National Institute for Health and Care Excellence

Health Technology Evaluation

Inhaled treprostinil for treating pulmonary hypertension with interstitial lung disease [ID6459]

Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Ferrer (company)	Ferrer agrees that an evaluation of this topic and the single technology appraisal route is appropriate.	Thank you for your comment
	NHSE	This proposal looks at the use of an existing drug (treprostinil) for a new indication pulmonary hypertension caused by interstitial lung disease (PH-ILD) and so agree would be suitable for a single technology appraisal (STA) approach	Thank you for your comment
	Action for Pulmonary Fibrosis	This seems like the appropriate route for this medicine.	Thank you for your comment
	Pulmonary Hypertension Association UK (PHA UK)	Patients with pulmonary hypertension caused by interstitial lung disease (ILD) are classified as Group 3. Currently available treatments (approved for groups 1 & 4) are not commissioned for this type of PH. As such, PH-ILD is a patient population that is currently without any effective licensed therapy.	Thank you for your comments. We have amended the treatments described in

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		Evaluation of treprostinil by STA would recognise the unmet clinical need for this group of patients who experience a high burden of symptoms of breathlessness and for whom undertaking activities of daily living is very challenging. Should this STA result in a positive outcome, there are significant challenges for effective implementation. Accurate diagnosis, phenotyping and appropriate expert follow-up to measure efficacy of treatment will need careful consideration as this group of patients currently fall outside the remit of the PH expert centres. The PHA UK recognise capacity issues at both the PH and ILD specialist centres. We also recognise that given the frail, co-morbid nature of the population in question, and in line with the transformation agenda within specialist respiratory medicine that care would ideally be delivered close to home.	the background and list of comparators. The implementation of inhaled treprostinil, if recommended, is outside the remit of this technology appraisal and so is not referenced in the scope.
	Association of Respiratory Nurses	There is a clinical need for evidence-based treatments for pulmonary hypertension in ILD. The only other relevant NICE technology appraisal (Sotatercept- ID6163) is not ILD-specific, so this suggested evaluation is welcomed, and the single technology approach is appropriate.	Thank you for your comment
Wording	Ferrer (company)	NICE describes the remit as: "*To appraise the clinical and cost effectiveness of inhaled treprostinil within its marketing authorisation for treating pulmonary hypertension caused by interstitial lung disease*". The appropriate wording would replace "caused by" with "associated with": "*To appraise the clinical and cost effectiveness of inhaled treprostinil within its*	We have amended the remit to: inhaled treprostinil for treating pulmonary hypertension with interstitial lung disease.

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		marketing authorisation for treating pulmonary hypertension associated with interstitial lung disease". This change is necessary to reflect that pulmonary hypertension associated with interstitial lung disease (PH-ILD) is a separate condition from both PH and ILD alone and is consistent with how PH-ILD is referred to within European guidelines.[1] In addition to this, the updated wording reflects the trial wording [redacted]	
	NHSE	We consider that it does. [reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider]	Thank you for your comment.
	Action for Pulmonary Fibrosis	[no comment]	No action
	Pulmonary Hypertension Association UK (PHA UK)	[no comment]	No action
	Association of Respiratory Nurses	Yes [the wording of the remit reflects the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider]	Thank you for your comment.
Timing issues	Ferrer (company)	Until now, there has been no approved treatment for patients with PH-ILD in the UK. PH-ILD represents a severe and progressive condition that is associated with greater mortality risk than either PH or ILD alone.[2] Indeed, a recent retrospective observational study using the UK Clinical Practice	Thank you for your comments. This topic has been scheduled

