Proposal for assessment of new health technologies

Important information – read this first!

- Submitted proposals for national health technologies (HTAs) will be published in full. If the proposer thinks there is information necessary for filling out the form, that should not be made public, please contact the secretariat (Nye Metoder) before submission.

  The proposer is aware that the form will be published in its entirety (tick): ☒

- Proposer has filled out point 19 below «Interests and, if any, conflicts of interest» (tick): ☒
- This form serves the purpose to submit proposals for health technology assessment (HTA) at the national level in Nye Metoder - the national system for managed introduction of new health technologies within the specialist health service in Norway. The form does not apply to proposals for research projects. A health technology assessment is a type of evidence review, and for this to be possible, documentation is required, e.g. from completed clinical trials. Lack of documentation may be one of the reasons why the Commissioning Forum (Bestillerforum RHF) does not assign a health technology assessment.
- If the proposal concerns a medical device, the proposer is familiar with the document «Guidance criteria for management of medical devices in the National System for Managed Introduction of New Health Technologies within the Specialist Health Service in Norway» (link) (tick): X

Contact information:

Name of the proposer (organization / institution / company / manufacturer)**:**

PulmonX International (Manufacturer)

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Date and locality:

Neuchatel, June 20th, 2019

1. Proposer's title on the proposal: *

*This may be changed during the course of the process"

Manufacturer

2. Brief description of the health technology proposed to be considered:

Endobronchial lung volume reduction with Zephyr endobronchial (duckbill) valves (EBV) for the treatment of patients suffering from severe and very severe emphysema who remain symptomatic despite optimal medical management.

The minimally invasive endobronchial lung volume reduction (BLVR) technique through the implantation of one-way duckbill valves has been established as a means of treating the hyperinflation associated with emphysema for a group of selected patients. Emphysema is a progressive, debilitating disease characterized by irreversible destruction of alveolar tissue resulting in reduced elastic recoil, progressive hyperinflation and gas trapping. Patients experience chronic dyspnea, limited exercise tolerance and poor health-related quality of life with current therapies unable to reverse or remove the hyperinflation caused by the alveolar destruction.

The Zephyr Endobronchial Valve (EBV) System is designed to occlude a hyperinflated lobe of the lungs with multiple valves (on average 4 valves per patient), allowing air to escape while blocking airflow into the treated lobe. This is intended to result in a reduction in lung volume and hyperinflation in the targeted area. As a consequence, the remaining lobes are able to expand more fully, the overall lung works more efficiently, with resultant improvement in overall lung function in patients with hyperinflation associated with severe emphysema.

The Zephyr EBV System consists of an implantable Zephyr EBV, which includes a single use, disposable Endobronchial Loader System (ELS), and a single-patient use, disposable Zephyr Endobronchial Delivery Catheter (EDC).

The Zephyr Endobronchial Valve (EBV) is a silicone, duckbill valve mounted in a nitinol, self-expanding retainer that is covered with a thin silicone membrane. The valve is implanted during bronchoscopy, with the aim to block inspiratory airflow into a targeted, hyperinflated lobe of the lung. The procedure is designed to be reversible as each EBV can easily be removed by refolding it and retracting it through the catheter. The Zephyr EBV is available in two sizes to accommodate variations in patient anatomy.

The Endobronchial Loader System (ELS) is designed to compress and load the Zephyr Endobronchial Valve (EBV) into the housing of the Zephyr Endobronchial Delivery Catheter (EDC). The Zephyr EBV is secured in an uncompressed or expanded state inside the ELS during manufacturing and is shipped and stored in its expanded state. Immediately prior to use, the Zephyr EBV is compressed within the ELS and then transferred into the Zephyr EDC. The ELS is a non-patient contacting, single use, disposable accessory.

