

Comments should be submitted not later than Wednesday 08/01/2020

Input from external experts and manufacturers on **2nd draft project plan:** **“Hypoglossal nerve stimulation systems for treatment of obstructive sleep apnoea”**

(Project ID: OTCA21)



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^b “minor”: the comment does not necessarily have to be answered in a detailed manner

^c “linguistic”: grammar, wording, spelling or comprehensibility

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EUnetHTA JA3 WP4 - other technologies, OTCA21
 All comments and author's replies on the 2nd draft project plan
 "Hypoglossal nerve stimulation systems for treatment of obstructive sleep apnoea"
 January 2020

External Experts

Comment from <i>Insert your name and organisation</i>	Page number <i>Insert 'general' if your comment relates to the whole document</i>	Line/ section number	Comment and suggestion for rewording <i>Please insert each new comment in a new row.</i>	Character of comment <ul style="list-style-type: none">• 'major'^a =1• 'minor'^b = 2• 'linguistic'^c =3 <i>Please indicate your choice by writing the according number in this field, e.g. for major choose "1".</i>	Author's reply
Dra. Irene Cano Pneumologist, Respiratory Sleep Unit. Madrid, Hospital Ramon y Cajal (HRC) Spain	1-7		Please, describe the acronym the first time it is used.	3	Changed
I. Cano (HRC)	7	Table 2.1	Presumably there's a mistake. It should say "hypoglossal nerve stimulation systems"	1	Thank you, corrected to Hypoglossal Nerve Stimulation (HGNS) after scoping e-meeting
I. Cano (HRC)	10	Comparison	The comparators are not clearly described	1	Changed as discussed during the scoping e-meeting.
I. Cano (HRC)	10	Outcomes	There is not a differentiation between primary and secondary outcomes	1	After discussion during scoping e-meeting the only classification for outcomes will be the GRADE rating. Outcomes will be rated as critical, important or not important according with Grading of Recommendations,

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					Assessment, Development and Evaluation (GRADE) system.
I. Cano (HRC)	14-15	Clinical effectiveness	I would add a topic issue about the treatment compliance at follow up	1	Added

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Inspire Medical Systems, Inc.	4	Line 41 Section 1.1: Project Participants	Inspire recommends inclusion of a physician highly experienced in treating this patient population and utilizing HGNS therapy as an external expert. We recommend any of the physicians who have published on HGNS therapy in recent years such as Prof. Clemens Heiser, Munich or Prof. Armin Steffen, Luebeck, Schleswig-Holstein, as both have significant experience with this therapy and other therapy alternatives for this patient population	1	Thank you. Two external experts with significant clinical experience in treating OSA patients, had already been contacted, selected and rated as suitable to support the development of the project: Dr. Irene Cano, Pneumologist, Respiratory Sleep Unit. Madrid, Hospital Ramon y Cajal (HRC); and Dr. Marina Carrasco, ENT, University Hospital, Valencia, Spain
Inspire Medical Systems, Inc.	6	Line 43 Section 1.2 Project Stakeholders	<p>Published clinical outcomes from the Inspire Upper Airway Stimulation HGNS system do not apply to ImThera or Nyxoah. Each of these technologies has a different clinical mechanism of action and only Inspire provides a closed-loop therapy where stimulation is clinically timed with the respiration cycle. There is no expectation that Inspire outcomes are relevant surrogates for ImThera or Nyxoah.</p> <p>This issue was raised by the GBA in Germany, and a hearing was held in December 2019 to determine whether Inspire clinical evidence evaluating the Inspire system can be used to anticipate outcomes from Nyxoah or ImThera. All German based physician clinical experts invited to present at</p>	1	This will be considered in the assessment

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EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