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		Research Datalink (CPRD) and Hospital Episode Statistics (HES) data has demonstrated a median overall survival of 15.1 months for people with PH-ILD.[2] Overall, there is a significant unmet need for an efficacious and safe treatment option that improves exercise capacity, delays disease progression, and extends survival in people with PH-ILD. Inhaled treprostinil is recommended within European guidelines for use in PH-ILD and offers the opportunity to address this unmet need in the UK.[1] Hence, it is important for NICE to provide a recommendation for the use of inhaled treprostinil within the NHS as close to marketing authorisation approval as possible.	into the work programme and NICE aims to provide timely guidance to the NHS.
	NHSE	Patients in the UK who develop PH-ILD currently have no licensed or commissioned treatment options open to them. Existing data suggests that once PH has developed these patients have a poor prognosis without treatment. The INCREASE and INCREASE-OLE studies conversely demonstrate long term benefits in this patient population from inhaled treprostinil – as a result inhaled treprostinil now has FDA approval and is available in the US. Inhaled treprostinil has also been recommended by the European Respiratory Society/European Cardiology Society 2022 guidelines with a Class IIb Level B recommendation. UK patients are currently therefore at a disadvantage to patients elsewhere in Europe and the US and potentially face a worse prognosis.	Thank you for your comments. This topic has been scheduled into the work programme and NICE aims to provide timely guidance to the NHS.
	Action for Pulmonary Fibrosis	There is currently no effective treatment for PH-ILD. Therefore, there is urgency to evaluate this treatment.	Thank you for your comments. This topic has been scheduled into the work

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			programme and NICE aims to provide timely guidance to the NHS.
	Pulmonary Hypertension Association UK (PHA UK)	There is an unmet need in this patient population that this technology seeks to fill but its urgency is unclear at present as data is still evolving. For example, there is currently limited data to provide proof of a meaningful improvement in quality of life, which is consistently identified as a treatment priority by the PH patient population. A 2023 PHA UK survey showed 52% of people with PH rate overall improvement in quality of life as what matters to them most from treatment (sample size 859). In the same survey conducted in 2016 (sample size 563), this figure was 56%. Whilst this research was completed mainly with those in groups one and four, we would extrapolate that it would be equally important to group three due to their high symptom burden.	Thank you for your comments. This topic has been scheduled into the work programme and NICE aims to provide timely guidance to the NHS.
	Association of Respiratory Nurses	Pulmonary hypertension is a common and serious complication of ILD for which there are no specific treatments currently available. As such, I believe this evaluation is relatively urgent.	Thank you for your comments. This topic has been scheduled into the work programme and NICE aims to provide timely guidance to the NHS.

Section	Stakeholder	Comments [sic]	Action
Additional comments on the draft remit	Ferrer (company)	[no comments]	No action
	NHSE	[no comments]	No action
	Action for Pulmonary Fibrosis	[no comments]	No action
	Pulmonary Hypertension Association UK (PHA UK)	In adult PH services across the UK, drugs are funded within the national commissioning policy – but infrastructure is not (this is left to individual Trusts). The majority of the diagnostic eligibility work involved with the delivery of this technology will fall to frontline staff in PH services, not simply those writing the prescription. There is a lack of clarity around where the ongoing management of these patients will sit. The PHA UK is aware n ongoing work in the CRG around diagnostic pathways and ongoing management. We feel strongly that given capacity issues with group one and four patients at specialist centres, group three must be regarded as an entirely separate cohort and managed in addition to current services. We are positive about this novel treatment option and the need for it to be commissioned, but the above does need to be considered.	Thank you for your comments. The implementation of inhaled treprostinil, if recommended, is outside the remit of this technology appraisal and so is not referenced in the scope.

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	Association of Respiratory Nurses	n/a	No action

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Ferrer (company)	We recommend rewording the background section to accurately reflect PH-ILD as a distinct clinical condition – PH associated with ILD. PH-ILD is separate from both PH and ILD as individual conditions, with distinct symptoms, treatments, and outcomes. Notably, PH-ILD generally has worse outcomes than either PH or ILD alone.[3-6] The current background section does not include any mention of the symptoms, burden or treatment of patients with PH-ILD. **Overview of PH-ILD, including burden of disease** The World Health Organization (WHO) categorises PH into five clinical groups to facilitate differential diagnoses and guide treatment choices. Among these, PH WHO Group 3, which includes PH due to lung diseases and/or hypoxia, has the poorest prognosis of all PH classifications.[3]	Thank you for your comments. We have amended the background section.