For EBV treatment to be effective, the targeted lobe must be isolated from airflow, both from airflow through the airways and from possible collateral ventilation between lobes (i.e. ventilation of alveolar structures through passages or channels that bypass the normal airways). This is more common in emphysema patients than healthy subjects. When the lobe is properly occluded and isolated from airflow, trapped air in the diseased lobe is able to escape only through the valves, resulting in reduced lung volume in the targeted lobe. Before the EBV procedure, the suitability of a patient for EBV treatment is assessed by measuring the extent of the collateral ventilation (CV) in the targeted lobe. One way this can be achieved is by the use of a specially designed balloon catheter with a flow sensor (CHARTIS Pulmonary Assessment System). The Chartis System, composed of the Chartis Catheter and Chartis Console, is designed to measure pressure and flow in order to calculate resistance to airflow and quantify collateral ventilation in isolated lung compartments. The CHARTIS system consists of a single patient use catheter with a central lumen and a balloon at its tip, and a console to allow for the assessment of airflow in the targeted lobe. When the balloon is inflated, the bronchus is blocked and air can only escape through the catheter's central lumen. Airflow and pressure are displayed on the CHARTIS console allowing for a simulation of an 'occluded lobe' and the measurement of any CV in the targeted lobe. Quantitative CT analysis (QCT) can be used in combination with CHARTIS to optimally diagnose patients appropriate for and most likely to benefit from EBV treatment (Koster, Respiration, 2017). This combined methodology has been supported by expert consensus as well (Slebos, Respiration, 2017).

3. Brief description of current standard of care (SOC) (Which health technology (ies) are currently used. What is the status of the technology (ies)? Whether it provides curative treatment, life extension, etc.)
   Will the proposed technology replace or be a supplement to today's SOC?

The current Standard of Care (SOC) for patients suffering from severe or very severe emphysema consists of either medical management and if symtoms persist, surgical or endobronchial intervention.

Medical Management is comprised of 2 complementary components:
1) reduction or stopping of exposure to risk factors (of which smoking is the most important and
2) symptomatic treatment to reduce symptoms: pharmacological treatment (for example bronchodilators and inhaled or systemic corticosteroids) with in addition, according to the stage of the disease, respiratory reeducation and at the stage of chronic respiratory failure, long term oxygen therapy and non-invasive ventilation (GOLD 2019).
For those patients in whom very invalidating symptoms persist after optimal standard of care medical care, complete smoking cessation, full pulmonary reeducation and/or an adapted physiotherapy program, a surgical intervention or an interventional bronchoscopy can be considered (GOLD 2019).

Surgical intervention:
Surgical lung volume reduction consists of the surgical excision of the diseased and hyperinflated area of the lung identified by High resolution CT scan. This surgery can be performed by median sternotomy or video assisted thoracoscopy. The aim of this surgery is to reduce the volume of the affected lung by 20 to 30%.

This surgery increases the elastic recoil of the lung, leading to a better mechanical efficacy of the healthy regions and thus an improved gas exchange. Surgical lung volume reduction is a complex procedure with significant associated mortality and morbidity risks, as identified during the NETT trial (Fishmann et al, 2003), which has led to a strong reduction of its use.

Lung transplant: Lung transplantation can be considered for patients suffering from very severe COPD. In carefully selected patients, lung transplantation improves health and functional capacity, but does not prolong life. Over 70% of the transplantations are bilateral, which allows a longer survival compared to unilateral transplantations, as demonstrated by Thabut et al, 2008 in patients aged 60years and younger.
The major limitations of lung transplantation are the scarcity of donor organs, early and late dysfunction of the graft, morbidity linked to the long term immunosuppression, and cost (GOLD 2018).

Other endobronchial therapies: Other endobronchial therapies are intrabronchial **umbrella-shaped valves, endobronchial coils, endobronchial foam or sealant and thermal vapor ablation.** Opposed to endobronchial (duckbill) valves, these other endobronchial treatments are not yet considered standard of care for emphysema.

