Oveporexton for Narcolepsy
Response to Public Comments on Draft Evidence Report

APRIL 29, 2026

Table of Contents

#	Comment	ICER Response
Manufacturers		
Jazz Pharmaceuticals		
1.	**Focus the Analysis on High Sodium Oxybates to Ensure Validity of Model Inputs** ICER's draft report groups oxybate products as a single class and includes both high sodium oxybates (Xyrem, Lumryz, generic variants) and low sodium oxybate (Xywav) within this grouping. The inclusion of low sodium oxybate is not appropriate, as it is a distinct formulation with a safety profile that differs from high-sodium oxybate formulations. Low sodium oxybate is a mixed-cation (calcium, magnesium, potassium, and sodium) oxybate with approximately 92% lower sodium content than high-sodium oxybate at equivalent doses. At the maximum Food and Drug Administration (FDA)-approved dose (9 g/night), this corresponds to approximately 1,600 mg (70% of the recommended daily amount) of daily sodium exposure with high-sodium oxybate compared to ~130 mg (6% of the recommended daily amount) with low sodium oxybate. This difference has clear clinical relevance. There is well-established global consensus that prolonged excess sodium intake is associated with increased blood pressure and cardiovascular risk, including coronary events and stroke. Given that NT1 requires chronic, often lifelong treatment, cumulative sodium exposure is an important consideration for long-term patient outcomes. Reflecting this, the FDA determined that low sodium oxybate is clinically superior to high-sodium oxybate due to its reduced sodium content and associated reduction in cardiovascular risk. By grouping different oxybates, ICER introduces significant uncertainty by combining data across heterogenous oxybate formulations and evidence sources. Efficacy	Thank you for your comments. While we appreciate that there are some differences among the oxybate products, in terms of efficacy, the three different formulations are comparable. In fact, Lumryz was approved via the 505(b)(2) pathway, which allows at least some of the information required for approval to come from existing studies of the active drug ingredient. Additionally, clinical evidence has shown similar efficacy between low sodium oxybate (LXB, Xywav) and high sodium oxybate (SXB) and supports using a similar dosage for LXB as used for SXB (Junnarkar et al., Expert Opinion on Drug Discovery 2022, 17(2), pp. 109–119) Thus, it seems reasonable to pool efficacy data from the different formulations, as we did for our network meta-analysis. We note that the majority of the data included in the network meta-analysis comes from studies of Xyrem and Lumryz, which are high sodium oxybate products. We have acknowledged the differences in harms from the low sodium formulation in the report, both in the clinical effectiveness section and in the Uncertainties and Controversies section (see Section 3). Although treatment with the low sodium formulation has been shown to reduce blood pressure, there is no direct data that suggests that treatment with the low sodium form of sodium oxybate compared with the high sodium form results in a reduction in cardiovascular events. In fact, although the American Heart Association's expert panel consensus recommendations on cardiovascular risks in people with narcolepsy recommends that clinicians educate patients that high sodium intake can increase the risk of hypertension and cardiovascular disease, the document also acknowledges that the evidence base for this recommendation is limited and is derived mainly from retrospective, nonrandomized clinical trials, and that some studies have shown that treatment with sodium oxybate does not increase risk of hypertension (Kwon et al., JAHA 2024; 13(16): 1-15).