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		When ILD progresses to PH-ILD (WHO Group 3), patient prognosis worsens significantly, with a median overall survival of 15.1 months (based on UK retrospective observational data, as described above).[2] Additionally, the symptoms of PH-ILD—such as shortness of breath, cough, and fatigue—significantly limit daily activities and physical functioning, leading to a notable reduction in patients' health-related quality of life.[5, 7, 8] The economic impact of PH-ILD is considerable as well, with substantial healthcare resource utilisation, including frequent hospital admissions, compared to patients with ILD who do not have PH.[9-12] Ferrer considers it important that the background section is updated to include mention of the symptoms and burden of PH-ILD, specifically. **Epidemiology** Consistent with recent retrospective data from HES and CPRD, Ferrer recommends that the epidemiology data within the scope be updated to reflect that PH-ILD in the UK has: • A prevalence of 0.66 per 10,000 people • An incidence of 0.16 per 10,000 people.[2] **Current treatment for PH-ILD** Ferrer recommends replacing the current text on conventional treatment for PH with text on the current treatment for PH-ILD. There are currently no indicated treatments specifically for PH-ILD, which is discussed in more details in the comparator section.	

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		The technology Tyvaso will no longer be the brand name for this product. It is anticipated that the brand name at launch will be [redacted] Ferrer would like to inform NICE that the other marketing authorisations listed within the draft scope are for different formulations of treprostinil (infused and subcutaneous products, rather than inhaled). Inhaled treprostinil has marketing authorisations from the Food and Drug Administration (FDA) for pulmonary arterial hypertension (WHO Group 1), and for PH-ILD (WHO Group 3) and no current UK or European marketing authorisations.	
	NHSE	Conventional treatment of Pulmonary Hypertension no longer includes use of anticoagulants (with the exception of a subgroup, Chronic Thromboembolic Pulmonary Hypertension or CTEPH)	Thank you for your comments. We have amended the background section.
	Action for Pulmonary Fibrosis	The scoping document uses the assumption that “Between 2,000 and 4,000 new patients are diagnosed with interstitial lung disease in England each year.” However, more recent estimations estimate that this number is significantly higher, with UK estimations 20,000 and 30,000 new diagnoses per year and English ILD cases at 16,000-18,000 per year. Gupta R, Morgan AD, George PM, Quint JK. Incidence, prevalence and mortality of idiopathic pulmonary fibrosis in England from 2008 to 2018: a cohort study. Thorax. 2024 Jun 14;79(7):624-631. doi: 10.1136/thorax-2023-220887. PMID: 38688708. Gonnelli, F. et al (2024). Incidence and survival of Interstitial Lung Diseases in the UK in 2010-2019. In ERJ Open Research (pp. 00823–02024).	Thank you for your comments. We have amended the background section to include updated prevalence and incidence estimates.

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		European Respiratory Society (ERS). https://doi.org/10.1183/23120541.00823-2024	
	Pulmonary Hypertension Association UK (PHA UK)	[no comment]	No action
	Association of Respiratory Nurses	It would be relevant to include prevalence as well as incidence of ILD, and acknowledge that, for various reasons (including better diagnosis and anti-fibrotic treatment) both are rising. It is also worth noting that pulmonary hypertension significantly impacts morbidity and mortality rates in ILD.	Thank you for your comments. We have amended the background section to include prevalence and incidence estimates.
Population	Ferrer (company)	The currently anticipated marketing authorisation wording for inhaled treprostinil in this indication is: [redacted] Ferrer would therefore suggest updating the wording to “associated with” rather than “caused by”, to reflect the population of the clinical trial and expected marketing authorisation.	Thank you for your comment. We have updated the wording.
	NHSE	We consider that it does. [defines the population appropriately]	Thank you for your comment.

