Ensifentrine for the Treatment of Chronic Obstructive Pulmonary Disease: Effectiveness and Value
Response to Public Comments on Draft Evidence Report

May 30, 2024

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#	Comment	Response/Integration
Manufacturers		
GSK		
1.	As outlined in our previous letter in response to ICER's draft scoping document, we believe it is inappropriate to include LAMA/LABAs and triple therapies (ICS/LABA/LAMA) in the comparator basket of maintenance therapies given that patients using these therapies were excluded from the ENHANCE trials of ensifentrine. Throughout the assessment, ICER applies data focused on a limited set of maintenance therapies to a broad set of available therapies, when there are significant differences in guideline recommendations, patient characteristics, disease severity, and outcomes across these therapies.	These therapies are being considered as background therapies, not comparators, and are present in both arms. We understand there is variability, both in the regimens that are used and in the specific treatments within each regimen that are used, in the current maintenance therapy that people living with COPD use. Regimen- and treatment-specific evidence for the current maintenance therapy was only used to inform the cost of current maintenance therapy. This cost of current maintenance therapy was applied to both arms of the model.
2.	In the draft evidence report, ICER acknowledges that triple therapy "has become standard of care in symptomatic patients and/or those with frequent exacerbations." ICER references evidence from an observational study of a different add-on product, roflumilast, to justify the inclusion of triple therapies in the comparator basket, but then goes on to note that the exclusion of triple therapies from the ENHANCE trials, along with LAMA/LABA therapies, "raises questions about the benefits of ensifentrine when added on to some of the most recommended regimens." Nonetheless, ICER concludes there is "high certainty that ensifentrine added to maintenance therapy, compared with maintenance therapy alone, results in at least a small net health benefit." We find it challenging to reconcile these two statements, and question ICER's "high certainty" in its conclusion of added benefit to the full set of maintenance therapies included in the comparator basket – especially LAMA/LABA and triple therapy.	Our evidence rating of B+ is based on the clinical trial evidence showing that ensifentrine added on to maintenance therapy results in benefits to lung function and COPD exacerbations, and a lack of harms. We do have higher certainty about the effect of ensifentrine in the population studied, and while the ENHANCE-1 and 2 trials did not include patients on dual LAMA/LABA or triple LAMA/LABA therapy, we did not see any evidence for effect modification by type of background therapy, and therefore have no reason to suspect that the results would differ based on type of background therapy. We have added language to both the Executive Summary and the report reflecting this.
3.	The inclusion of LABA/LAMA and triple therapies in the comparator group of maintenance therapies also results in questionable results in the cost-effectiveness analysis. ICER applies an exacerbation rate ratio taken from pooled data from the ENHANCE trials and applies it to all maintenance therapies, despite the fact that LAMA/LABA and triple therapies were excluded. There is no scientific basis for assuming that exacerbation rate ratio applies to LAMA/LABA and triple therapies, which have demonstrated a more significant impact on exacerbation rates than other maintenance therapies. The exacerbation rate ratio is by far	As noted above in more detail, we did not see evidence for effect modification by background therapy.

	the most significant factor in the results of the cost-effectiveness analysis, as shown in the tornado diagram (Figure 4.2); the relative impact of this input and the lack of direct evidence supporting its application to some of the most widely used therapies creates significant uncertainty in the results of the cost-effectiveness analysis.	
4.	Finally, in the cost-effectiveness analysis ICER uses data from a 2011 systematic review as the model inputs for baseline exacerbation rates. Data from the studies included in the systematic review were largely from placebo and "minimal treatment" arms in various trials that pre-date the introduction of modern COPD therapies that have demonstrated greater effectiveness in reducing exacerbations. Thus, baseline exacerbation rates in the current general population of COPD patients on maintenance therapy are unlikely to match the rates included as model inputs. This results in additional uncertainty in the cost-effectiveness model results, especially as applied to newer regimens like triple therapies.	An alternative source was not suggested within this comment. We used best available evidence to inform the deterministic estimate for these model inputs, but importantly, we also varied each input across a wide range in the sensitivity analyses because we acknowledge uncertainty and variability within model inputs.
5.	In conclusion, we can understand the decision to pool together maintenance therapies into one general comparator, given that ensifentrine is an add-on therapy. However, we are concerned that conclusions will be drawn regarding the additional benefit and value of ensifentrine added on to LAMA/LABA and triple therapies that have little clinical or scientific basis. At a minimum, we suggest that ICER reconsider the level of confidence in its results.	See above.

