National Institute for Health and Care Excellence

Health Technology Evaluation

Brensocatib for treating non-cystic fibrosis bronchiectasis in people 12 years and over ID6448

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	Insmed (company)	The Company agrees that NICE should consider this topic for appraisal. The single technology appraisal route is most appropriate for brensocatib.	Thank you for your comment. No action required.
	Association of Respiratory Nurses	This is very appropriate, Bronchiectasis is a long tern condition which is becoming more prevalent with limited current treatment available. It is proposed as a single technology appraisal which I think is right route.	Thank you for your comment. No action required.
	Taskforce for Lung Health and Asthma + Lung UK	Yes, we believe the evaluation route is appropriate.	Thank you for your comment. No action required.

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	British Paediatric Respiratory Society	The route of proposed evaluation is appropriate. We recommend particular focus on bronchiectasis in childhood (the 12-18 year group) when bronchiectasis may still be reversible with effective treatment (Mills AJRCCM 2024). We would recommend appropriate paediatric clinician representation during the evaluation to ensure equality across the ages.	Thank you for your comment. Clinical experts will be selected in line with NICE's health technology evaluations manual. Consultee organisations will be invited to nominate relevant clinical experts. No action required.
	British Thoracic Society	There is an unmet need in bronchiectasis treatments . The evaluation of a novel approach to a condition with no current licensed therapies is appropriate. The proposed approach may offer a bridge between current anti infective treatments and anti inflammatory options. It may sit as an adjunct to current treatments (macrolides) or second line in refractory cases. Agreed needed because of the two published randomised controlled trials of brensocatib in bronchiectasis. It should be a multiple technology appraisal as the main debate in those with recurrent infections whether they should be started on a long-term macrolide vs. brensocatib.	Thank you for your comment. The committee will consider unmet need during the development of the evaluation. A multiple technology appraisal can be used if multiple technologies which are not considered current clinical practice need to be evaluated for a condition. Multiple treatments which are already considered

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			clinical practice, such as long-term macrolides, can be considered as comparators within a single technology appraisal. Antibiotic prophylaxis (such as long-term macrolide) is included as part of established clinical management, which is a comparator in the scope.
	Royal College of Paediatrics and Child Health	This is an important evaluation. The route of proposed evaluation is appropriate. Bronchiectasis is known to be reversible with effective treatment in childhood (Mills AJRCCM 2024). Therefore, we recommend particular focus on the 12-18 year group). We recommend appropriate paediatric representation during the evaluation to ensure paediatric specific issues are taken into account.	Thank you for your comments. Clinical experts for the committee meeting will be selected in line with NICE's health technology evaluations manual. No action required.
Wording	Insmed (company)	The wording of the remit is accurate, and the Company suggests no further changes.	Thank you for your comment. No action required.

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	Association of Respiratory Nurses	The wording reflects the issue effectively and the need for new treatment. It explains clearly the indications for use and how it could clinically benefit patients with outcome measures. It addresses costs with regards to different perspectives but not how much the treatment will cost if marketed.	Thank you for your comment. No action required.
	Taskforce for Lung Health and Asthma + Lung UK	Yes, the wording is appropriate.	Thank you for your comment. No action required
	British Paediatric Respiratory Society	Wording of the remit is appropriate.	Thank you for your comment. No action required
	British Thoracic Society	We have an issue with the age as this crosses both paediatrics and adult medicine. Can optimal patients be identified and biomarkers (eg CRP, IL-8) predict response, can they be measured to stratify ongoing treatment. Does novel approach increase infection risk if response and what impact may this have on healthcare usage. How can cost effectiveness be justified eg what is the cost per QALY gained? Cost per exacerbation avoided? Benchmark against current therapies eg macrolides and inhaled antibiotics.	Thank you for your comments. NICE can only appraise a treatment within its marketing authorisation, which will specify the age range licensed for use. If evidence allows the company can present subgroups (e.g. biomarker status or age) in its submission

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		Will evaluation consider personalised access strategy via sub group effectiveness?	for the committee to consider. The cost effectiveness of brensocatib will be assessed in line with NICE's health technology evaluations manual.
	Royal College of Paediatrics and Child Health	Appropriate	Thank you for your comment. No action required.
Timing issues	Insmed (company)	To the NHS, the urgency of evaluating this technology is high, given the importance to clinical, economic, and patient outcomes of reducing chronic exacerbation burden beneath prognostically important thresholds in non-cystic fibrosis bronchiectasis (NCFBE). Notably, at present, there are no Medicines and Healthcare products Regulatory Agency (MHRA)-approved therapies specifically indicated for the treatment of NCFBE, and no treatment options that directly intervene in the predominantly neutrophilic inflammatory pathology that underlies the disease's pathogenesis. Frequent pulmonary exacerbations (PEx), defined as two or more in the last 12 months, are a strong predictor for their own recurrence. Experiencing ≥2 PEx is also strongly associated with symptom severity, lung function decline, hospitalisations, long-term serious comorbidities, and [redacted] (1, 2). PEx episodes last more than 2 weeks on average. Even aside from exacerbations, respiratory symptoms (especially cough, sputum production,	Thank you for your comments. NICE aims to publish guidance as soon as possible after the company receives the marketing authorisation and introduces the technology in the UK. NICE has scheduled this topic into its work programme.

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		and breathlessness), are frequent, intense, and highly debilitating, [redacted](3). Health-related quality of life (HRQoL) is greatly impacted. On the disease-specific Quality of Life–Bronchiectasis (QoL-B) instrument, impairment is seen across all domains [redacted] (3, 4). Items in these domains echo commonly cited themes for poor life experience: [redacted](5). On an indexed basis, having ≥2 PEx in the last 12 months worsens HRQoL by [redacted] versus UK population norms for the same mean age (based on SF-6v2 utilities) (3, 6). Additionally, during an exacerbation HRQoL deteriorates by [redacted] of age-similar normative values on EQ5D-3L (4, 7, 8). Importantly, quality of life on all these measures substantially improves with fewer than 2 PEx in a year (3, 6, 9-11). Notably, caregivers register a significant impact on their quality of life too; most patients have at least one informal caregiver who provides many hours of care a week (3). Mental health outcomes are poor in NCFBE. In the overall UK NCFBE population, possible anxiety and depression is measured in approximately 30% and 20% of patients, respectively (12). Probable anxiety and/or depression are [redacted] more likely in patients with ≥2 PEx than <2 PEx per year (3). Moderate to severe sleep disturbances affect over [redacted] of patients, and improve with fewer PEx (3). The age standardised mortality rate (ASMR) for the indicated population in the UK was estimated at [redacted] in 2019, nearly five times the age-matched background rate (13). Furthermore, ASMR was [redacted] lower in patients with <2 PEx in the prior year than those with ≥2 (13).	