Will the proposed technology replace or be a supplement to today's SOC?
The Zephyr Valve treatment is intended to be provided to patients on top of optimal medical management when symptoms and/or disease progression remains. Candidates for this treatment must have little to no collateral ventilation between the target and ipsilateral lobes, which is confirmed just prior to treatment.
In some cases these patients may also be candidates for lung volume reduction surgery (LVRS). U.S. FDA granted the Zephyr Valve «*breakthrough medical status» because «the device offers bronchoscopic lung volume reduciton without surgery and its associated risks. This device offers significant clinically meaningful advantage over the current standared of care and therefore its availabilty is also in the best interest of patients.*»
Thanks to the less invasive character of endobronchial valves treatment and the reversibility of the therapy, endobronchial lung volume reduction with Zephyr duckbill EBV can also be used to treat patients that due to comorbidities would not be candidates for lung volume reduction surgery.

4. This proposal concerns:	Yes	No
A brand new and innovative health technology	☐	☒
Anew application, or a new indication for an established method	☐	☒
A comparison between several methods	☐	☒
A technology that is already in use	☒	☐
If yes – technology used in clinical practice	☒	☐
If yes – technology used in research/clinical trials	☐	☒
A re-evaluation of technology used in clinical practice	☐	☒
The technology is relevant for disinvestment	☐	☒

The safety and effectiveness of Zephyr duckbill endobronchial valves treatment has already been demonstrated by solid clinical evidence (5 randomized controlled trials), and this treatment is used as routine care throughout Europe. NICE (UK), ZIN (NL), HAS (F) and G-BA (G) have each evaluated Zephyr EBV treatment and recommended its uptake into the basic healthcare package as primary therapeutic option for patients with severe emphysema who are symptomatic despite optimal medical management.

5. This health technology involves (Multiple ticks are possible)

Pharmaceutical	☐
Medical device/IVD medical device that is CE-marked*	☒

The Zephyr® Endobronchial Valve System is a Class III Implantable Medical Device according to Council Directive 93/42/EEC.

Description

The Zephyr Endobronchial Valve (Zephyr EBV) is an endobronchial prosthesis that is intended to control airflow. The device consists of a one-way, silicone, duckbill valve attached to a nickel-titanium (Nitinol), self-expanding retainer that is covered with a silicone membrane. It is implanted in the target bronchus using a flexible delivery catheter that is guided to the targeted bronchus by inserting it through the working channel of an adult bronchoscope.

When reduction of trapped air is indicated, the Zephyr EBV allows distal air to vent from the isolated lung segment during exhalation but does not allow refilling of this region during inhalation. With each respiratory cycle, the amount of air in the target lung segment is reduced (pneumoreduction).

Intended / Indications for Use

The Zephyr EBV is an implantable bronchial valve intended to control airflow in order to improve lung function in patients with hyperinflation associated with severe emphysema and/or to reduce air leaks.

Medical device/IVD medical device that is not CE-marked	☐
Procedure	☐
Screening	☐
Highly specialized services / national offers	☐
Organization of the health services	☐
Other (describe)	☐

"If relevant, please include who should be responsible for developing the technology."

6. Application of the technology:

Prevention	☐
Assessment and diagnostics	☐
Treatment	☒
Rehabilitation	☐
Specialist health care	☐
Primary health care	☐

The Zephyr Endobronchial Valve (EBV) is a silicone, duckbill valve mounted in a nitinol, self-expanding retainer that is covered with a thin silicone membrane. The valve is implanted during bronchoscopy, with the aim to block inspiratory airflow into a targeted, hyperinflated lobe of the lung. The procedure is designed to be reversible as each EBV can easily be removed by refolding it and retracting it through the catheter. The Zephyr EBV is available in two sizes to accommodate variations in patient anatomy.

The aim of insertion of Zephyr endobronchial valves is to reduce lung volume in patients suffering from severe or very severe emphysema and to achieve atelectasis of selected lung segments, improving lung function in the other lung segments that are less affected. The clinical trials /5 RCTs) demonstrate that treatment results in statistically and clinically significantly improved lung function, exercise capacity and quality of life.

This treatment uses an endoscopic approach, which is less invasive than open or thoracoscopic lung volume reduction surgery.