#	Comment	Response/Integration
Patient/Patient Groups		
COPD Foundation		
1.	Using outdated approaches as the foundation of the model hinders this review and sets a dangerous precedent for future assessments of new COPD treatments. The current model structure uses a dated approach to COPD severity classification based solely on lung function. Current GOLD guidance uses symptoms and exacerbations (moderate and severe) to classify a patient's severity for guiding therapy. We again encourage ICER to update the analysis approach to better represent current guidance to classify COPD severity important for treatment decisions.	The health states in the model were defined by the GOLD classification which considers lung function to define disease severity and disease progression. There are newer classifications, such as the GOLD ABE classification, that factor in both symptoms and exacerbations to classify a patient's severity. These newer classifications are primarily used for guiding treatment recommendations, but the underlying severity progression largely remains the same. We chose the GOLD classification to define our health states due to the vast amount of data for transitions, costs, and consequences stratified by the GOLD classifications. We do not anticipate dramatically different findings if a different classification was used for disease severity/progression due to the differential impact of the treatment that is primarily on exacerbations and not disease severity/progression.
2.	ICER should update the model structure to include all possible health states. In the current GOLD guidance paradigm, patients can become worse or better (if exacerbations and/or other symptoms decrease). The model only allows staying in the same health state or worsening. Allowing for a change to a less severe health state with treatment could be a key benefit of new treatments for COPD. Model structures described in similar assessments have previously allowed patients to transition to less severe health states.	We did not allow for transitions to less severe health states because it has not been suggested that this intervention is disease modifying. During initial calls with the manufacturer, we asked the manufacturer about improvement in functional class health states and they did not provide or suggest that they were looking at these data.
3.	Capturing all aspects of lived experience is critical when quantifying disease impacts and treatment potential. The current model includes treatment benefits centered around exacerbation. While exacerbations are important, these events do not represent the everyday impacts of those living with COPD. Treatment effects that matter most to patients include the relief for daily symptoms of breathlessness, cough and sputum, and fatigue. The current model approach should include treatment effects	We agree and share your concerns that we may be undervaluing the potential quality of life benefits of this intervention. Because of this, we even provided a sensitivity analysis assuming the intervention would improve health state quality of life. We also have concerns about double counting. We asked the manufacturer to provide us the quality of life data for patients not experiencing an exacerbation, which was a request that

	on daily symptoms and associated impacts on health-related quality of life (HRQoL) that are reported in the ENHANCE 1 and 2 trial results. The importance of inclusion of HRQoL is confirmed in the Report, where ICER notes that cost-effectiveness would improve if HRQoL results were included independent of exacerbations. Instead, ICER assumed that the full effect of treatment on HRQoL should be attributed to exacerbation events only. The rationale for this assumption is unclear when considering the specific patient reported outcome (PRO) assessments included in the trials for several reasons: • The recall period of relevant PROs is limited to either "now/today" or over a short timeframe prior to a study visit. • Based on the frequency of exacerbations, most patients would not have experienced an exacerbation when they completed the PROs at study visits. Therefore, most of the responses for relevant HRQoL PROs would not be influenced by an ongoing or recent exacerbation. • PRO results were directionally consistent across a variety of symptom and impact measures. • Inclusion of the EQ-5D-5L in the ENHANCE 2 trial provides a simple way to incorporate HRQoL impacts in the model beyond exacerbations. As noted in the Report, in ENHANCE 2, a statistically significant increase in EQ-5D-5L at week 24 was observed compared to placebo (MD versus placebo: 0.027; 95% CI: 0.004, 0.050; P=0.019). By this timepoint (i.e., week 24) most of the patients had not experienced an exacerbation providing confidence that these results represent everyday experience with COPD. Based on the frequency of exacerbations, the timing of the PRO responses, and the PRO recall periods, ICER should incorporate HRQoL impacts independent of exacerbation into this model to better represent all patient important impacts of treatment.	we thought would be feasible and would alleviate all concerns around double counting. Despite multiple requests to the manufacturer, they did not provide us these data. This leaves us hesitant to assume a significant benefit. As such, we made more conservative assumptions. In the future, if these data become available, we can revisit this decision.
4.	ICER should reconsider the data source for healthcare costs to ensure the current experience of COPD patients in the United States is accurately represented. Healthcare costs for exacerbations were estimated based on analysis from a clinical trial. Estimating healthcare	Thank you for sharing this more recent source. This source uses the first 12 months of data to classify patients into one of five exacerbation categories: 0 exacerbations=Category A, 1 moderate exacerbation=Category B, 2 or more