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		Mortality occurs alongside serious clinical comorbidities that emerge over time. Respiratory complications, in particular pneumonia, lower respiratory tract infections (LTRI), bronchitis, respiratory failure, and collapsed lung, have all been observed as attributable causes of death (14). Other common comorbidities include gastrointestinal reflux disease, osteoporosis, arthritic conditions, diabetes, atrial fibrillation, congestive heart disease and failure, myocardial infarction, peripheral vascular disease, and stroke. These are particularly prevalent among patients who die and may reflect underlying long-term systemic inflammation (15). Analyses of The Health Improvement Network (THIN) and Clinical Practice Research Datalink (CPRD) data show that the incidences of most of these comorbidities were elevated in patients with ≥2 versus <2 PEx in the last 12 months (13, 16). NCFBE incurs substantial healthcare-related costs to the NHS that are accentuated in patients with ≥2 PEx per year or increasing disease severity (1, 17-20). Approximately 20% to 45% of UK patients with ≥2 PEx in the last 12 months are hospitalised annually (1, 21). Among exacerbating patients overall, the rate of hospitalisations was [redacted], rising to [redacted] among those hospitalised. The mean hospital stay was [redacted] days, with nearly [redacted] of admission days spent in ICU (22). Each hospitalised patient cost NHS Trusts over [redacted] in 2022-23, totalling [redacted] across England. In the European EMBARC registry, hospitalisation incidence was 2% per year in patients with <2 PEx in the last 12 months, compared to 44% in those with ≥2 PEx (23). Existing treatments are largely symptomatic and targeted on managing the key pathological features of NCFBE, that is: infection (e.g. antibiotics), impaired mucociliary clearance (e.g. mucoactives, airway clearance techniques, and physiotherapy), and airway obstruction (e.g. bronchodilator and corticosteroids).	

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		However, British and European guidelines recommend routine use of chronic mucoactives, bronchodilators, and inhaled corticosteroids only in restricted circumstances when managing bronchiectasis alone, reflecting the limited levels of evidence for their benefits weighed against long-term safety and tolerability concerns. Oral corticosteroids are recommended only for comorbid conditions (14, 24). Long-term antibiotics, which are dominated by oral macrolides, are recommended sparingly in guidelines, specifically due to the very real risks of drug-resistant infections and long-term complications (24, 25). Multidrug-resistant infections occur in 10-15% of NCFBE isolates following exacerbation, mostly *Pseudomonas aueginosa*, MRSA, and beta-lactam-resistant *Enterobacteriaceae* (26). Macrolide resistance was observed in nearly 90% of pathogen isolates after just a year of treatment with azithromycin (as the dominant macrolide in use) (27). Non-tuberculosis mycobacteria (NTM) resistance is a very serious clinical complication of taking long-term macrolides (24, 25). Macrolide use is further cross-linked to resistance against other antibiotic classes (28). In May 2025, the European Medicines Agency (EMA) updated and harmonised azithromycin's label to strongly reflect these risks (29). Hearing loss is a recognised long-term toxicity associated with guideline-recommended antibiotics. Cardiotoxicity, gastrointestinal intolerance, and hepatotoxicity are known long-term safety concerns with macrolides (25, 30), while nephrotoxicity and bronchospasm-induced intolerance are concerns with inhaled antibiotics (14, 31, 32). Collectively, these chronic safety risks mean that a significant proportion of patients are medically ineligible for antibiotics, particularly given the average age of the patient population. It also means that initiation of these therapies imposes considerable service complexities (33). Notably, a 2017 British Thoracic Society (BTS) Quality Standards audit uncovered that nearly 50% of	

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		patients did not have microbial culture testing when starting or continuing antibiotics, which is a key service requirement to enforce microbial stewardship (34). Despite these risks, all chronic treatment classes are widely used in patients with ≥2 PEx in the last 12 months. This was reflected in a 2012 audit examining uptake of the BTS bronchiectasis guidelines, which showed that levels of use are generally consistent across subgroups, regardless of co-diagnoses of asthma and chronic obstructive pulmonary disease (COPD), active infection status, and exacerbation frequency (35). This probably reflects the level of necessity in the indicated population Crucially, there are currently no available treatment options that directly intervene in the predominantly neutrophil-mediated inflammatory pathology that underlies bronchiectasis (36). Brensocatib is a first-in-class oral, selective, competitive, and reversible inhibitor of dipeptidyl peptidase-1 (DPP-1) (37). DPP-1 activates pro-inflammatory neutrophil serine proteases, which are implicated in bronchiectasis pathogenesis. Brensocatib reduces neutrophil-mediated inflammatory markers in NCFBE, and has demonstrated efficacy in reducing PEx, improving lung function and respiratory symptoms, and increasing HRQoL (38). If licensed, it will be the only drug with a specific indication for the chronic treatment of NCFBE. ***Chronic Airways Assessment test, which has been validated in bronchiectasis (39).**	
	Association of Respiratory Nurses	This is relative to the needs of patients in the NHS who have moderate to severe bronchiectasis and still symptomatic or exacerbate, it is however still in phase 3 clinical trials I believes so not yet available.	Thank you for your comment. NICE aims to publish guidance as soon as possible after the company receives the marketing authorisation

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			and introduces the technology in the UK. NICE has scheduled this topic into its work programme.
	Taskforce for Lung Health and Asthma + Lung UK	This evaluation should be viewed as urgent, due to the significant and growing burden of bronchiectasis. Between 1999-2020, there was a 2.87-fold increase in the rate of hospitalisations for bronchiectasis.[1] The rise of hospitalisations over the last two decades illustrates that there is huge unmet need among people living with bronchiectasis. Frequent exacerbations and hospitalisations cause considerable disruption to the daily activities and quality of life of bronchiectasis patients. Currently, people with bronchiectasis have no approved treatments to address these damaging exacerbations. Many patients rely on long-term antibiotic therapy, but for many, this approach fails to effectively reduce exacerbations and increases their risk of antibiotic resistance. Brensocatib would be the first licensed medication for bronchiectasis, offering new hope to thousands of patients. In the clinical trial, patients on brensocatib experienced a 21% lower exacerbation rate when compared to the placebo group.[2] This evaluation offers the opportunity to introduce a new treatment that could potentially transform patients' lives, by significantly reducing exacerbations, hospitalisations and reliance on long courses of antibiotics. By	Thank you for your comments. NICE aims to publish guidance as soon as possible after the company receives the marketing authorisation and introduces the technology in the UK. NICE has scheduled this topic into its work programme.