	inputs are derived from multiple trials of oxybates, while discontinuation rates are sourced from a combination of trial-based estimates and long-term extension studies across different formulations.	
2.	In addition, utility inputs are derived from multiple preference-based measures, including a mix of directly observed and mapped estimates across instruments. As documented in the literature and in ICER's limitations section, these approaches capture different dimensions and may respond differently to clinical change, which may introduce additional uncertainty into the model. As a result, treatment benefit and treatment persistence may not be fully aligned to a common evidence base.	While we agree that utilities derived from multiple preference-based measures may introduce uncertainty, these trial-based utilities are the best available evidence for the utility impact of the treatments under evaluation. Narcolepsy is a multi-dimensional condition, restricting utility estimation to a single factor such as ESS risks underrepresenting quality of life impacts that treatment provides, introducing its own source of uncertainty. We therefore believe utilities derived from trial evidence albeit from multiple measures, better reflects the full burden of narcolepsy compared to the other possible source, anchoring solely on the ESS. As a result, we explored applying ESS-based utilities in a scenario analysis.
3.	The underlying studies differ in patient populations, including variation in disease subtype and baseline severity, as well as in study design, duration, and use of concomitant therapies. We appreciate that ICER also acknowledges these differences and the resulting uncertainty, noting that variation in trial protocols, baseline characteristics, and treatment context may affect comparability across treatments. These sources of heterogeneity may not be fully captured when combining inputs across evidence sources, which could contribute to additional uncertainty in the model. Combining different oxybates may not fully capture clinically meaningful differences in safety and could introduce additional complexity, given that discontinuation is the primary pathway through which adverse events influence model outcomes. In addition, inputs are drawn from multiple sources across different oxybate formulations, with limited data specific to low sodium oxybate, which may limit the model's ability to reflect product-specific outcomes. Taken together,	As we state above in Response 1, the majority of the data in the network meta-analysis is derived from studies using high sodium oxybate. We agree that the heterogeneity in studies introduces uncertainty in the estimates, as we have acknowledged in the report. We have also acknowledged that our analysis may not capture all the differences between the forms of sodium oxybate. However, efficacy is similar across forms of sodium oxybate, and studies have not yet demonstrated that taking a lower sodium form of sodium oxybate results in reduction of cardiovascular events. We agree that clinicians and patients may choose medications based on their individual circumstances, we have added two scenario analyses to reflect real-world sodium oxybate utilization, one incorporating market share data across all sodium oxybate products, and another applying clinician informed dose distributions.

	these factors may influence estimates of treatment value and contribute to uncertainty in the results. Moreover, this approach may not fully reflect clinical practice, where treatment decisions are made based on product-specific characteristics, including sodium content, tolerability, and patient comorbidities. Given that a majority of the inputs in the model are sourced from high sodium oxybate studies, we recommend that ICER consider limiting the generalizability of the findings to high sodium oxybates.	
4.	**An ESS-based Approach to Utilities May Improve Consistency and Reduce Cross-trial Differences** ICER's base case combines utilities derived from multiple preference-based measures (PBMs). This approach may introduce uncertainty, as different instruments capture different health dimensions and may respond differently to clinical change—an issue ICER also acknowledges. Importantly, while ICER's updated model structure—where health states are defined based on treatment phase and response status (e.g., ESS ≤10 vs. >10)—is a meaningful step forward, some differences may remain between how health states are defined and how corresponding utilities are measured. A symptom-based utility framework resolves these issues. Under an ESS-based approach: Utilities are anchored to clinically meaningful disease severity categories, A consistent method is applied across all treatments, and Utility estimation is aligned with the clinical endpoint used to define response in the model. Importantly, this approach is supported in the literature. Prior economic models in NT1 have linked ESS changes to utility, reflecting the central role of EDS in driving quality of life.[18] Health technology assessment bodies, including both the National Institute for Health and Care Excellence and Canada's Drug	Please see response 2. Additionally, ESS based utilities are derived from a population of majority obstructive sleep apnea patients, introducing uncertainty in its applicability to a NT1 population. Additionally, the National Institute for Health and Care Excellence noted that changes in quality of life may not be adequately captured by mapping the ESS to the EQ-5D. We therefore maintain that trial derived utilities represent the best available evidence and explored ESS-based utilities in a scenario analysis.

	Agency, have also recognized the limitations of generic PBMs in this condition and have accepted approaches that directly reflect symptom burden. In ICER's scenario analysis, shifting to an ESS-based utility approach shifts the incremental cost-effectiveness ratio by approximately 171%, suggesting that results are highly sensitive to this assumption. In this context, the choice of utility approach in the base case may warrant further consideration. These concerns are especially pronounced in NT1, where EDS is a primary driver of disease burden and quality of life.	
5.	**Consider Uncertainty and Evolving Market Dynamics in Sodium Oxybate Pricing** We appreciate that ICER revised the assumed price for generic sodium oxybate to better reflect real-world costs. That said, the current assumption of approximately $160,000 is based on a single point estimate and may not fully capture the evolving and heterogenous pricing landscape. Pricing for oxybate is expected to vary substantially across formulations, manufacturers, and contracting arrangements, particularly as the market continues to evolve. Pricing is an important input in cost-effectiveness analyses and can meaningfully influence results. Reliance on a single point estimate, especially in a market undergoing change, may not fully reflect the range of plausible comparator costs. In addition, changes in market structure, including increased competition and potential differentiation across products, may lead to variability in pricing over time rather than a uniform trajectory. This dynamic is well described in the literature, as generic entry is often associated with price erosion over time. Given this uncertainty, incorporating a broader range of pricing assumptions may help support more robust interpretation of results. To enhance transparency and decision relevance, ICER may consider including alternative sodium oxybate pricing scenarios and presenting results across a range of plausible values. Including sodium oxybate pricing as a	Thank you for your comment. We agree that the price of sodium oxybate may vary over time and across individuals for a range of reasons. However, explicitly modeling temporal price changes is challenging given the uncertainty around future trends. To address uncertainty in the estimated price—particularly that driven by differences in market share and pricing across products—we conducted additional scenario analyses using sodium oxybate prices that reflect real-world market shares across branded and generic products, as well as real-world dosing patterns.