	resource use (HRU) and associated costs from clinical trial populations is not representative of the overall population and typically underestimates HRU and cost. An alternative source for this input should be used to represent costs of COPD.	moderate exacerbations=Category C, 1 severe exacerbation=Category D, and 2 or more exacerbations with at least one being severe=Category E. At first, we thought we could use the incremental cost of Category B to Category A to approximate a moderate exacerbation cost and we thought we could use the incremental cost of Category D to Category A to approximate a severe exacerbation cost given all-costs are reported, not exacerbation-specific costs. However, the all-cause costs are only reported for years 2 and year 3. Costs were not reported for year 1, which was the year their exacerbation status was classified.
5.	ICER should acknowledge the limitations of the current analysis approach in fully representing the full impact of COPD on patients and caregivers. The current analysis approach does not include other important impacts of COPD due to limited available evidence. The current modified societal perspective does consider patient and caregiver productivity and unpaid caregiver time. Data on other indirect impacts such as, caregiver health and quality of life, patient and caregiver out-of-pocket costs, or other support services, were not available for inclusion. ICER should clearly note in the Report the limited inclusion of broader impacts of COPD.	We appreciate this comment and have added the following to the "Uncertainty and Controversies" section of the report: "The findings from the modified societal perspective scenario analysis may not fully represent the impact of COPD on patients and caregivers. The current modified societal perspective includes patient productivity and caregiver time spent caregiving. Data on other indirect impacts such as caregiver quality of life were not available for inclusion."
6.	The current model assumes ensifentrine will be used as an add-on therapy for all patients (currently treated with mono, dual or triple therapy), although clinical trials for ensifentrine included adults with COPD of all levels of severity, including people on no maintenance therapy. Additionally, no more that 50% of patients were allowed on either LAMA or LABA maintenance therapy at inclusion. At model entry, the cohort should include an option to better mirror the trial population, with patients transitioning to alternative maintenance treatment basket options in later cycles of the model. Scenarios that include additional comparisons or treatment options across cycles would be more aligned with the current treatment approaches (e.g., LABA + LAMA versus LABA + ensifentrine, or LABA+LAMA+ICS versus LABA+LAMA+ensifentrine). Altering the approach could	As noted above in more detail, we did not see evidence for effect modification. Further, the objective of our analysis is not to mirror the trial population but rather approximate the likely population who will use the drug.