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		improving disease control, brensocatib could ease the pressures on the NHS and help reverse the trend of increasing bronchiectasis hospital admissions.	
	British Paediatric Respiratory Society	Currently, only supportive management is available for bronchiectasis. Prevalence of bronchiectasis is increasing, with wide ranging effects on the health economy. Bronchiectasis in childhood may be reversible and effective treatment is needed to prevent long term lung injury. Therefore this evaluation is urgent.	Thank you for your comment. NICE aims to publish guidance as soon as possible after the company receives the marketing authorisation and introduces the technology in the UK. NICE has scheduled this topic into its work programme.
	British Thoracic Society	Not urgent as we have other available treatments. This will be the first licensed bronchiectasis treatment. There is an unmet need but other treatments are available that we know work despite not being licensed and the evaluation doesn't and shouldn't be rushed.	Thank you for your comments. The evaluation will follow scheduled timelines. No action required.

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	Royal College of Paediatrics and Child Health	Prevalence of bronchiectasis is increasing, with wide ranging effects on the health economy. Currently, only supportive management is available for bronchiectasis. Therefore, a specific treatment for this condition should be evaluated rapidly, so that it can be offered as soon as possible if found to be effective. In particular, in childhood, bronchiectasis may be reversible, and effective treatment is needed to prevent long term lung injury. Therefore, this evaluation is urgent.	Thank you for your comments. NICE aims to publish guidance as soon as possible after the company receives the marketing authorisation and introduces the technology in the UK. NICE has scheduled this topic into its work programme.
Additional comments on the draft remit	N/A	-	-

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Insmed (company)	Overall, the information is broadly accurate and complete. However, the Company would recommend the following amendments to improve the accuracy and completeness of the background section: **Clarification of terminology** The current description of non-cystic fibrosis bronchiectasis is factually incorrect. Bronchiectasis is formally a syndrome defined by characteristic	Thank you for your comments. The scope is intended to be a broad overview of the topic. However, the following amendments

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		widening and damage of the large airways (bronchi) that is permanent. *Non-cystic fibrosis bronchiectasis* refers specifically to cases that are not concomitant with a diagnosis of cystic fibrosis (CF). Patients with CF can also have bronchiectasis. Where this occurs it is classified as CF-related bronchiectasis, which is its own endotype due to a distinct aetiology, clinical presentation, and prognostic signature (40). We suggest revising the definition to reflect this distinction clearly. Importantly, bronchiectasis and CF itself do not necessarily have similar symptoms. Additionally, we would like to add in the first sentence, that the lungs are *permanently* widened. This is a key point to make, as bronchiectasis is a chronic, lifelong condition, for which there is a characteristic remodelling of the airways that is a key pathology. This remodelling is permanent, progressive, and contributes to the morbidity of the condition. **Disease progression and lung function decline** The Company has covered in some detail the burden of disease and unmet need associated with the population of the proposed indication in its responses to the section "*What is the relative urgency of this evaluation to the NHS?".* As described in that section, bronchiectasis is a long-term, incurable, and debilitating condition in which the airways of the lungs become permanently widened and damaged, alongside a build-up of excess mucus, chronic inflammation, and increased vulnerability to infection (1, 41, 42). These four key pathological processes (inflammation, infection, mucociliary dysfunction, and lung remodelling) have been described in the literature as a 'vicious vortex', because of their complex interplay in a self-perpetuating cycle. Operating together, these pathologies drive progressive lung damage and	have been made to the background information: - the definition of non-cystic fibrosis has been updated - the first paragraph has been updated to state 'the lungs are permanently widened' and the condition is associated with inflammation - the prevalence estimates have been updated to include estimates in females and males separately - the third paragraph has been updated to highlight that there are currently no licensed treatments for

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		disease activity (43, 44). While spirometric patterns vary, the disease is marked by a slow and insidious decline in lung function over time (43, 44). Importantly, modern understanding considers bronchiectasis to be fundamentally an inflammatory condition. Neutrophilic inflammation is both a hallmark and key driver of the disease. Finally, the background currently states: *"People with bronchiectasis can also experience flare-ups, known as exacerbations".* It is worth noting that exacerbations are a cardinal feature of the condition and represent periods of symptom worsening that have precise clinical definitions in the literature. They are highly morbid events in of themselves but also occur against a baseline in which symptoms are generally present and already debilitating. These are relevant aspects of the disease's natural history and pathogenesis which should be reflected in the background information. **Correction of prevalence** The background states *"The prevalence of bronchiectasis is increasing worldwide. In the UK, the estimated prevalence is up to 566 per 100,000 women"*; however, this figure reflects the female-only incidence and may overestimate the total population prevalence. For transparency, we would suggest that the male prevalence reported in the same study, that is, 485.5 per 100,000, be included too (45). Also to note, the quoted figures are gross prevalence estimates for all NCFBE patients in the UK based on coded diagnosis. The proposed indication is for patients with ≥2 PEx in the last 12 months, which is a small, severe, and high-risk subpopulation for whom care should be specialist-led. Based on current evidence using proxy coding for PEx in CPRD (13) and THIN (16) (likely underestimates), and PEx as recorded in the European and UK	bronchiectasis in the UK.