7. Responsibility for funding

	Yes	No
Is the specialized health service responsible for financing the technology today?	☒	☐
May the specialized health service become responsible for funding the health technology?	☐	☐

8. Is the technology mentioned in the national guidelines or action programs prepared by the Norwegian Directorate of Health?

Yes	No
?	☒

We could not identify any relevant national guidelines or action program prepared by the Norwegian Directorate of Health, however, the Zephyr duckbill endobronchial valve treatment is recognized as standard of care in national recommendations and in International and European treatment guidelines for this group of patients:

Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD treatment guidelines, 2017/2018 and 2019 reports recommend endobronchial valves as a treatment in selected patient

UK: NICE IPG 600 (on the use of endobronchial valves), NICE NG150 (on the management of COPD and when to consider valves) and NHS England Commissioning Policy Proposition (NHS ENGLAND 1622 on Lung Volume Reduction by surgery or endobronchial valves);

The Netherlands: ZIN, decision 22.11.2017 on inclusion of endobronchial valves in the basic Health Care package;

Germany: G-BA 21.12.2018 decision to include endobronchial valves on the hospital guideline as treatment necessary within hospital care; and

France: 26.2.2019 HAS recommendation to include Zephyr endobronchial valves on the list of reimbursed devices.

9. Does the technology involve the use of radiation (ionizing/ non- ionizing)? Yes ☐ No ☒

"Give a short description of type of radiation source, device and degree of radiation exposure"

10. Which discipline(s) does the health technology apply to, and which patients are affected? (Could the health technology also affect other groups (e.g. health personnel or relatives)?)

Pneumology, interventional Pneumology

Patient population:

Patients suffering from severe (COPD stage III) or very severe (COPD stage IV) heterogeneous or homogeneous pulmonary emphysema of the superior or inferior lobe with a significant hyperinflation (Residual volume > 175%) and with absence of collateral ventilation.

11. Which aspects are relevant to the assessment? (Multiple ticks are possible)

Clinical efficacy	☒
Safety/adverse effects	☒
Costs/resource use	☒
Cost-effectiveness	☒
Organizational consequences	☒

Ethical	☒
Legal	☐

12. Please suggest the main scope/objective for the health technology assessment, as well as secondary scopes/objectives (in compliance with question 10). For those familiar with "PICO" (Patient, Intervention, Comparator, Outcome) – please include tentative suggestions for PICO.

Patient: Patients with emphysema

Intervention: Endobronchial valves insertion to reduce lung volume in emphysema (Zephyr)

Comparator: Optimal medical care or standard medical care, and as appropriate, LVRS

Outcome: efficacy and safety

Outcome measures

Pulmonary function tests and measures of lung volumes

FEV1 (forced expiratory volume) – the volume of air that the patient is able to exhale in the first second of forced expiration. An increase with 12% indicates a meaningful change.

FVC (forced vital capacity) – the total volume of air that one can forcibly exhale after a full inspiration.

TLC (total lung capacity) – maximum volume of air present in the lungs.

RV (residual volume) – volume of air remaining in the lungs after a full exhalation.

6MWD (6-minute walking distance test) – assesses distance walked over 6 minutes as a sub-maximal test of aerobic capacity or endurance. An increase with 26 meters indicates a meaningful change.

Modified Medical Research Council dyspnoea scale

Measures perceive respiratory disability ranging from none (grade 0) to almost incomplete incapacity (grade 4)

St. George's Respiratory Questionnaire (SGRQ)

The SGRQ is designed to measure health impairment in patients with respiratory disease. A reduction with 4 points suggests a meaningful change.

COPD assessment test (CAT)

The CAT is a validated 8-question self-completed questionnaire designed to measure the health status of patients with chronic obstructive pulmonary disease (COPD) being responsive to change and to treatment. The CAT has a scoring range of 0 (low impact on daily activities) to 40 (very high impact on daily activities). A change of 2 units suggests a meaningful difference.