	show more cost-effective scenarios and improve the utility of the overall analysis and Report. Updating the model treatment approach to allow for treatment discontinuation and changes also provides the opportunity to align with impacts of longer-term adverse events associated with current treatments, such as infections and cardiovascular disease, and better represents the current recommendations for COPD Action Plans to be updated every six months.	
7.	Additional causes of discontinuation should be included in the model to accurately represent treatment duration. It seems unrealistic that discontinuation is only driven by adverse events at week 12 in a life-time model. In most models, there is a waning effect or a move to later lines of therapy. ICER should account for other causes of discontinuation and discontinuations after week 12.	The objective of our model is to estimate the cost-effectiveness of ensifentrine and is not to model the real-world treatment patterns of patients. For this model specifically, if other discontinuation was modeled, then the treatment cost would go away, and so would the treatment effect. Therefore, the incremental findings would not be dramatically different.
8.	Clarify how the model applies disutilities for exacerbations. Additional detail is needed in the Report to clarify if the decrement is applied for the entire one-year cycle length and how more than one exacerbation during the cycle is handled. Note, other models use 1-month cycles which allow for a more granular assessment of exacerbation impact and capture these disutilities more intuitively.	We have added more detail to section E of the supplement to better describe how exacerbation disutilities were applied. Exacerbations were modeled as an event, rather than a health state, to allow for more flexibility (allowing multiple exacerbations per cycle).
9.	Clarify how productivity costs are scaled to reflect the proportion of patients/caregivers who are likely retired or non-working. The current Report is unclear how productivity costs are applied at a population level. ICER should clarify if the proportion of non-working is accounted for in the model calculations for productivity.	We did not make any adjustments for the proportion of the population working versus not working. Rather we monetized a loss in productivity, acknowledging that loss in productive time may not be work-related. We do not monetize time missed from work directly, in which we would need to account for the percent of the population working. Rather we monetize productive time lost.

10.	Additional detail should be included to clarify specific healthcare costs included in the assumptions. While the healthcare total cost inputs may be appropriate, ICER should note what costs are specifically included in assumptions/inputs for full transparency and so others can determine if potential costs are missing from the inputs (e.g., primary or specialist care, rescue medications, device costs, oxygen).	We have added more detail to Section E of the supplement in response to this comment. The text now says, "These costs include COPD-related health care utilization costs excluding emergency department, inpatient, and pharmacy costs as those costs were included elsewhere in the model but include office visits and other outpatient costs which includes oxygen therapy."
Global Allergy & Airways Patient Platform		
1.	COPD Continues to Exact a High Clinical Burden COPD is not just a medical condition – it is a pervasive crisis that represents the third leading cause of death globally. COPD-associated deaths have increased by 30% worldwide between 1990 and 2010, further underscoring the fatality of the disease. The symptom burden associated with COPD is significant, especially dyspnea, or shortness of breath, which remains the most bothersome symptom that patients note experiencing. Dyspnea and other symptoms are also associated with an increased risk of exacerbations. The health risks associated with exacerbations are acute, with patients facing an almost fourfold increase in the risk of cardiovascular events, such as heart attacks, within 30 days post-exacerbation. Experiencing two or more moderate exacerbations can increase a patient's risk of a future severe exacerbation by 61%. The healthcare resource use associated with these exacerbations is significant, with up to 20% of patients requiring at least one hospital admission per year. COPD-related hospitalizations are also associated with an increased mortality risk, especially in the period post-admission, where mortality has been observed to increase by 43% two years post-discharge.	We appreciate the additional information provided about the clinical burden of COPD. We have added relevant details to the background section of the Evidence Report.
2.	Quantifying the Impact of COPD on Patient Quality of Life Remains Difficult While COPD-specific quality of life instruments exist – such as St. George's Respiratory Questionnaire for COPD Patients (SGRQ-C), the COPD Assessment Test (CAT), and the Clinical COPD Questionnaire (CCQ) – these tools are designed to help clinicians assess patients' health status and tend to focus on physical symptoms and limitations. They do not fully address the psychosocial aspects of COPD that affect a patient's ability to engage in meaningful activities such as	We agree that current COPD quality of life instruments may not fully capture the impact of COPD on patients. We have added this concern to the Stakeholder Perspectives section.

