

Thank you for this opportunity to address you. I speak on behalf of the National Forum for Heart Disease & Stroke Prevention, a nonprofit hub for public-private collaboration to improve cardiovascular health, and the Value & Access Steering Committee. Committee members represent patients, providers, public health, payers, purchasers, and pharma and biotech companies. The Committee provides consensus input to ICER on various reviews.

The first point I would like to address is ezetimibe as a comparator. The analytic model should accurately reflect what happens in the real world. This is not the case with use of ezetimibe. For example, NHANES data show that only 4.2 percent of people with prior ASCVD and LDL-C greater than 70 on statin therapy take ezetimibe. Yet ICER's model assumes that all patients take ezetimibe.

The National Forum and Value & Access Steering Committee support evidence-based medicine. We recognize that the ACC/AHA guidelines for management of blood cholesterol call for ezetimibe to be used before more aggressive therapies. However, two significant factors should affect the weight that current modeling gives to the guidelines.

1) The guidelines added ezetimibe as a step-through for PCSK9 inhibitors because of the high cost of those therapies. The guidelines explicitly refer to "mid-2018 list prices," before the manufacturers cut the cost of PCSK9 inhibitors by about half. The price cut significantly affected cost-effectiveness.

2) The data tell all of us that real-world use of ezetimibe is low (less than 7%).

We understand that clinicians ICER consulted said they would likely consider ezetimibe as the first treatment. However, clinicians consulted by the National Forum said that because many patients with high residual CV risk and / or high LDL-C will need more than ezetimibe, many physicians will bypass that and go to a more potent therapy.

Therefore, ezetimibe is not a realistic comparator for either treatment being considered. Furthermore, if more people benefit from ezetimibe's lipid-lowering power when it is combined with bempedoic acid, either because more clinicians will prescribe it in the combination pill, or because patients are more likely to take a combination pill, LDL-C reduction is achieved, and it benefits cardiovascular health. This is sound justification for the value-based price of bempedoic acid to include the lipid-lowering benefit of ezetimibe.

The second point is the baseline LDL-C level among patients on maximally tolerated statin and ezetimibe used in the model. For the reasons I have just covered, this is not grounded in real world practice. The value of 88.8 mg/dL (milligrams per deciliter) is significantly lower than

baseline LDL-C levels in Phase III trials. The more accurate, or realistic baseline to use would be the population average without applying the effect of ezetimibe to the entire population. Using the lower LDL-C level of 88.8 negatively impacts the cost-effectiveness analysis. As the primary goal of high cholesterol treatment is absolute lowering of LDL-C, starting at an artificially lower number in effect, lowers the ceiling on the impact that can be achieved with both inclisiran and bempedoic acid.

One option ICER might consider is an additional stratified analysis by base LDL-C. Many clinicians are used to LDL-based thresholds. Looking at cost effectiveness in those with LDL-C 70-99 vs 100-129 vs 130+ would be useful. The other challenge is that ICER uses LDL-C reduction to estimate treatment efficacy. These estimates should be updated after cardiovascular outcome trial (CVOT) data are released.

Finally, high-risk patients need effective therapeutic options. As ICER's review and Dr. Lin's presentation show, bempedoic acid and inclisiran are effective in reducing LDL-C in high-risk populations. They provide alternative treatment options to patients and society to address the most prevalent and costly chronic conditions impacting Americans today.

Payers who are on the Value & Access Steering Committee have reported that multiple payers currently have bempedoic acid on Tier 2 formularies without restrictions. They have determined it is cost effective. There is concern that were ICER to judge its cost effectiveness based on modeling assumptions that do not obtain in the real world, it could open the door for formulary changes that would have the effect of reducing treatment options for patients.

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