	key parameter in one-way sensitivity analyses may also help illustrate its impact on model outcomes.	
6.	**Ensure Analyses Reflect Uncertainty Around Oveporexton Pricing, Including the Potential for Higher Launch Pricing** ICER's cost-effectiveness analysis relies on a placeholder price of $175,000 for oveporexton. Given that oveporexton has not yet launched, there remains uncertainty around its eventual price, which may differ from this placeholder value. Historically, newly launched mechanistically novel therapies that are first in class are often launched at a substantial premium to existing therapies. Launch pricing is expected to be $200,000 or higher, underscoring the importance of evaluating a range of plausible price points. To support robust interpretation of results, ICER may consider presenting findings across a range of pricing scenarios and highlighting the sensitivity of results to this key input. Including oveporexton pricing in one-way sensitivity analyses would further illustrate its impact on model outcomes. As additional information becomes available, ICER may also consider updating the analysis to reflect real-world pricing to ensure that conclusions remain decision relevant.	Thanks for your comment. Although it is still uncertain what the actual price of oveporexton will be, we have updated the placeholder price to $ 250,000 in our analysis based on more recent estimates by IPD analytics. However, there are always uncertainties around the placeholder price, and as we noted in various sections in our report, the actual cost-effectiveness of oveporexton will depend on its actual price. The most informative sections of our report on pricing are the section on threshold analyses and the section on ICER's Health Benefit Price Benchmark. We have presented threshold analyses versus each comparator in our report to show the price range at which oveporexton remains cost-effective at commonly used US cost-effectiveness thresholds for the various comparators. And central to ICER's cost-effectiveness analysis is the estimation of the Health Benefit Price Benchmark, which is ICER's judgment on the price range that aligns with oveporexton's added benefits relative to a common first-line and cost-effective treatment option.
7.	**Characterize Uncertainty Around the $150,000 per Quality-Adjusted Life Year (QALY) Result** The proximity of the base case incremental cost-effectiveness ratio for oveporexton versus sodium oxybate to a commonly cited cost-effectiveness threshold highlights uncertainty in the model and may make interpretation of the results for voting purposes more challenging. When an incremental cost-effectiveness ratio falls at or near a decision threshold, even modest changes in assumptions can shift results above or below that threshold. As a	Thank you for your comment. The incremental cost-effectiveness ratio has changed due to other changes made to the model.

	result, the interpretation of cost-effectiveness becomes highly sensitive to inputs, including those subject to uncertainty in the current model. These include assumptions related to utility estimation, comparator pricing, discontinuation, placeholder pricing, and the long-term durability of oveporexton, which remains uncertain given the relatively short duration of available clinical data. In this context, presenting a single point estimate that aligns with the cost-effectiveness threshold may overstate the certainty of the model and its conclusions. To support more appropriate interpretation, ICER may consider: Emphasizing the uncertainty surrounding the base case incremental cost-effectiveness ratio, given its proximity to the $150,000 per QALY threshold, and Illustrating how variation in key inputs affects whether results fall above or below this threshold. Highlighting this uncertainty could help ensure that decision-makers understand that conclusions regarding cost-effectiveness are contingent on assumptions that remain uncertain.	
Takeda Pharmaceuticals		
1.	**"No treatment" is not an appropriate clinical comparator, but rather a real-world manifestation of unmet need and access/tolerability barriers** ICER evaluated the clinical efficacy and safety of oveporexton versus "no treatment", as represented by the placebo arms of the Phase 3 TAK-861-3001 and TAK-861-3002 trials. While Takeda recognizes that anchoring the cost-effectiveness model on "no treatment" was a necessary statistical approach to provide a common comparator for indirect analyses, ICER's emphasis on conclusions that	Thank you for your comment. We agree that standard of care for the treatment of NT1 involves active treatment with current FDA approved medications. However, our comparison of oveporexton vs no treatment was done to align with the inclusion criteria of the pivotal trials, FirstLight and RadiantLight, in which the participants were required to have a washout period of previous medications for narcolepsy and were not permitted to be on other narcolepsy treatments during the trial. If oveporexton is approved and comes to market, this particular scenario would present itself in patients who are newly diagnosed and naïve to therapy, along with the small proportion of patients