	remaining employed, playing with grandchildren, traveling, or participating in community events.	
3.	COPD Imposes a High Burden on the Health System Due to Direct and Indirect Costs The economic impact associated with COPD is expected to rise to $4.8 trillion globally by 2030, reflecting the extensive resources required to manage this disease. In many countries, including the United Kingdom (UK) and Canada, COPD is the second most common cause of emergency admissions. This high rate of hospitalization places a significant strain on healthcare systems, with nearly 50% of COPD costs in Europe attributed to these hospital stays. Among patients who are employed, COPD leads to substantial income losses, with a survey across six countries estimating an average loss of $7,365 due to missed work. Moreover, approximately 40% of patients are forced into premature retirement due to COPD, resulting in lifetime income losses of $316,000.	We appreciate the additional data and have added relevant information to the Background section of the report.
4.	Conclusion There continues to be a high unmet need for patients with COPD. It is imperative during value assessments of new innovations that we acknowledge the full spectrum of its impact – from the direct costs of medical care to the indirect costs borne by patients and their families. As we consider future healthcare policy and resource allocation in COPD, access to a new drug class with a novel mechanism of action will provide hope and increased health for patients whose COPD is not adequately managed with the current drug classes available. As a global advocacy community, we urge ICER to consider the broader scope of physical, mental, psychosocial & financial impact to the COPD patient and carer community and society.	Thank you for your detailed comments. We will discuss the broader scope of physical, mental, and psychosocial and financial impact during the public meeting on June 14th. Many of these dimensions are included in our voting questions, which you can find here.

#	Comment	Response/Integration
Other		
Partnership to Improve Patient Care		
1.	ICER's sources of data do not accurately capture the reality for COPD patients in the United States. ICER's choice of data for costs per exacerbation appear to underestimate the true cost of exacerbations in the United States. The ICER model uses a single study that found the cost of moderate exacerbation estimated at $2,415 and a severe exacerbation at $26,047. This study relies on a sample of 300,000 patients. A much larger recent study that utilized data from CMS suggested a range of cost per exacerbation of between $26,544 - $43,774 based on category of severity. This data relied on a much larger sample size of just under four million patients. In this instance, the more recent study with a larger sample population appears to provide more credible data. We would suggest that, where available, ICER should be using the most recent and largest studies.	Thank you for sharing this more recent source. This source uses the first 12 months of data to classify patients into one of five exacerbation categories: 0 exacerbations=Category A, 1 moderate exacerbation=Category B, 2 or more moderate exacerbations=Category C, 1 severe exacerbation=Category D, and 2 or more exacerbations with at least one being severe=Category E. At first, we thought we could use the incremental cost of Category B to Category A to approximate a moderate exacerbation cost and we thought we could use the incremental cost of Category D to Category A to approximate a severe exacerbation cost given all-costs are reported, not exacerbation-specific costs. However, the all-cause costs are only reported for years 2 and year 3. Costs were not reported for year 1, which was the year their exacerbation status was classified. Importantly, the study did not suggest a range of cost per exacerbation of between $26,544-$43,774. The study suggested a range of annual (not per exacerbation) all-cause healthcare costs (not exacerbation specific) for patients with COPD.
2.	We are also concerned that the sources used for mortality modifiers by COPD severity may underestimate the years of life lost due to COPD. The ICER model assumes standardized mortality ratios compared to those without COPD as 1.3 for moderate, 1.6 for severe and 1.9 for very severe. The original source is a European study using Eurostat data from 21 countries, and states that the measures of severity varied widely by country. The paper itself is a request to improve standardization of outcome measures in COPD. There is a better source for mortality ratios that is based on United States data. This study estimates standardized mortality ratios compared to those without COPD as 1.6 for moderate COPD and 2.7 for severe COPD. As ICER's assessments are conducted for an American audience and meant to drive decision making within the United States	Thank you for sharing this other source. The reason we did not use that source is because it does not remove mortality due to exacerbations from the reported standardized mortality ratios. Due to ensifentrine's effect largely being on fewer exacerbations, it was important to have an exacerbation-specific mortality assigned. To avoid double counting, we then needed COPD standardized mortality ratios for COPD patients not experiencing an exacerbation. The source we used allows us to model COPD-specific, but non-exacerbation-related mortality, and then allows us to add in exacerbation-