Section	Consultee/ Commentator	Comments [sic]	Action
		bronchiectasis registries (likely overestimates) (21), this subgroup represents between approximately 0 to <50% of the total NCFBE population. The Company recommends that it is clarified qualitatively but not quantitatively in the background information that the clinically relevant high-risk subpopulation for which the technology will be indicated represents only a portion of this overall gross prevalence for NCFBE. **Prognostic importance of frequent exacerbations** Patients experiencing ≥2 PEx in the last 12 months represent a small but clinically significant and severe subgroup with substantially worse outcomes. This subgroup is associated with increased morbidity, poorer lung function, reduced HRQoL, and higher mortality than patients with <2 PEx per year. Recognising this subgroup is essential for understanding disease severity and unmet need (1, 46, 47). **Current treatment paradigm** The Company feels that there are four important points related to current treatment that should be clarified in the third paragraph of the background information: 1. There are currently no licensed treatments for bronchiectasis in the UK, and there is no cure for the condition. 2. No treatments are currently available that directly intervene in the inflammatory pathology which underlies the disease. 3. Existing off label chronic treatments (bronchodilators, ICS, mucoactives, and antibiotics) are widely used in clinical practice, even in patients without comorbidities, despite NICE and BTS guidelines recommending their use only in limited contexts based on the evidential level of benefit-risk.	

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		4. Long-term use of antibiotics, and most prominently macrolides, present long-term tolerability, toxicity, and drug-resistant infection risks. Consequently, a significant proportion of people are clinically inappropriate for these agents, especially considering the older average age of patients (who are more likely to have comorbidities such as cardiovascular disease and poor hearing). Of note, azithromycin, which is the most prescribed long-term antibiotic in the UK (used in 75.6% of patients on long-term antibiotics for more than 28 days, per the 2017 BTS audit (34)), has been subject to recent regulatory scrutiny. The European Medicines Agency issued a notice in May 2025 requiring changes and harmonisation to azithromycin's label to emphasise growing concerns around antimicrobial resistance, long-term safety risks, and appropriate prescribing practices (48).	
	Association of Respiratory Nurses	The background information is very good with relevant and up to date statistics and data, it highlights the need for effective treatment in bronchiectasis delivery.	Thank you for your comment. No action required
	Taskforce for Lung Health and Asthma + Lung UK	Yes, the background information is complete. We note that the current wording states that "surgery may also be considered for people who have bronchiectasis". Clinicians have told us that surgery is used very rarely. Therefore, we believe this wording should be amended to: "in a small number of cases, surgery may be considered for people who have bronchiectasis." This revised wording ensures clinical accuracy while aligning with current treatment patterns, where surgery is a last resort for a highly selective patient group.	Thank you for your comment. The text has been updated as suggested.
	British Paediatric Respiratory Society	While the information is accurate, 2 issues need highlighting – 1. difference in prognosis and natural course of illness between adults vs children and young people (CYP): In particular, the potential for halting the disease process or	Thank you for your comment. The scope is intended to be a broad

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		reversal of bronchiectasis with appropriate and adequate treatment in CYP (Mills AJRCCM 2024), and 2. QALYs lost due to bronchiectasis (and potential improvement with treatment) and impact on family of the CYP.	overview of the topic. No action required.
	British Thoracic Society	The mucus is variable depending on the severity of the bronchiectasis. Presume rounded fingertips is finger clubbing? The BTS guidelines in bronchiectasis recommend consideration of a long term antibiotic in patients with three or more exacerbations annually.	Thank you for your comment. The scope is intended to be a broad overview of the topic. Yes, 'rounded fingertips' is referring to finger clubbing. This has now been added in brackets.
	Royal College of Paediatrics and Child Health	The information is accurate, but we consider it is incomplete. Please could the following issues be highlighted – 1. difference in prognosis and natural course of illness between adults vs children and young people (CYP): In particular, the potential for halting the disease process or reversal of bronchiectasis with appropriate and adequate treatment in CYP (Mills AJRCCM 2024), and 2. QALYs lost due to bronchiectasis (and potential improvement with treatment) and impact on family of the CYP.	Thank you for your comment. The scope is intended to be a broad overview of the topic. No action required.
Population	Insmed (company)	We recommend refining the population definition to align to the anticipated licensed indication, the ASPEN inclusion criteria, and the group of highest unmet need in the NCFBE population (38). Specifically, the population should be described as: "People aged 12 years and over with non-cystic fibrosis bronchiectasis who have experienced at least two pulmonary exacerbations in the previous 12 months".	Thank you for your comment. The population has been updated as suggested.

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	Association of Respiratory Nurses	Yes	Thank you for your comment. No action required.
	Taskforce for Lung Health and Asthma + Lung UK	Yes, we believe the population is defined appropriately.	Thank you for your comment. No action required.
	British Paediatric Respiratory Society	Yes, the population is appropriate. It may be appropriate to also state that the population includes those with primary ciliary dyskinesia (PCD).	Thank you for your comment. The population in the scope is intended to be broad to cover the final marketing authorisation. No action required.
	British Thoracic Society	Would prefer we separate paediatric and adult bronchiectasis. The study population was people with bronchiectasis and at least 2 exacerbations in the preceding 12 months. This should be the population and not all people with bronchiectasis over 12 years of age	If evidence allows the company can present subgroups. The committee will consider the relevance of these subgroups in line with NICE's health technology evaluations manual. The population has been updated to specify

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			people who 'have experienced at least two pulmonary exacerbations in the previous 12 months'.
	Royal College of Paediatrics and Child Health	Appropriate.	Thank you for your comment. No action required
Subgroups	Insmed (company)	Clinical heterogeneity is a hallmark of NCFBE. There is great variety of presentation in terms of demographics, pathologies, aetiologies, comorbidities, symptomology, microbiology, spirometry, lung radiology, and immunological profiles (36, 49, 50). For this reason, disease severity, prognosis, and treatments are very individualised notions in this disease. From a prognostic perspective, varied and nuanced individual risk patterns exist, and clinical specialists are 'skilled-in-the-art' of identifying them. However, the common risk factor, which is a well-defined clinical subtype, is having frequent exacerbations (≥2 per year) (23). This already aligns to the proposed indication for the technology, and the population studied in the ASPEN Phase 3 study for brensocatib (4). From a treatment perspective, the specific mix of interventions prescribed to a given patient is targeted against the pathologies in their particular clinical presentation and, where relevant, known aetiologies. This gives rise to the endotype-led notion of 'treatable traits', which has recently been published on (51). As such, there are no clinically well-defined subgroups, beyond that of the label itself, which distinguish between prognoses, and none that distinguish between therapeutic alternatives.	Thank you for your comment. No action required.

