similar motor symptoms to the slow progression cluster. This subgroup showed moderate progression and a prognosis closer to that of the first subgroup. The final group, Cluster III or diffuse/malignant subtype, had predominant nOH, MCI, and RBD at baseline with more severe motor symptoms and color discrimination disturbances. This last subgroup showed the worst course of the disease and the most rapid progression. Other studies also supported the findings of this cohort where the co-existence of severe motor and non-motor symptoms suggested simultaneous impairment in very different anatomical systems which may mark a relatively diffuse neurodegenerative process. [30,31]
Educational Needs	Patients with nOH are seen by a variety of specialties including neurology and cardiology. However, a recent survey conducted by CE Outcomes LLC found a disparity between the number of neurologists (64%) vs cardiologist (36%) who participated in nOH CME activities. There is a need for tailored disease state education to increase awareness of nOH to cardiologists in order to better identify and manage patients seen in a cardiology setting. This same survey also found that physicians had trouble distinguishing between orthostatic hypotension and nOH and did not have consensus regarding the use of non-pharmacologic and pharmacologic treatment strategies. Other topics that represent an educational gap in physician knowledge include, proper testing and work-up of patients with nOH and how to best manage a patient with complicating comorbid conditions such as supine hypertension or history of cardiac events.
Outcomes measures	The educational evaluation plan must be designed to objectively measure improvements in HCP knowledge and competence (Moore's Expanded Outcomes Level 4). Ideally, the evaluation plan will include quantitative and qualitative evidence that the intervention(s) has had an impact on health care professional behavior.
Funding Guide	• Multi or sole support. The budget should demonstrate fiscal responsibility and cost effectiveness.

	• Each budgetary item must be clearly delineated and be in line with fair market value(FMV) • Input from Lundbeck regarding selection of speaker(s) or the content of the program is not permissible • Lundbeck personnel cannot be utilized as speakers or consultants
Submission Guidelines	Please utilize the Lundbeck medical education grant portal at www.Lundbeckincgrants.com Please include RFP code **RFP-NOH-1901** in the activity title. Only eligible registered Lundbeck grant portal users who do not currently have any overdue outcomes data or financial reconciliations may submit a request in response to this RFP. Information on how to register can be found at www.Lundbeckincgrants.com. The education should offer credits for physicians, nurses and pharmacists. The education must be accredited by the appropriate accrediting bodies, be fully compliant with ACCME criteria and the Standards for Commercial Support and must be in accordance with the U.S. Food and Drug Administration's Guidance on Industry-Supported Scientific and Educational Activities. If accepted, must attest to the terms, conditions, and purposes of an educational grant as described in the Lundbeck letter of agreement.
Contact Information	Please email mededgrants@lundbeck.com or call 844-634-7867

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