	health care system, the paper based on United States data would be the more accurate source.	specific mortality without double counting.
3.	Finally, ICER's health state utility values are derived from a randomized clinical trial when real world data is available and more accurate. ICER uses utility scores of 0.787 for moderate, 0.750 for severe and 0.647 for very severe COPD. These are second hand and taken from a multi-center randomized clinical trial (RCT) using the UK value set. Over the years, PIPC has laid out the many limitations that result from using utility data derived solely from the trial setting. RCT populations are generally much healthier than real-world disease-specific populations. There are always explicit and implicit exclusion criteria for recruitment into trial settings, including age, the existence of co-morbidities and levels of healthcare access and utilization, that make RCT populations rarely representative of real-world populations of need.	We agree that it would be ideal to use both real-world evidence and data from randomized clinical trials. However, there is rarely real-world evidence available during the time of an FDA decision, therefore all stakeholders in the healthcare system rely on data from trials, and data provided by the manufacturer, for their decision-making.
4.	In addition, utilities in RCTs tend to be inflated compared to non-RCT samples of patients as EQ5D gains are often generated for patients in RCTs that are non-disease or treatment related socio-emotive components, that can occur because of receiving greater care and attention from healthcare professionals. There is also a placebo effect from patients in both arms of the trial. Numerous studies have highlighted the utilities generated in RCTs are generally much higher than the equivalents would be for a real-world population. Ultimately, ICER should be looking to use the best possible sources that are most representative of the population in need of treatment. This should include prioritizing sources based on United States data, large sample sizes, real-world data, and the most recent publications.	We agree that it is important to use all available high-quality sources of evidence. ICER conducts a thorough literature search, and we send a detailed data request to the manufacturer of the drug to ask for all available data, including real-world evidence and publications that have not yet been published.
5.	Evidence suggests that frequency of exacerbations is related to significantly worse survival outcomes, a dynamic that is not captured in ICER's model. Exacerbations, whether treated or untreated, have a detrimental and prolonged impact on patients' health status and outcomes, and have cumulative negative effects on lung function over time. COPD exacerbations are highly heterogeneous, varying in severity and phenotype. Evidence has shown that exacerbations are related to worse survival outcomes, yet the model only bases risk of mortality modifiers on severity level, not rate of exacerbations. The frequency of exacerbations is also a marker of both disease burden and mortality risk. Frequent	We assign an increase in mortality due to a severe exacerbation, which isn't universally done and benefits the treatment. We also model exacerbations as events which allowed us to model a higher mortality risk for a higher rate of severe exacerbations. Therefore our approach to modeling exacerbations and exacerbation-specific mortality accounts for this heterogeneity in survival and mortality as it relates to severity and rate of exacerbations. We did not assume that exacerbations impact disease progression. This