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		For prognosis, it has been shown that ppFEV$_1$, active *Pseudomonas aeruginosa* infection, and COPD co-diagnosis independently predict for PEx reoccurrence, albeit more weakly than recent PEx frequency itself (23). Severity scores in bronchiectasis, which are predictive for hospitalisation and mortality, also include age, BMI, recent hospitalisation, breathlessness scoring (on MRC), and radiological involvement as scoring parameters (52, 53). However, [redacted]. As such, there are no subgroups within the indicated population that are clinically relevant for the purposes of clearly demarcating clinical and cost effectiveness, nor for defining different comparators.	
	Association of Respiratory Nurses	Maybe the degree or severity of bronchiectasis, should it be sub-grouped into mild, moderate, severe disease? Where should it be prescribed? Primary care by clinicians with specialist interest in bronchiectasis or general care or specialist secondary bronchiectasis clinics.	If evidence allows the company can present subgroups in its submission for the committee to consider. The committee will consider the relevance of these subgroups in line with NICE's health technology evaluations manual.
	Taskforce for Lung Health and Asthma + Lung UK	We believe this technology could be more clinically and cost-effective for patients who exacerbate frequently and/or have frequent hospitalisations.	If evidence allows the company can present subgroups in its submission for the committee to consider. The committee will consider the relevance

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			of these subgroups in line with NICE's health technology evaluations manual.
	British Paediatric Respiratory Society	Specific focus should be given to CYP as highlighted above given the potential for reversal of bronchiectasis (or prevention of deterioration) and QALY lost.	If evidence allows the company can present subgroups in their submission for the committee to consider. The committee will consider the relevance of these subgroups in line with NICE's health technology evaluations manual.
	British Thoracic Society	Those with <3 and >=3 exacerbations per year (see BTS guidelines). Groups of patients with pseudomonas infection / colonisation.	If evidence allows the company can present subgroups in their submission for the committee to consider. The committee will consider the relevance of these subgroups in line with NICE's health technology evaluations manual.

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	Royal College of Paediatrics and Child Health	Specific focus should be given to CYP as highlighted above given the potential for reversal of bronchiectasis (or prevention of deterioration) and QALY lost.	If evidence allows the company can present subgroups in their submission for the committee to consider. The committee will consider the relevance of these subgroups in line with NICE's health technology evaluations manual.
Comparators	Insmed (company)	The comparator as listed, "Established clinical management without brensocatib", that is, continued use of existing care alone in an individual patient, is the correct comparator. In clinical practice, frequently exacerbating patients are generally individually optimised on a given mix of treatments, in line with their particular pathological and clinical presentation, risk profile, and tolerance. These patients have ongoing symptoms and exacerbations despite use of existing treatment options. While this treatment mix might be amended over time as patients' clinical presentation fluctuates, they are unlikely to see significant and sustained improvements in their disease status. As written, the treatment classes listed within established clinical management are correct. The Company does, however, note that bronchodilators, as well as inhaled corticosteroids, are the other classes which, if added, would complete the treatment categories included in British and European guidelines. The Company also points out that all of these treatments are used both acutely and chronically, depending on individual patient need.	Thank you for your comment. The examples of treatments that comprise established clinical management without brensocatib are not intended to be exhaustive but 'inhaled corticosteroids' have been added. 'Antibiotic prophylaxis' has been included as part of the first bullet point as suggested.

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		Furthermore, chronic antibiotics (i.e. antibiotic prophylaxis) are also just part of the individually optimised mix of drugs used in established clinical management, and not a distinct therapeutic intervention in themselves. Guidelines define circumstances in which they are appropriate treatment options, which are aligned to the indicated population for brensocatib. In clinical practice, they are used quite broadly for patients with ≥2 PEx in the last 12 months, and present risk and tolerability profiles that make them medically inappropriate for many individuals. As such, the Company advises that, for clarity, antibiotic prophylaxis be included within the brackets of the first bullet, and not as a separate bullet. Established clinical management, with the mix of constituent treatments as stated above, is consistent with the comparator studied in the Phase 3 ASPEN study for brensocatib. The ASPEN study allowed for maintenance doses of these medication classes to be continued from baseline, and for them to be used acutely as clinically required over the treatment period. Oral and inhaled chronic antibiotics had to be started more than 3 months prior to baseline to ensure stable dosing. Airway clearance techniques and physiotherapy were also permitted and continued.	
	Association of Respiratory Nurses	Established treatments that are already available such as oral, inhaled, nebulised mucolytics and antibiotic treatment.	Thank you for your comment. No action required.
	Taskforce for Lung Health and Asthma + Lung UK	We believe that antibiotic prophylaxis is not an appropriate comparator for bensocatib. Clinicians have told us they don't use antibiotics as prophylaxis in the treatment of bronchiectasis, as per the BTS Guideline for Bronchiectasis.[3] Antibiotics are used as treatment for acute infection or as chronic suppression	Thank you for your comments. The list of comparators is intended to be kept

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		of bacterial growth rather than prophylaxis. Therefore, established clinical management without brensocatib should be used as the comparator.	inclusive in the scope. The committee will discuss the most appropriate comparator(s) during the development of this evaluation. This will depend on the final marketing authorisation, the current treatment pathway, and current clinical practice. No action required.
	British Paediatric Respiratory Society	Yes, the listed treatments are the current standard treatments. However, the intervention group should be Brensocatib + established clinical management. It is noted that ASPEN trial (Chalmers NEJM 2025) was Brensocatib vs. Placebo (with other established clinical management similar in both groups)	Thank you for your comment. The intervention has been updated as suggested.
	British Thoracic Society	Comparators should be long term macrolides, long term other oral antibiotics, long term inhaled antibiotics, long term muco-active treatments, long term other anti-inflammatory treatments (long term = 3 months or longer). Could also include airway clearance (without medication).	Thank you for your comment. The examples of treatments that comprise established clinical management without brensocatib are not intended to be