	oveporexton is not cost-effective versus "no treatment" warrants additional context to avoid misinterpretation. Highlighting such results without clear caveats risks implying that "no treatment" is a clinically acceptable treatment strategy for NT1 and that patients can manage the substantial and persistent burden of NT1 symptoms without therapy. We strongly encourage ICER to add explicit context clarifying that "no treatment" is not a guideline-concordant treatment option in NT1 and should not be interpreted as a normative comparator. In real-world settings, periods of untreated disease more likely reflect unmet need and systemic barriers (e.g., access, affordability, coverage restrictions, tolerability limitations, contraindications, discontinuation), rather than an evidence-based or ethical standard of care. Accordingly, "no treatment" should be presented as a limited real-world benchmark (i.e., a manifestation of gaps in care) rather than a guideline-aligned clinical alternative.	observed in this state in real-world data. Thus, we felt that it was an important part of our evaluation of oveporexton. We have added language in the Uncertainties and Controversies section to reflect this reasoning.
2.	ICER should clarify that cost-effectiveness results versus "no treatment" may be sensitive to uncertain disease burden inputs and to limitations in translating trial endpoints into broader real-world benefits. In particular, incomplete capture of the full spectrum of NT1 symptoms and longer-term functional outcomes and disease-related harms (e.g., accident/injury risk, workplace safety, increased long-term risk of cardiovascular disease (CVD), and downstream mental health consequences) may lead the model to understate the impact patients experience with effective treatment. For these reasons, conclusions drawn from a "no treatment" anchor should be clearly caveated, with greater emphasis placed on the fact "no treatment" is not an evidence-based or ethical standard of care.	Disease burden inputs in NT1 carry meaningful uncertainty, and we acknowledge the gaps this commenter has highlighted. The no treatment comparator was included because a proportion of NT1 patients are observed in this state in real-world data, regardless of whether this reflects an evidence-based standard of care. We agree that cost-effectiveness results relative to no treatment should be interpreted with caution, and a finding that a treatment is not cost-effective relative to no treatment may reflect limitations in capturing the full disease burden in the untreated state, or the high acquisition costs of active treatment relative to the lack of acquisition costs with no treatment.
3.	**The consequences for poorly controlled disease are not fully captured** ICER's model appears to limit the consequences of poorly controlled NT1 largely to productivity losses, modest incremental	We agree that the model does not directly capture all potential downstream effects of poorly controlled NT1. The model indirectly captured some of these consequences via the productivity impacts, healthcare utilization costs, and HRQoL decrements. The lack of direct impacts in the model reflects gaps