	exacerbations, mainly in patients with severe COPD, accelerate disease progression and mortality. This is a dynamic also ignored in the ICER model. Exacerbations of COPD also have a cumulative effect on lung function. Patients in the 3-year TORCH study who experienced 0–1.0 moderate to severe exacerbations per year had a 37% faster decline in lung function than those with no exacerbations. Among those patients who experienced more than one moderate to severe exacerbation, the rate of decline in lung function was 65% faster.3 Rate of exacerbations also varies strongly not just by severity but also by age and gender , the dynamic nature of which is not adequately represented using a single estimate of exacerbations per cycle used in the model. The ICER model largely ignores the complexity of this dynamic between lung function and exacerbation rate over time, and the impact of exacerbation rate on mortality and disease progression. This is a stark omission, as it will not allow ICER's assessment to capture an accurate value of treatment of COPD.	assumption was aligned with the majority of economic models in COPD; however, a few models have incorporated a reduction in FEV_1 following an exacerbation. Most of those models were modeling FEV_1 decline over time, rather than modeling defined health states. We engaged with economic experts who had previously incorporated a link between an exacerbation and lung function and heard that the evidence to support this assumption is limited and it was not a key driver of the cost-effectiveness.
6.	ICER Continues to Use the Discriminatory QALY and the Similar Measure evLYG. Multiple studies have shown that cost-effectiveness models using the quality-adjusted life year (QALY) discriminate against patients with chronic conditions, like COPD, and people with disabilities. There is widespread recognition that the use of the QALY is discriminatory, reflected in laws that bar its use in government decision-making. The National Council on Disability (NCD), an independent federal agency advising Congress and the administration on disability policy, concluded in a 2019 report that QALYs discriminate by placing a lower value on treatments which extend the lives of people with chronic illnesses and disabilities. NCD recommended that policymakers and insurers reject QALYs as a method of measuring value for medical treatments. Additionally, we share the concerns of NCD about the equal value of life year gained (evLYG), a similar measure created by ICER to supplement the QALY. The evLYG is a simplistic fix attempting to address criticism that the QALY devalues life years lived with a disability, yet it fails to account for oversimplified measures of quality-of-life gains in expected life years (not extended life years) and it does not account	Thank you for this comment. We invite you to review our Value Assessment Framework for a detailed overview of the different methods and concepts we use in our reviews: https://icer.org/our-approach/methods-process/value-assessment-framework/ The quality-adjusted life year (QALY) is the academic standard for measuring how well all different kinds of medical treatments lengthen and/or improve patients' lives, and therefore the metric has served as a fundamental component of cost-effectiveness analyses in the US and around the world for more than 30 years. If evidence shows that a treatment helps lengthen life or improve quality of life, these benefits are comprehensively summed up to calculate how many additional QALYs the treatment provides, and this added health benefit is then compared to the added health benefit of other treatments for the same patient population.

	for any health improvements in extended life years. Like the QALY, the evLYG relies on average estimates based on generic survey data and obscures important differences in patients' clinical needs and preferences, particularly those with complex diseases and from underrepresented communities. It assumes that people value life year gains more than quality of life improvements, giving a lower value to health interventions in patient populations that have a lower life expectancy or fewer life years gained from treatment, which may include people with disabilities, underlying chronic conditions, the elderly, and certain communities of color. With the evLYG and the QALY, ICER promotes two compromised and flawed measures of health gain. Deciding which to choose is confusing and inconsistent.	To complement the use of the QALY, ICER's reports also include a calculation of the Equal Value of Life Years Gained (evLYG), which evenly measures any gains in length of life, regardless of the treatment's ability to improve patients' quality of life. In other words, if a treatment adds a year of life to a vulnerable patient population – whether treating individuals with cancer, multiple sclerosis, diabetes, epilepsy, or a severe lifelong disability – that treatment will receive the same evLYG as a different treatment that adds a year of life for healthier members of the community. By understanding a treatment's cost per evLYG, as well as its traditional cost per QALY, policymakers can take a broader view of cost-effectiveness and be reassured that they are considering information that poses no risk of discrimination against any patient group.
7.	ICER fails to capture the heterogeneous nature of COPD. As ICER notes in its report, COPD is a widely heterogenous disease both in terms of the cause, the level of comorbidity, and its impact on patient experience. This points to a larger issue with respect to value assessment reporting is that the archetypal cost-effectiveness model relies heavily on producing effect size based on population averages, and rarely are results specific to subpopulations released in results. It is well established that generating and reporting of differential value assessment across subgroups leads to substantial health gains, both through treatment selection and coverage. If ICER is to take seriously its role of informing health policy decision makers about the value of new therapies, it needs to move away from the assumption that all patients are the same. No patient is average, and it is essential that ICER moves to acknowledge this and incorporate analysis of subpopulations and produce ranges of value rather than relying on an archetypal patient.	Please provide a source for the statement "it is well established that generating and reporting of differential value assessment across subgroups leads to substantial health gains, both through treatment selection and coverage." To clarify--ICER reports evaluate drugs (therapies or treatments) and we look at the average price for these drugs in our analyses.