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			exhaustive. No action required.
	Royal College of Paediatrics and Child Health	Yes, the listed treatments are the current standard treatments. However, the intervention group should be Brensocatib + established clinical management. It is noted that ASPEN trial (Chalmers NEJM 2025) was Brensocatib vs. Placebo (with other established clinical management similar in both groups)	Thank you for your comment. The intervention has been updated as suggested.
Outcomes	Insmed (company)	The Company supports the inclusion of the listed outcomes, but recommends the following refinements to better reflect clinical priorities and evidence interpretation: • Pulmonary exacerbations should be listed first, as they constitute the primary outcome in the Phase 3 ASPEN clinical trial, and are the key driver of prognosis, including symptom severity, lung function decline, HRQoL, hospitalisation, and mortality (1, 46, 47). • Inclusion of acute infections is redundant as a distinct outcome, as they are typically captured within the occurrence of PEx. The Company suggests removing these to avoid duplication. • The hospitalisation outcome is incorporated into the endpoint of severe PEx, which was included in the ASPEN study. Thus, this endpoint should be changed to severe exacerbations. Importantly, ASPEN was run during the COVID-19 lockdown (November 2020 to March 2024). As such, hospitalisation rates were suppressed relative to those seen in clinical datasets before this time. This likely affected the event rate and statistical outcomes for severe exacerbations as an endpoint in the study. • Given the heterogeneity of established clinical management and its individualised optimisation in practice (as reflected in the ASPEN study	Thank you for your comments. The outcomes have not been listed in any particular order. Acute infections has been removed as an outcome as suggested. The key outcomes relevant to the population are outlined in the scope but this is not an exhaustive list. Where relevant, the company is welcome to provide the evidence on

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		population), the need for other treatments or reduction in existing therapies is not considered a key clinical outcome. However, this aspect remains relevant for capturing potential cost offsets in cost-utility modelling. • Mortality is a relevant consideration in cost-utility modelling due to its established prognostic association with exacerbation frequency and lung function decline. However, it was not evaluable as an efficacy endpoint in the Phase 3 ASPEN study, as the study duration (12 months) was insufficient to observe mortality outcomes. Most patients have at least one informal caregiver who provides substantial weekly support. As such, caregiver quality of life is an important outcome for cost-utility modelling, reflecting the broader societal impact of the disease.	all outcomes that are important for people with the condition and their carers including specific outcomes related to 'exacerbations' during the evaluation, which is captured under 'pulmonary exacerbations'. 'Need for hospitalisation and other treatments' captures the desired outcome measure, and any confounding which affected the measurements of this outcome in the ASPEN trial should be fully explained and adjusted for or replaced with a proxy outcome in the company's submission.

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	Association of Respiratory Nurses	Yes – these are good outcome measures to measure and record effectiveness of treatment.	Thank you for your comment. No action required.
	Taskforce for Lung Health and Asthma + Lung UK	We believe that “pulmonary exacerbations”, “adverse side-effects”, and “health-related quality of life” are appropriate outcomes that will capture the most important health benefits related to brensocatib. However, we are calling on the Committee to consider: • “Frequency and severity of acute infections” may overlap with the “need for hospitalisation and other treatments” outcome. We suggest amending the wording to “need for hospitalisation and need for intravenous antibiotic courses.” This wording reflects that not all intravenous antibiotics are given in a hospital. • A one-off measurement of lung function cannot capture the fluctuating and progressive nature of the condition. To meaningfully assess health-related benefits, clinicians must monitor changes in lung function over time. Therefore, we suggest amending the wording to “change in lung function over time.” • Given that there is a high comorbidity burden in people with bronchiectasis, with estimates suggesting that up to 70% of bronchiectasis patients have comorbidities,[4] It may be difficult to capture the health-related benefits of brensocatib through the outcomes “symptom	Thank you for your comments. Acute infections has been removed as an outcome based on comments received during consultation. The outcome has been updated to ‘changes in lung function’. The key outcomes relevant to the population are outlined in the scope but this is not an exhaustive list. Where relevant, the

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		control" and "mortality". An international review found that the most common comorbidities were chronic obstructive pulmonary disease (58%), cardiovascular disease (53%) and asthma (40%).[5] These overlapping conditions can obscure the direct clinical impact of a new intervention, especially when evaluating symptom burden or cause-specific mortality. Therefore, additional or stratified outcome measures may be needed to accurately assess treatment benefit in this complex patient population.	company and consultees are welcome to provide evidence on all outcomes that are important for people with the condition during the evaluation.
	British Paediatric Respiratory Society	Outcomes listed are appropriate and capture the most important health related benefits. An additional outcome in CYP would be reversal of bronchiectasis (although it is appreciated that no data is currently available for this outcome). Also, of note: EQ5D not used in original ASPEN trial, so there maybe some undisclosed benefits although the QoLB resp domain maps well to the VAS in EQ5D, this is not part of health utility scoring. Time off work* /education not in the ASPEN study (For the CYP group: Time off work for parents, time off school for CYP)	Thank you for your comments. The key outcomes relevant to the population are outlined in the scope but this is not an exhaustive list. Where relevant, the company and consultees are welcome to provide evidence on all outcomes that are important for people with the condition during the evaluation. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	British Thoracic Society	These are good.	Thank you for your comment. No action required.
	Royal College of Paediatrics and Child Health	Outcomes listed are appropriate and capture the most important health related benefits. Additional outcomes in CYP would be a. reversal of bronchiectasis (although it is appreciated that no data is currently available for this outcome). Some aspects of Quality of life – ensuring that the evaluation takes into account specific issues for CYP (E.g. time off school)	Thank you for your comments. The key outcomes relevant to the population are outlined in the scope but this is not an exhaustive list. Where relevant, the company and consultees are welcome to provide evidence on all outcomes that are important for people with the condition during the evaluation. No action required.
Equality	Insmed (company)	Although the Company does not recommend changes to the remit or scope, we would like to highlight several equality-related issues associated with NCFBE that should be considered throughout the appraisal: • Evidence suggests that the burden of NCFBE varies across regions of England and may be influenced by socioeconomic status. This variation can affect access to diagnosis, specialist services, and new treatments. For example, data from Scotland indicate regional inequalities in service	Thank you for your comments. We have noted your comments on the equality impact assessment (EIA) form.