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			this hearing argued that Inspire outcomes cannot be used to predict outcomes from Nyxoah or ImThera's technologies, and that these two systems should be assessed solely on the basis of their own unique published outcomes. Please see the attached rationale provided to the GBA. A decision from the GBA hearing is imminent (should be finalized before the end of January 2020).		
Inspire Medical Systems, Inc.	7	Line 53	Globally, Hypoglossal Nerve Stimulation System is referred to as "HGNS" vs "HNSS". It would be helpful to use the same acronym as in other countries to facilitate literature searches, so we recommend the acronym "HGNS".	3	Changed
Inspire Medical Systems, Inc.	8	Line 62 Table 2-3	We recommend expansion of the controlled terms and free text to ensure all relevant publications are detected. We recommend the following search terms be added / included: <ul style="list-style-type: none"> • Hypoglossal Nerve Stimulation • Cranial Nerve XII 	1	Changed
Inspire Medical Systems, Inc.	10	Line 67 Table 2-5 Section: Comparison	There is a typographical error in the last paragraph of the Comparison section of the PICO table. The last sentence says "...In this scenario RCTs comparing HSSS...." This should say "...comparing HNSS...". This is a very minor point, but probably worth clarifying.	3	Changed
Inspire Medical Systems, Inc.	10	Line 67 Table 2-5 Section: Clinical Setting	We recommend expanding the clinical setting to include both Hospital Inpatient and Hospital Outpatient. In Germany, HGNS procedures are performed in Hospital Inpatient, in the Netherlands, they are performed in both the Inpatient and Outpatient (Ambulatory) setting	2	Changed
Inspire	12	Line 117 and	The references included here are older publications. There are more recent	2	Thank you, they have been

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Medical Systems, Inc.		Line 120	publications/updates for each of these studies. The STAR trial includes 5 year follow up (Woodson et al. 2018) and the most recent ADHERE analysis includes over 1000 enrolled patients (Heiser et al 2019). Both articles are attached.		included
LivaNova PLC	6	43	Please change from ImThera Inc US to LivaNova PLC London	1	Changed
LivaNova PLC	7	51	Assume this is meant to read hypoglossal nerve stimulation systems for treatment of OSA?	1	Thank you, it has been corrected.
LivaNova PLC	7	61	Any unpublished trial results may only be submitted in confidence, is it possible to submit information in confidence if this were possible?	1	Any confidential data, although useful, could not be published or included in the results without specific authorisation from the data owner.
LivaNova PLC	9	70	Please define for clarification purposes 'inadequate adherence'	1	It is now defined.
LivaNova PLC	9	70	Upper Airway Stimulation is the name used for Inspire's therapy, please therefore add 'targeted hypoglossal nerve stimulation'	1	Added
LivaNova PLC	10	70	Table 2.5 project scope - outcome measures: AHI We would like to note that this measure in particular should be examined from the perspective of "response" as well as change from baseline. Important in this analysis are several factors which we believe should be	1	Included. These considerations will be taken into account in the assessment.

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			<p>considered to ensure the quality of the assessment:</p> <ol style="list-style-type: none"> 1. How AHI is measured (polysomnography, home sleep test, a mixture of the two, etc.). we would suggest not to mix methods in so far as is possible. 2. Understanding the baseline level of AHI, how it is defined and what is the change. 3. How the mean and median levels of AHI and the change either agree or disagree and what this means from a public health perspective. 4. Assessment of the relationship between baseline AHI value and the likelihood of AHI 'response'. <p>Sleep measures/QOL</p> <p>Would any other QOL or sleep measures such as EQ5D or the Pittsburgh sleep quality interest be of interest for this assessment?</p> <p>Technical and procedural success</p> <p>We would like to suggest that the length of surgery be considered as this could affect outcomes.</p>		

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	11	70	<p>Clinical setting</p> <p>We would like to note that it is not always the case that HGNS surgery is carried out in a 'tertiary referral hospital' which may be defined as a specialist sleep center implanting more than 10 patients per year. This may be too restrictive and not reflect real world practice. It may be useful to consider other clinical setting selection criteria.</p> <p>Please could the 'tertiary referral hospital' be defined for clarity.</p>	1	Changed

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