BODE Index for COPD survival prediction

BODE stands for **B**ody mass index, airflow **O**bstruction, **D**yspnoea and **E**xercise capacity This score combines FEV1, 6MWD, mMRC dyspnoea Scale and Body Mass Index. A reduction of the BODE index with 1 point is clinically meaningfull and indicates a significant reduction of mortality.

13. Please give a brief explanation of why it is important that the health technology assessment proposed should be conducted.

The impact of severe emphysema is substantial. Patients with severe emphysema are limited in the activities they can perform including inability to walk through their homes, bathe, or prepare food. Their social, family, and work lives are limited by their disability, with resulting isolation and depression. Patients panic when emphysema symptoms occur and are afraid of having to go to the emergency room or hospital. Even with medications, symptoms persist, and these symptoms can lead to hospitalization and even death. In the controlled setting of the National Emphysema Treatment Trial (NETT), approximately 50% of patients with severe emphysema on medical management died within 5 years (Naunheim, Annals of Thor Surgery, 2006).

Endobronchial lung volume reduction with Zephyr duckbill valves is a treatment option for these patients. Multiple randomized controlled trials of the Zephyr Valve in patients with severe emphysema with hyperinflation and little or no collateral ventilation between the target and ipsilateral lobe(s) have been published in top-tier journals and demonstrated clinically and statistically significant improvements in various effectiveness outcomes that are important to patients and their physicians, with the benefits persisting out to at least one year. These include improvements in lung function (FEV1), quality of life (SGRQ), exercise capacity (6MWD) and prognostic predictor of survival (BODE). The benefits of Zephyr Valve are consistent across trials in patients with little or no collateral ventilation in both heterogeneous and homogeneous emphysema phenotype. These are clinically meaningful benefits that are recognized by subject matter experts.

The endobronchial lung volume reduction with Zephyr duckbill valves is supported by solid clinical evidence from 5 randomized clinical trials and has been recognized as standard of care and included in the base healthcare package in several European countries (England, The Netherlands, France, Germany and Austria).

This treatment has to our knowledge not yet been the subject of a formal evaluation in Norway, and is for the moment not being provided to the Norwegian patients.

A formal HTA can provide objective information as to why this treatment should be made available also to Norwegian patients.

14. Please comment on the technology that is proposed to be assessed with regard to the following points:

The severity of the disease/condition the health technology targets

Zephyr Valve treatment is for patients with severe or very severe emphysema due to significant hyperinflation, who have poor lung function and experience significant symptom burden.

Chronic Obstructive Pulmonary Disease (COPD) is a severe, progressive disease with an important impact on quality of life and survival.

The predominant and most troublesome symptom experienced by the majority of patients with emphysema is breathlessness. Patients with COPD and a predominate emphysema phenotype have the most severe breathlessness due to increased pronounced air trapping or hyperinflation. As hyperinflation progresses, breathlessness worsens, and patients not only reduce their level of physical activity but also report an impact of their disease on all aspects of their quality of life including everyday tasks such as bathing, dressing themselves or walking up stairs. Depression and social isolation also occur since most patients can no longer participate in activities they once enjoyed like light exercise, travel and group/community activities. Patients experience fear, anxiety and panic associated with increasing breathlessness, with the fear of being unable to breathe just as disabling as breathlessness itself. The quality of life for patients with emphysema is reported to be worse than those with lung cancer (Gore et al, Thorax 2000). In addition to these profound effects on patients, COPD also has significant effects on the families and caregivers who bear the burden of providing support to patients with a reduced ability to engage in social activities, take holidays, and enjoy a normal life (Miravitlles, Int Jrnl COPD 2015).

COPD is the 4th cause of death in the world with 3 million deaths in 2012, representing 6% of the global mortality. COPD is an important public health issue causing major disability, morbidity and mortality.

Chronic diseases in the lower respiratory tract (including COPD) were the third most frequently reported cause of death in Norway in 2015, after cardiovascular disease and cancer (NIPH; Cause of Death Registry).