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	Action for Pulmonary Fibrosis	Yes [the population is defined appropriately]	Thank you for your comment.
	Pulmonary Hypertension Association UK (PHA UK)	No, we do not feel the population is defined appropriately. As there is no current licensed treatment for this cohort, estimating the volume of these patients is difficult and quantifying the likely referral rate is challenging. Little or no work as been done in the UK to date to a accurately quantify this cohort because there is no current available treatment option. The scope states that 'between 2,000 and 4,000 new patients are diagnosed with interstitial lung disease in England each year.' There is a large variation between these figures, making it difficult to consider appropriately. How will a cost be assigned based on this very broad parameter? The scope adds that up to 86% of people with ILD may also have pulmonary hypertension, but "the accuracy of this figure depends on the definition". Again, this makes it difficult to define the population appropriately.	Thank you for your comment. The incidence and prevalence rates of PH-ILD have been updated in the background section of the scope. The implementation of inhaled treprostinil, if recommended, is outside the remit of this technology appraisal and so is not referenced in the scope. A minor change to the population has been made, to clarify it is for pulmonary hypertension with interstitial lung disease but broader changes are not needed.
	Association of Respiratory Nurses	Yes [the population is defined appropriately]	Thank you for your comment.

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Subgroups	Ferrer (company)	Ferrer agrees that it may be appropriate to consider subgroups based on ILD form. However, would like to bring to NICE's attention that there are over 200 types of ILDs. Because of this, there is likely to be a limited number of subgroup analyses that are feasible to conduct. The most appropriate ILD subgroup analysis is anticipated to be idiopathic pulmonary fibrosis, which represents the most common type of ILD.	NICE keeps the subgroups list inclusive. We have added idiopathic pulmonary fibrosis. Subgroups will be discussed by the committee if it feels they are appropriate and evidence allows.
	NHSE	May be worth considering sarcoidosis separately as this is currently viewed as a separate form of PH ie Group V PH (whereas PH-ILD is typically viewed as Group III PH). We agree it would be sensible to also consider combined pulmonary fibrosis and emphysema separately to other forms of ILD as a subgroup analysis of INCREASE data suggested this cohort did less well with treatment.	Thank you for your comment. The appropriate subgroups will be discussed by the committee depending on the evidence available.
	Action for Pulmonary Fibrosis	Extrinsic allergic alveolitis should be known as hypersensitivity pneumonitis (HP)	Thank you for your comment, we've amended this.
	Pulmonary Hypertension Association UK (PHA UK)	No. [there are no groups within the population that should be considered separately] Accurate phenotyping within group three PH relies on expert diagnostic pathways.	NICE keeps the subgroups list inclusive. We have added idiopathic pulmonary fibrosis. Subgroups will be discussed by the

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		Many people with PH (of all types) have lots of comorbidities so it needs to be considered that those taking part in the trials resulting in the data being evaluated may not realistically represent those seen in everyday clinical practice.	committee if it feels they are appropriate and evidence allows.
	Association of Respiratory Nurses	The subgroups defined are appropriate. If possible, subgroup analysis based on disease severity would also be helpful.	Thank you for your comment. The list of possible subgroups is not intended to be exhaustive. The committee will consider other subgroups if it considers these appropriate and the evidence allows.
Comparators	Ferrer (company)	**Overall comments on comparators listed** Based on the currently anticipated marketing authorisation wording for inhaled treprostinil, Ferrer considers that the comparators listed in the draft scope are <u>not relevant.</u> This is because the listed technologies are used to treat PH (WHO Group 1 & Group 4) rather than PH-ILD specifically. As such, these treatments are anticipated to be continued as background therapies as needed for PH in patients with PH-ILD who receive inhaled treprostinil. Additionally, patients are expected to continue being initiated on PH treatments as needed, apart from phosphodiesterase 5 inhibitors (PDE-5i). Inhaled treprostinil is not anticipated to be replacing other therapies. None of the listed treatments have a marketing authorisation for PH-ILD.	Thank you for your comments. We have amended the comparators to only include established clinical management and PDE-5is. NICE keeps the comparators list inclusive. The appropriate comparators will be