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		provision and outcomes, which may reflect broader patterns across the UK (54). • Related to this, there is significant variation in how patients with chronic respiratory conditions are reviewed and managed across the UK. In many areas, only patients with severe or worsening symptoms are regularly monitored, and/or can access specialist care only non-electively when their disease severity becomes acute. If prescribing is restricted narrowly within secondary care service pathways, rather than being broadly permitted within secondary care, this could lead to unequal access to brensocatib. • Additionally, adults with paediatric-onset bronchiectasis may experience more severe disease over time. If access to brensocatib is restricted based on age, this group could be disproportionately disadvantaged despite having long-standing disease (55).	No changes required to the scope.
	Association of Respiratory Nurses	Not to my knowledge	Thank you for your comment. No action required.
	Taskforce for Lung Health and Asthma + Lung UK	It does not appear that this draft remit and scope could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed.	Thank you for your comment. No action required.
	British Paediatric Respiratory Society	It is our suggestion that children younger than 12 years to be included in the consultation, in order to highlight the a. lack of evidence and lack of studies in this age group, and to b. evaluate potential off-label use of this drug in this age group.	Thank you for your comment. NICE can only appraise a treatment within its

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		This would ensure equality across the age groups.	marketing authorisation. No action required
	British Thoracic Society	No issues.	Thank you for your comment. No action required.
	Royal College of Paediatrics and Child Health	It is our suggestion that children younger than 12 years be included in the consultation, in order to highlight the a. lack of evidence and lack of studies in this age group, and to b. evaluate potential off-label use of this drug in this age group. This would ensure equality across the age groups.	Thank you for your comment. NICE can only appraise a treatment within its marketing authorisation. No action required.
Other considerations	Insmed (company)	For clarity and transparency, we recommend that the 'intervention' element of the Population, Intervention, Comparators, Outcomes (PICO) explicitly specify the formulation and dosing of the treatment: "Brensocatib (oral tablet, once daily)".	Thank you for your comment. The scope is intended to be a broad overview of the topic. However, the committee will consider the dosage and form of brensocatib during the development of the evaluation.
	Association of Respiratory Nurses	When will the treatment be licenced for use.	Thank you for your comment. The information relating to the license will be published by the

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			Medicines and Healthcare products Regulatory Agency. The expected licence date is considered confidential by the company.
	British Paediatric Respiratory Society	Recommendations for future research, including post-authorisation safety studies (PASS) in both CYP and adults.	Thank you for your comment. No action required.
	Royal College of Paediatrics and Child Health	Recommendations for future research, including post-authorisation safety studies (PASS) in both CYP and adults.	Thank you for your comment. No action required.
Questions for consultation	Insmed (company)	Where do you consider brensocatib will fit into the existing care pathway for non-cystic fibrosis bronchiectasis? Brensocatib is expected to be used as an add-on therapy to individually optimised existing care in patients with ongoing disease activity that confers a particularly poor prognosis (i.e. ≥2 PEx in the last 12 months), despite treatment. Please select from the following, will brensocatib be: • ~~Prescribed in primary care with routine follow-up in primary care~~ • ~~Prescribed in secondary care with routine follow-up in primary care~~ • ***Prescribed in secondary care with routine follow-up in secondary care***	Thank you for your comments. The positioning of the technology in the treatment pathway will be considered by the committee during the evaluation.

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		• ~~Other (please give details~~): Brensocatib will be prescribed in secondary care, with routine follow-up in secondary care. However, the Company believes it is important to qualify the term 'routine' in this context. In current UK practice, there is significant variation in how patients with NCFBE are routinely monitored. In many regions, only patients with severe or worsening symptoms are reviewed regularly in secondary care, and access may be limited to non-elective referrals when disease becomes acute. Others may be managed primarily in primary care, with infrequent or reactive specialist input. As such, 'routine' in this context is assumed by the Company to refer to the setting in which decisions about continuing treatment with brensocatib, or not, will be made (i.e. by a specialist). Furthermore, there is a need for clearer guidance on referral and prescribing pathways, as proposed by the British Thoracic Society Quality Standard for Clinically Significant Bronchiectasis, to ensure consistent and equitable access to drugs to treat NCFBE, including brensocatib (56). <u>For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.</u> The setting for the comparator treatments would not differ from that of the intervention. <u>Would brensocatib be a candidate for managed access?</u> No, the Company does not envisage brensocatib being a candidate for managed access. It has a chronic dosing schedule, is not an orphan drug, and is supported by a large Phase 3 trial of 12 months duration, with a	

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		clinically well-defined indicated population that aligns to the population studied in the trial. <u>Do you consider that the use of brensocatib can result in any potential substantial health-related benefits that are unlikely to be included in the quality-adjusted life year (QALY) calculation?</u> Yes, there may be broader health-related benefits associated with brensocatib that are unlikely to be included in the QALY calculation. • The ASPEN trial showed that brensocatib significantly reduced the frequency of PEx. Poor mental health, particularly anxiety and depression, is observed in the disease, and worsens with exacerbation frequency. These potential mental health benefits will not be explicitly captured from a cost and utility perspective in the QALY calculation (15, 57). • The cost-utility model will consider the utility gains associated with improved lung function outcomes on ppFEV$_1$, which was a key secondary endpoint in ASPEN. This spirometric endpoint relates to predominantly obstructive pathologies associated with mucus plugging, airway wall damage, luminal distortion, and distal airway collapse. However, restrictive pathologies also occur in NCFBE, driven by volume loss that is at least partly a result of alternative pathologies. Gas trapping and hyperinflation also occur. These benefits would be more strongly linked to improvements in Forced Vital Capacity (FVC), Residual Volume (RV), and Total Lung Capacity (TLC). [redacted] These lung function benefits that are not related to FEV$_1$ will not be captured in the QALY framework.	During the evaluation, it will be discussed if all benefits of brensocatib were captured in the cost-effectiveness analyses.