(Nielsen et al, 2009) analysed data on utilisation of healthcare resources from the BOLD survey existing literature and unit costs from national sources and concluded that COPD has a significant economic burden in Norway and will grow in the future.

☐

Expected effect

Multiple randomized controlled trials of the Zephyr Valve in patients with severe emphysema have demonstrated clinically and statistically significant improvements in various effectiveness outcomes that are important to patients and their physicians, with the benefits persisting out to at least one year. These include improvements in lung function (FEV1), quality of life (SGRQ), exercise capacity (6MWD) and the prognostic factor for survival (BODE). The benefits of Zephyr Valve are consistent across trials and clinically meaningful in patients with little or no collateral ventilation in both heterogeneous and homogeneous emphysema phenotype.

Safety

Around the time of the procedure, as expected, more Zephyr patients experienced serious adverse events than patients who do not receive a procedure. This is primarily driven by an increased risk of patients experiencing a pneumothorax around the time of the procedure (approximately 27% of Zephyr patients in the Liberate Trial, with the median time to occurrence 1 day). This compares favorably to LVRS where greater than 90% of patients experience a pneumothorax within the first 30 days. Importantly, in the longer term in the same Liberate Trial, there were statistically fewer respiratory failures in the Zephyr-treated group compared to SoC (p=0.033) and numerically fewer COPD hospitalizations, although not statistically significant (p=0.053).

Total number of patients in Norway the health technology is applicable to

According to the latest Tromsø Study, about 6% of the population over 40 years old has COPD. This corresponds to 150,000 people in Norway.

Most COPD patients display mild symptoms and many are unaware that they have the disease and approximately 55,000 people were treated for COPD in 2016.

Approximately 11,000 patients were admitted to hospital for acute COPD deterioration in Norway in 2015. On average, they were admitted 1.6 times during that year. On average, 29.3 per cent of all primary admissions were followed by readmission within 30 days. This is shown by figures from the Centre for Clinical Documentation and Evaluation (SKDE, 2017). The acute admissions are those with the most severe symptoms (Public Health Report, Per Nafstad et al, COPD in Norway, 2.2018 ; https://www.fhi.no/en/op/hin/health-disease/copd/)

We estimate that Zephyr therapy could be applicable to about 350 patients suffering from severe or very severe emphysema accompanied by hyperinflation (and without collateral ventilation in the target lobe) per year in Norway.

Consequences for resource use in the public health service

Resources may be redirected from acute management of COPD-related adverse events to Zephyr valve procedures and may be shifted from surgical lung volume reduction to endobronchial lung volume reduction with Zephyr valves.

Need for revision of existing national guidelines or preparation of new guidelines

We could not identify any current COPD treatment guidelines. If existing guidelines do not include endobronchial lung volume reduction therapies, and in particular Zephyr endobronchial valves therapy, for the treatment of emphysema, then this could be added, as is currently being proposed in the new NHS clinical commissioning policy proposition for Lung volume reduction by surgery or endobronchial valve for severe emphysema in adults.

15. Please provide references to documentation of the health technology's effect and safety (i.e. previous technology assessments). (Up to 10 key references can be provided, please do not send attachments in this step of the process):

RCTs

1. BELIEVER

a. Davey et al. Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (theBeLieVeR-HIFi study): a randomised controlled trial. Lancet, 2015, 386(9998), 1066-1073.

b. Zoumot et al. A randomised controlled study of Bronchoscopic Lung Volume Reduction with endobronchial valves for patients with Heterogeneous emphysema and Intact interlobar Fissures: the BeLieVeR-HIFi study. NIHR Journals Library; Efficacy Mech Eval 2015;2(5)

2. STELVIO

a. Klooster et al. Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation. NEJM 2015, 373(24), 2325-2335

b. Klooster, k., Hartman, J. et al. One-Year Follow-Up after Endobronchial Valve Treatment in Patients with Emphysema without Collateral Ventilation Treated in the STELVIO Trial; Respiration 2017 Jan; 93(2): 112–121