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		This position aligns with clinical guidelines, insights provided to Ferrer by key opinion leaders and feedback gained during a NICE system engagement meeting. Indeed, European Society of Cardiology/ European Respiratory Society (ESC/ERS) Guidelines specifically state that treatment options for PH are not efficacious in the PH-ILD population.[1] It is also important to note that two of the listed technologies within the draft scope are specifically contraindicated for use in PH-ILD patients: • Ambrisentan is contraindicated in patients with IPF[13] • Riociguat is contraindicated in patients with pulmonary hypertension associated with idiopathic interstitial pneumonias[14] 1. **Use of PDE-5is** Ferrer understands that PDE-5i is used in some cases within the UK PH-ILD population. However, engagement with experts in the UK has further led to the understanding that PDE-5 inhibitors are only used in a small percentage of very severe PH-ILD patients (in the absence of any licensed treatment) and are not standard of care in the overall population. Ferrer therefore does not consider these products to be relevant comparators. European guidelines state that whilst PDE-5 inhibitors (such as sildenafil and tadalafil) can be used on a case-by-case basis for people with severe PH-ILD (defined in the guidelines as people with a PVR status of >5 wood units (WU)), the recommendation is based on conflicting and limited evidence, and is rated “very low” (i.e., very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect). **Summary** Overall, there is significant unmet need within PH-ILD. The technologies listed within the scope are typically PH technologies and (with the exception	discussed by the committee.

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		of PDE-5i, which is used in only a small minority of patients) are not anticipated to be replaced by inhaled treprostinil. Because of this, they are not considered to be relevant comparators.	
	NHSE	We believe so. [the comparators listed are standard treatments currently used in the NHS with which the technology should be compared]	Thank you for your comment. We have amended the comparators to only include established clinical management and PDE-5is. NICE keeps the comparators list inclusive. The most appropriate comparators will be discussed by the committee.
	Action for Pulmonary Fibrosis	The regular comparator of care for those with PH-ILD should be best supportive care. Given access to right heart catheterisation is varied, and patient numbers willing or able to travel to PH centres being low, the majority receive limited care specifically for their PH-ILD.	Thank you for your comments. We have amended the comparators to only include established clinical management and PDE-5is. NICE keeps the comparators list

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			inclusive. The appropriate comparators will be discussed by the committee.
	Pulmonary Hypertension Association UK (PHA UK)	These are not appropriate comparators as this group has not been treated before. The comparators listed are licensed for patients in groups one and four; none have been shown to be effective in group three patients.	Thank you for your comments. We have amended the comparators to only include established clinical management and PDE-5is. NICE keeps the comparators list inclusive. The appropriate comparators will be discussed by the committee.
	Association of Respiratory Nurses	Yes [the comparators listed are considered to be the standard treatments currently used in the NHS with which the technology should be compared]	Thank you for your comments. We have amended the comparators to only include established

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			clinical management and PDE-5is. NICE keeps the comparators list inclusive. The appropriate comparators will be discussed by the committee.
Outcomes	Ferrer (company)	Inhaled treprostinil is aimed at the treatment of PH-ILD (and not only PH). As such, pulmonary function is also a relevant outcome.	Thank you, we have added lung function to the list of outcomes.
	NHSE	Also important to include lung function parameters such as FVC. INCREASE and INCREASE-OLE suggested treprostinil could have a beneficial effect on FVC in both the short and longer term.	Thank you, we have added lung function to the list of outcomes.
	Action for Pulmonary Fibrosis	Unable to comment	No action
	Pulmonary Hypertension Association UK (PHA UK)	The PHA UK is unaware of robust randomised controlled trial data showing improvement in all cause mortality or in haemodynamics. As demonstrated in the INCREASE study, improvement in NT-proBNP could be considered an additional outcome measure.	Thank you for your comments. NICE keeps the outcomes list inclusive.