	non-drug direct medical costs, and health-related quality-of-life (HRQoL) decrements. By design, the model does not incorporate potentially important lifetime downstream outcomes such as CVD, major adverse cardiovascular events (MACE), accidents/injuries, mental health comorbidities, and excess mortality due to gaps in evidence directly linking treatment to reductions in these outcomes. While we recognize the evidentiary challenges, excluding the costs, mortality, and HRQoL associated with infrequent but serious NT1 consequences systematically underestimates the burden of uncontrolled disease and therefore the value of effective treatment. This concern is supported by ICER's own QALY shortfall findings, which highlight the substantial unmet need and lifelong burden experienced by people with NT1.	in the available evidence. To our knowledge, there is no direct evidence demonstrating that the drugs under review decreased the outcomes listed, e.g. CVD, mortality, etc. However, we explored uncertainty related to mortality impacts through a scenario analysis, removing the excess mortality associated with narcolepsy in treatment responders. The uncertainties and controversies section has also been updated to more explicitly acknowledge these gaps and their possible impact on the models' results.
4.	In addition, direct costs related to healthcare resource use (HCRU) for uncontrolled NT1 are thought to be underestimated in the current framework, which creates minimal modeled disadvantage for untreated patients. This risks contradicting clinical practice and stakeholder expectations, where poorly controlled NT1 is associated with meaningful morbidity, safety risks, and broader societal and economic impacts that extend beyond what is typically captured in claims-based HCRU alone, including safety risks and downstream harms (e.g., motor vehicle accidents, other injuries, and suicidality) and potential excess mortality (e.g., ~40% higher risk reported in NT1/NT2 modeling).10,12 In addition, the model does not readily capture the broader "life course" consequences of symptoms beginning early in life (including impacts on educational and professional attainment and loss of independence), caregiver burden and out-of-pocket costs, or cognitive impairment and psychosocial impacts frequently reported by patients and families. ICER should therefore consider adding explicit context that cost-effectiveness results may not capture the full burden of NT1, including the full spectrum of NT1 symptoms and potential	While these limitations are meaningful, their magnitude of impact on cost-effectiveness results is unknown and cannot be readily quantified given the absence of robust evidence linking NT1 symptom control to outcomes such as accident rates, mortality risk, and life course consequences; incorporating speculative estimates for these domains risks introducing bias of uncertain direction. We note that some of these downstream harms may be partially captured indirectly through excess mortality inputs and healthcare resource utilization costs sourced from narcolepsy populations broadly, though these are unlikely to fully reflect the burden of uncontrolled disease specifically. We have updated the uncertainties and controversies section to highlight these data gaps, including downstream harms, caregiver burden, education, and professional attainment.

	longer-term benefits conferred by effective treatment, and that the clinical and utility inputs underpinning the model may not fully reflect the benefits experienced by patients. At a minimum, ICER should clearly characterize these omissions as limitations that may bias results against treatments that improve multi-domain symptoms and functioning.	
5.	**Xyrem, Xywav, and Lumryz are distinct products and are not substitutable** ICER's analysis groups different oxybate formulations (Xyrem and generics, Xywav, and Lumryz) into a single treatment category, assuming comparable efficacy, pooling discontinuation rates, and applying the cost of generic sodium oxybate as a class-level proxy in the reference case. However, these products are not therapeutically equivalent or substitutable, as evidenced by the fact that they are not designated as therapeutically equivalent in the FDA Orange Book. While ICER acknowledges that product-specific differences are not fully captured in their analysis, we have several concerns about how this approach limits the real-world relevance. First, oxybate formulations differ in clinical efficacy, side effects and tolerability, which may meaningfully influence adherence, persistence, and HRQoL. For example, nausea, dizziness, and vomiting are reported across formulations (≥5% in clinical trial participants), but lower-sodium oxybate is more often associated with loss of appetite, anxiety, and diarrhea.17-21 Differences in taste/texture, once- vs. twice-nightly dosing,23 and pharmacokinetic profiles may also affect compliance, effectiveness, and lifestyle. Furthermore, using generic sodium oxybate as a cost proxy for the entire class understates real-world treatment costs, as only Xyrem has an authorized generic;17,20,21 Xywav and Lumryz, neither of which has a generic alternative,18,19 represent a large and growing share of oxybate use,24,25,26 and payers do not treat these products as	See above responses 1 and 4 to Jazz Pharmaceuticals' comments. We understand that the FDA Orange Book may not designate the different formulations as therapeutically equivalent; however, our grouping of sodium oxybate formulations is based on the fact that efficacy data across formulations is similar, not on therapeutic equivalence. We also understand that there may be differences in prescribing based on certain drug characteristics – in order to capture some of the variability in the model, we have added scenario analyses that vary the costs based on market share data for the three oxybate products and on dose distributions informed by clinical experts.