3. IMPACT

a. Valipour et al. Endobronchial Valve Therapy in Patients with Homogeneous Emphysema: Results from the IMPACT Study. Am J Respir Crit Care Med. 2016; Nov. 1; 194(9): 1073-1082

4. TRANSFORM

a. Kemp S, Slebos DJ, Kirk A et al, A Multicenter RCT of Zephyr® Endobronchial Valve Treatment in Heterogeneous Emphysema (TRANSFORM). Am J Respir Crit Care Med. 2017 http://www.medengine.com/Redeem/CC1DF0600D898B6E

5. LIBERATE

a. Criner , Sue, Wright et al, A Multicenter RCT of Zephyr® Endobronchial Valve Treatment in Heterogeneous Emphysema (LIBERATE) , Am. J. Resp. Care 2018, vol 198 ; Iss 9, 1151-1164

Systematic and HTA reviews

1. NICE Interventional procedure guidance (IPG600) - Endobronchial valve insertion to reduce lung volume in emphysema and NICE COPD Management document – when to refer for LVR (https://www.nice.org.uk/guidance/ng115)

2. **NHS England** : Clinical Commissioning Policy Proposition : Lung volume reduction by surgery or endobronchial valve for severe emphysema in adults ; Reference : NHS England 1622

3. ZIN (NL) On November 22nd, 2017, the Dutch ZIN published its decision to fund endobronchial valves for lung volume reduction in severe emphysema patients. This decision entered into force with retroactive effect as from September 14th, 2017.

4. **Lancet Respir. 2019** : van Geffen, Slebos, Herth et al, Surgical and endoscopic interventions that reduce lung volume for emphysema : a systematic review and meta-analysis ; Lancet Respir. http://dx.doi.org/10.1016/S2213-2600(18)30431-4

5.**Respiration 2019** : Labarca, Uribe, Pacheco et al, Bronchoscopic Lung Volume Reduction with Endobronchial Zephyr Valves for Severe Emphysema: A Systematic Review and Meta-Analysis, Respiration, May 2019, DOI: 10.1159/000499508

16. Please provide the name of the marketing authorization holder/manufacturer/supplier of the health technology (if applicable/available):

PulmonX International

17. Marketing Authorization Status (MA) or CE-marking: When is MA or CE- marking expected? If possible, provide the time of planned marketing:

The device has a CE mark and is also FDA approved as a breakthrough device

18. Additional relevant information (up to 300 words.)

Mansfield et al recently published a patient preference survey, using the discrete-choice experiment (DCE) survey method, aimed to assess whether there are a set of patients willing to accept the key risks associated with Zephyr Valve to get the benefits of the device, and whether there are a set of patients that would prefer a hypothetical device with characteristics like the Zephyr Valve over their current medical management. The survey involved 294 respondents with severe emphysema and demographic characteristics similar to the LIBERATE study subjects. The risks evaluated in the survey included risk of pneumothorax, hospitalization for breathing problems (i.e. COPD exacerbation requiring hospitalization) and death. The 1-year benefits were expressed in terms of outcomes from patient-specific answers to the Activities Domain questions from the SGRQ questionnaire. The results of the survey showed more than 70% of the survey respondents would choose a hypothetical device with a benefit/risk profile like the Zephyr valve procedure over both lung volume reduction surgery and medical management. This corroborates the strong evidence base on the efficacy and safety of bronchoscopic lung volume reduction treatment using Zephyr EBV duckbill valves and has led to its inclusion in international treatment guidelines, US Food and Drug Administration approval and inclusion in routine care in an increasing number of countries. The one-way duckbill valve treatment has become a routine treatment option in these countries.

19. Interests and potential conflicts of interests

Please describe the proposer's relationships or activities that may affect, be influenced by, or be perceived by others to be important for further management of the health technology that is proposed assessed. (E.g. proposer has financial interests in the matter. Proposer has or has had assignments in connection with the technology or to other actors with interest in the technology)

The proposer has financial interests in the matter since the proposal was made by the manufacturer and distributor of the Zephyr endobronchial valve system.