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		It should be noted that quality of life has not been a primary endpoint in any of the studies, despite PHA UK research showing how valued it is by patients. The list of outcome measures to be considered places walk-test improvements at the top, and health-related quality of life at the bottom. Whilst this may not be in ranking order, we would suggest it would be more helpful to flip this, given the importance this patient population places on improved quality of life from effective treatments. A 2023 PHA UK survey showed 52% of people with PH rate overall improvement in quality of life as what matters to them most from treatment (sample size 859). In the same survey conducted in 2016 (sample size 563), this figure was 56%.	The most appropriate outcomes will be discussed by the committee. The order of outcomes does not reflect their importance. The committee will discuss all relevant outcomes, including input from relevant stakeholders on the outcomes most important to people with pulmonary hypertension with interstitial lung disease.
	Association of Respiratory Nurses	Alongside the outcomes listed, it would be helpful to see more patient-centred outcomes, for example patient-reported measures examining symptoms such as breathless and fatigue (for example, Dyspnoea-12 or FACIT Fatigue Scale). Capturing daily activity levels via technology like actigraphy may also be a more meaningful way of measuring physical function for patients beyond the 6MWT.	Thank you, we have added the outcomes suggested.
Equality	Ferrer (company)	No equality issues have been identified.	Thank you for your comment.
	NHSE	Currently PH therapies can only be accessed through commissioned PH centres. These centres do not currently routinely see all patients with potential PH-ILD, as there are no licensed therapies available for this patient	Thank you for your comments. Equalities

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		cohort. Consideration would need to be given therefore to increase the capacity of PH services to be able to screen and treat a larger group of patients to avoid any inequity. We also consider that the need for appropriate investigations should be carried out locally, as patients may be unwilling to travel long distances for investigations and this may also entrench inequalities in access to treatment. As the treatment under appraisal comes in an inhaled form patients would need to be educated on how to prime and use the device. Consideration would therefore need to be given to how this would be administered in patients who have issues with dexterity or carrying out complicated processes, to again avoid any inequity.	issues will be considered as part of the evaluation.
	Action for Pulmonary Fibrosis	n/a	No action needed
	Pulmonary Hypertension Association UK (PHA UK)	We have no concerns over equality or access.	Thank you for your comment
	Association of Respiratory Nurses	No comments to add	No action needed

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Other considerations	Ferrer (company)	There is an NHS England Commissioning Policy for targeted therapies for use in adults with PH listed in the relevant documents section of the draft scope. However, Ferrer would like to highlight this document outlines treatments for patients with pulmonary arterial hypertension (WHO Group 1 PH) and chronic thromboembolic pulmonary hypertension (WHO Group 4 PH), and is not relevant for patients with PH associated with ILD (WHO Group 3, i.e., the relevant population for inhaled treprostinil).	Thank you, this has been removed from the related national policy section.
	NHSE	We do not have other suggestions.	Thank you for your comment
	Action for Pulmonary Fibrosis	n/a	No action needed
	Pulmonary Hypertension Association UK (PHA UK)	[no comment]	No action needed
	Association of Respiratory Nurses	No comments to add	No action needed
Questions for consultation	Ferrer (company)	**Question:** Where do you consider inhaled treprostinil will fit into the existing care pathway for pulmonary hypertension caused by interstitial lung disease? **Response:**	Thank you for your comments.

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		Ferrer considers that, aligned with its anticipated marketing authorisation, inhaled treprostinil would be a first-line treatment option for PH-ILD. Considering that data for inhaled treprostinil demonstrates earlier initiation of treatment is associated with improved outcomes, Ferrer expects that the product could be initiated after diagnosis by either PH or ILD specialists. Ferrer is open to further discussions with stakeholders on optimising the treatment pathway. **Question:** What treatments for pulmonary hypertension caused by interstitial lung disease might inhaled treprostinil replace in clinical practice? Which treatments would continue as supportive care, used alongside inhaled treprostinil? **Response:** Patients are expected to continue their existing supportive care which may include oxygen, PH medications, or ILD products (e.g., nintedanib). It is anticipated that in the small percentage of patients in which clinicians would currently consider initiating PDE5-i's, inhaled treprostinil would be initiated instead. **Question:** Please select from the following, will inhaled treprostinil be: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details) **Response:** C. Inhaled treprostinil will be prescribed in secondary care with routine follow-up in secondary care. It is important to distinguish PH-ILD from PH alone. As discussed earlier, PH-ILD is associated with greater severity and mortality impact. Given the severity of PH-ILD, management does not occur in primary care. Diagnosis of PH-ILD occurs within specialist PH centres. Following this, those with a PVR status of between 2 and 5 WUs are	