	interchangeable but instead make formulation-specific coverage decisions based on distinct clinical and cost profiles. Taken together, this aggregation obscures real differences that matter in practice and ultimately limits the ability of stakeholders to draw clinically relevant conclusions from the ICER analysis.	
6.	**Dosing assumptions in the cost-effectiveness model may not reflect real-world use** In the current cost-effectiveness model, ICER's pricing assumptions for key comparators do not fully reflect real-world use. Real-world dosing patterns for pitolisant and sodium oxybates suggest a greater proportion of patients use higher doses than those currently modeled to achieve the desired treatment effect. Understating real-world dosing patterns can underestimate comparator costs and, in turn, influence incremental cost-effectiveness results. To better align the analysis with clinical practice, Takeda recommends that ICER estimate comparator drug costs using a weighted average that reflects observed real-world dosing across the distinct drug products.	Dosing in the model is currently based around the clinical trials used to inform treatment effectiveness. This may differ from real-world practice. Using real-world dosing in the model without corresponding effectiveness estimates risks introducing bias, as changes in dose may affect both costs and effects. To address this uncertainty around impacts of dosing and other sodium oxybate products, we have added scenario analyses exploring dosing that more aligns with real-world use by applying a distribution of all sodium oxybate products with the caveat that clinical effects may not align with these doses.
7.	**Oveporexton data demonstrates that it has the potential to be a highly efficacious monotherapy treatment if FDA approved; there is no evidence indicating routine supplemental treatment is needed** One of the key uncertainties ICER raises is whether oveporexton will be used in combination with other treatments in real-world practice. While it is true that current NT1 management often involves multiple medications, ICER should avoid implying that oveporexton will likely require add-on therapy to achieve adequate symptom control. Importantly, the reason combination therapy is common today is that available options are largely symptom-directed and often address only a subset of the spectrum of NT1 symptoms, necessitating multi-drug regimens, as well as possible switching and dose	Thank you for your comment. We agree that oveporexton was studied as a monotherapy, and our report reflects those data. However, both clinical experts and patients we spoke with brought up the possibility that some patients may require combination therapy for optimal management of their NT1 symptoms. We did not mean to imply that this would be the norm; rather, by discussing it in our Uncertainties and Controversies section, we wanted to highlight this possibility and that there are currently no data on the use of oveporexton as part of combination therapy, as clinicians, patients, and payers will be seeking this kind of information. We have updated the Uncertainties and Controversies section to reflect the uncertainty in this area.

	adjustments to balance incomplete efficacy and tolerability. Oveporexton is meaningfully different: with a novel mechanism of action aimed at the underlying cause of NT1. In clinical trials it has demonstrated robust and durable efficacy as a monotherapy across multiple symptom domains. In a dose-blinded Phase 2 study, data showed no discontinuations due to loss of efficacy at 6 months,31 and Phase 3 data indicates that approximately 84% of patients achieved normal ESS scores (no EDS) on oveporexton monotherapy. In addition, oveporexton monotherapy substantially improved hallucinations or sleep paralysis in ~85% of Phase 3 participants, and 67% of patients experienced meaningful improvement in disturbed nighttime sleep. Taken together, these results suggest that oveporexton monotherapy has the potential to reduce, not increase, the need for multi-drug symptom-directed regimens in NT1 and its real-world use should be based on joint patient and clinician decision making. Currently, the efficacy and safety of oveporexton in combination with other drugs requires further study. As such, strong inferences about routine combination use introduce unnecessary uncertainty and risk conflating two distinct concepts: (1) background real-world polypharmacy driven by the limitations of existing symptom-directed therapies, and (2) a clinical need for add-on therapy because oveporexton may be insufficient on its own. There is no evidence or expert consensus indicating that oveporexton would require supplemental treatment for optimal symptom control. Assuming that oveporexton will “likely” require combination therapy based primarily on experience with therapies that treat individual symptoms risks mischaracterizing the clinical evidence to date and understating the potential for oveporexton to simplify treatment in NT1. ICER should therefore consider reassessing its assumptions and more carefully qualify statements regarding likely combination use	

8.	**The ESS severity–based utility scenario should be clearly caveated regarding applicability to the NT1 population** We would also like to note ICER's scenario analysis applying utilities mapped from ESS severity to isolate the impact of EDS on quality of life. ESS severity–based utilities should be interpreted cautiously in NT1. NT1 burden extends beyond EDS, and oveporexton's potential treatment benefits may not be fully reflected when utility is driven solely by ESS. In addition, the ESS-based utility estimates used in this scenario were elicited largely from an obstructive sleep apnea population, which may limit applicability to people with NT1.34 ICER should explicitly qualify this scenario analysis with these limitations and avoid over-weighting its results relative to the base case using oveporexton trial-based utilities.	Thank you for your comment. These points were caveated in the supplement but have been moved to the main report.