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		• NCFBE is associated with serious respiratory complications and long-term comorbidities, which worsen in their incidence with greater exacerbation frequency. These are discussed in more detail in the section "*What is the relative urgency of this evaluation to the NHS?".* The cost and quality of life benefits of potentially avoiding these expensive and morbid concomitant conditions with better long-term control of PEx and systemic inflammation will not be captured. • The capacity of brensocatib to reduce PEx may also lead to reductions in long-term antibiotic use, thus facilitating more judicious stewardship. The current 2024-29 UK National Action Plan on Antimicrobial Awareness specifically highlights the need for greater control of macrolide use. NICE NG15 also identified macrolides as a class for monitoring inappropriate levels of use (58). While the direct drug cost offsets of reduced antibiotic use will be factored into cost-utility modelling, broader benefits, such as economic, health, and policy benefits of potentially lower levels of drug-resistant infections, as well as the cost and QoL benefits of avoiding other long-term complications of macrolide use such as ototoxicity and cardiovascular events, will not be captured. <u>Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.</u> In addition to the pivotal Phase 3 ASPEN study and supporting Phase 2 WILLOW study, the Company has undertaken a comprehensive programme of evidence development to enhance understanding of the burden of NCFBE and the broader impact of brensocatib. The available data sources will include: • THIN and CPRD analyses (13, 16): UK databases used to analyse epidemiology, exacerbation patterns, treatment trends, and healthcare resource use.	

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		• ADELPHI DSP (3): A real-world study using validated generic and disease-specific instruments to quantitatively measure symptom burden and patient HRQoL. • BURDEN Survey (6): Structured qualitative research exploring the lived experience of patients and caregivers, including emotional, social, and functional impacts. SF6v2 outcomes will also be cross sectionally measured. Additional sources informing clinical and modelling assumptions will include: • Modified Delphi and York expert panels: Convened to support the development of clinical assumptions through expert consensus. • Vignettes study: To elicit health state utility values for patients and their caregivers. <u>How is 'moderate to severe' non-cystic fibrosis bronchiectasis defined in clinical practice? How does this compare to the population included in the key clinical trial informing this evaluation?</u> In clinical practice, moderate to severe NCFBE is defined by the frequency and severity of exacerbations: • High-risk patients with a high chronic symptom morbidity and particularly poor prognosis are those who have had two or more PEx in the last 12 months. Furthermore, the ASPEN study population aligns to this definition in its inclusion criteria. <u>Which treatments are considered established clinical management in the NHS for non-cystic fibrosis bronchiectasis in people 12 years and over?</u> Established clinical management in the NHS is highly heterogeneous, due to the clinical and pathological heterogeneity of NCFBE. Existing off label	

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		treatment options are individually optimised based on a patient's symptom severity, exacerbation history, aetiology (where known), and comorbid conditions (16). As previously described, the major treatment categories within existing care are bronchodilators, mucoactives, antibiotics, and ICS. These are the agents defined in British and European guidelines and are used both acutely and chronically. They are included as constituents of existing care in the scope as written (subject to the refinements suggested previously). As previously explained, for the treatment of bronchiectasis itself (i.e. not its comorbidities), guidelines recommend use of all these agents only in restricted circumstances, given the level of formal evidence for their benefit weighed against the long-term safety risks. Chronic antibiotics in particular, and most notably macrolides, have known long-term toxicities and complications, and are medically inappropriate for many patients. The generally broad use of all these agents in UK clinical practice despite recommendations, presumably out of necessity, highlights the unmet need in NCFBE. Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics (SPCs). For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the SPCs. All existing constituent treatments within existing care are used off label, although there is no evidence to suggest that dosing schedules in clinical practice generally differ to the SPCs.	The committee will discuss the most appropriate comparator(s) during the development of this evaluation. This will depend on the final marketing authorisation, the current treatment pathway and current clinical practice.

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		NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which brensocatib will be licensed. • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology. • could have any adverse impact on people with a particular disability or disabilities. **Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.** Please see Comment 1, Equality section for the potential issues pertaining to equality. To support the consideration of equality impacts in the appraisal, it would be helpful to gather evidence that illustrates how different groups (i.e., socioeconomic groups, or paediatric-onset NCFBE patients) may experience varying levels of access to care, diagnosis, and treatment for NCFBE.	We have noted your comments on the equality impact assessment (EIA) form.

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	Taskforce for Lung Health and Asthma + Lung UK	Where do you consider brensocatib will fit into the existing care pathway? We need some understanding of the volume of patients who may qualify for assessment for brensocatib – this will require a pathway that covers primary care identification and referral, and assessment in secondary care. Secondary care is appropriate for the prescribing and management of brensocatib, but capacity must be considered as brensocatib (and other drugs like it) will need an increase in workload and therefore resource.	Thank you for your comment. No action required.

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	British Paediatric Respiratory Society	Questions are appropriate. An additional separate question on cost effectiveness would be valuable. (We assume, we are not supposed to answer the questions in appendix B here but that this will be part of the actual evaluation process. Please let us know otherwise).	Thank you for your comments. The questions in appendix B were intended to be answered during the scoping consultation process.
	British Thoracic Society	Please select from the following, will brensocatib 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) **Option C** For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. Would brensocatib be a candidate for managed access? **I would consider this to be the case to assess cost-effectiveness.** Do you consider that the use of brensocatib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?	Thank you for your comments. The positioning of the technology in the treatment pathway will be considered by the committee during the evaluation.

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		No How is 'moderate to severe' non-cystic fibrosis bronchiectasis defined in clinical practice? How does this compare to the population included in the key clinical trial informing this evaluation? **There are criteria such as bronchiectasis severity index.** Which treatments are considered established clinical management in the NHS for non-cystic fibrosis bronchiectasis in people 12 years and over? **Chest physiotherapy** **Nebulised saline** **Mucolytic oral agents** **Prophylactic antibiotics including oral such as azithromycin and nebulised such as colomycin** **Oral and IV antibiotics**	The committee will discuss the most appropriate comparator(s) during the development of this evaluation. This will depend on the final marketing authorisation, the current treatment pathway and current clinical practice. No action required.
	Royal College of Paediatrics and Child Health	Covered as above	Thank you for your comment. No action required

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Additional comments on the draft scope	Insmed (company)	Blue highlighted and underlined confidential content relates to figures that are academic in confidence at the current time, for which public release could jeopardise future peer review publication. It cannot be determined yet when this information can be made publicly available. At this time content in the company's responses that is referenced to Insmed data on file is included in the reference list but is not provided in the reference pack. These sources will be provided as part of the full evidence submission.	Thank you for your comment. Information marked as confidential will be redacted accordingly in this document. But, please note the principles for marking and redacting confidential information ahead of the evidence submission. This outlines NICE's position on the confidential status of data which is awaiting publication in peer reviewed journals.

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

N/A