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		managed at ILD specialist centres, typically receiving treatments for ILD aspects only. Patients with a PVR of ≥5 WU typically receive care at a PH specialist centre, with some continuing to be monitored at an ILD centre. Following the launch of inhaled treprostinil, it is anticipated that patients will continue to be managed within specialist secondary care centres (i.e., specialist PH and ILD centres), reflecting the severity of the disease. **Question:** For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. **Response:** The small minority of patients who receive PDE-5 inhibitors (on a case-by-case basis) for PH-ILD are prescribed them in PH specialist centres. **Question:** Would inhaled treprostinil be a candidate for managed access? **Response:** Ferrer anticipate inhaled treprostinil may be eligible for managed access, as there are additional data collection activities initiating and ongoing that could be supportive. **Question:** Do you consider that the use of inhaled treprostinil can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? **Response:** There are several additional benefits Ferrer considers unlikely to be included in the QALY calculations. **Quality of life considerations** During the INCREASE trial, the St. George's respiratory questionnaire (SGRQ) measured quality of life. Ferrer considers that this tool may have underestimated the quality of life impact on patients with PH-ILD. It is important to note the SGRQ was developed for the measurement of quality of life in patients with asthma and COPD (conditions where cough is the most	

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		prevalent symptom). There is currently no quality of life tool validated for use specifically in PH-ILD. In addition to potential underestimation of patient quality of life, PH-ILD represents a severe disease area and therefore has significant carer impact. **Wider additional benefits** As described earlier, the current pathways for managing PH-ILD are fragmented between PH and ILD specialist centres. There are a limited number of specialist centres, and some patients have to travel far to either a PH centre or an ILD centre (depending on their PVR status). Based on this, Ferrer considers there could be additional benefits not captured. This could include wider system and patient benefits due to standardisation of the treatment pathway. For example, it is anticipated that inhaled treprostinil will be potentially administered at both PH and ILD centres, irrespective of PVR status (reducing travel needs of many patients).	
	NHSE	*Where do you consider inhaled treprostinil will fit into the existing care pathway for pulmonary hypertension caused by interstitial lung disease?* We would consider inhaled treprostinil to be first line therapy for patients with PH-ILD who fulfil the INCREASE recruitment criteria ie >18 years old, diagnosed with diffuse parenchymal lung disease with PVR>3WU *What treatments for pulmonary hypertension caused by interstitial lung disease might inhaled treprostinil replace in clinical practice?* As there are currently no licensed therapies for PH-ILD, inhaled treprostinil would not replace any existing commissioned medications.	Thank you for your comments.

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		Which treatments would continue as supportive care, used alongside inhaled treprostinil? Treatments such as home oxygen, diuretics and digoxin would potentially continue as part of supportive care. *Where will inhaled trepostinil be prescribed from?* We would envisage that treprostinil would be prescribed by recognised PH centres (ie D 'other'), with close collaboration with recognised ILD centres who already work closely with this patient cohort. *For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.* Many of the comparators listed are targeted PH therapies which would normally be prescribed by a recognised PH centre. Other listed therapies are supportive (ie digoxin, home oxygen, and diuretics) could be prescribed by primary or secondary care. *Would inhaled treprostinil be a candidate for managed access?* A managed access scheme would potentially be appropriate, especially if this facilitated access to therapy sooner. As the PH national network already has robust data collection processes it would be feasible to manage this using existing infrastructure. *Do you consider that the use of inhaled treprostinil can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?* No *Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.* The most robust	

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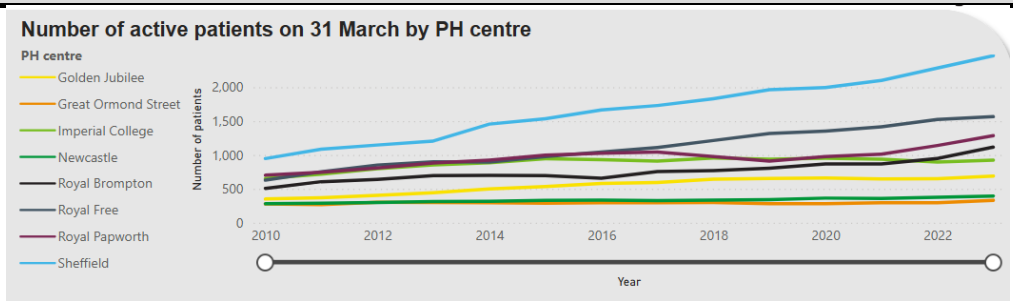
		data is available from the INCREASE and INCREASE-OLE studies. A number of other papers have been published, examining subgroup analyses from the original data. *Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.* As discussed in Equality section there may be issues around using the inhaler device in some patient groups – we would suggest obtaining information from the manufacturer as to how they plan to avoid this. There are also potential issues around how and where ILD patients would be seen by appropriately skilled specialists to access treatment. This may require more detailed liaison with Specialised Commissioning who commission both ILD and PH services nationally.	
	Action for Pulmonary Fibrosis	Where do you consider inhaled treprostinil will fit into the existing care pathway for pulmonary hypertension caused by interstitial lung disease? There is currently no standardised pathway for people with PH-ILD. Many do not reach PAH centres for treatment given low access to right heart catheterisation, combined with inability or unwillingness to travel long distances to PAH centres. Please select from the following, will inhaled treprostinil be: D Other – We would expect that, given the number of patients who may be eligible for this treatment and also the number of PAH specialist centres (as well as the context of the expanding numbers of expected prescribing ILD centres across England as part of the roll-out of the OneVoiceILD integrated care pathway), treatment decisions would be taken jointly between the PAH and ILD MDTs. We expect that treatment would likely be given prescribed by the ILD service following joint decision-making.	Thank you for your comments.

Section	Consultee/ Commentator	Comments [sic]	Action
	Pulmonary Hypertension Association UK (PHA UK)	As previously stated, there is no existing treatment pathway for this population, so it is impossible to say where it would fit into an existing care pathway. Additionally, whilst we are very keen for patients to have access to this new therapy, passing judgement on where it sits in the treatment pathway is outside our remit as the PHA UK. As part of patient assessment for this therapy, we would expect all current treatments for them to be re-evaluated, prior to initiation of this new therapy. We would expect inhaled treprostinil to be prescribed in secondary care with routine follow-up in secondary care. It is unlikely that many of the eligible population will still be working. Given the likely older and frail nature of the cohort, existing substantial health-related benefits are unlikely.	Thank you for your comments.
	Association of Respiratory Nurses	No comments to add	No action needed
Additional comments on the draft scope	Ferrer (company)	Ferrer suggests a scoping workshop would be beneficial. This is because there has been no NICE evaluation to date specifically for the treatment of PH-ILD.	Thank you for your comments. NICE has considered the appropriateness of a scoping workshop after considering all

Section	Consultee/ Commentator	Comments [sic]	Action
			consultation comments. No scoping workshop was held for this evaluation.
	NHSE	We have no further comments on the draft scope.	Thank you for your comment.
	Action for Pulmonary Fibrosis	[no comment]	No action needed
	Pulmonary Hypertension Association UK (PHA UK)	ECONOMIC ANALYSIS: The cost of delivering this technology needs to be considered from the perspective of infrastructure and capacity as well as the cost of the therapy itself. PH centres managing group one and four patients may already be working at capacity – the graph below is taken from the most recent National Audit of Pulmonary Hypertension and shows how the numbers of managed patients continues to rise. Is consideration being given to the delivery of this technology through ILD services?	Thank you for your comments. NICE's reference case considers evidence on resource use from an NHS and Personal and Social Services perspectives. This will include consideration of all costs to the NHS associated with introducing this technology, not only the acquisition cost of the drug.

Section	Consultee/ Commentator	Comments [sic]	Action
		 As a patient organisation we sit between NHS commissioning and industry, which is novel, so we hope you take our comments in this consultation as constructive rather than critical	
	Association of Respiratory Nurses	[no comment]	No action needed

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

GSK