

August 22, 2018

Mr. Matt Seidner
Program Manager
Institute for Clinical and Economic Review
Two Liberty Square, 9th Floor
Boston, MA 02109

Dear Mr. Seidner,

Thank you for the opportunity to provide feedback to ICER on its draft scoping document for the review of canakinumab's ASCVD indication. We appreciate your willingness to review comments and recommendations from the National Forum's Value & Access Steering Committee and partners working on these issues.

The Value and Access Steering Committee and partners reviewed the draft scoping document and jointly offer the following feedback for ICER's consideration.

Positives:

The Steering Committee and partners appreciate that other benefits and contextual considerations (e.g., health disparities and access to care issues) will be evaluated. They are supportive of ICER's progress in this direction; and look forward to patient advocacy groups continuing to be involved throughout the process.

Opportunities:

The Steering Committee and partners identified the following opportunities for the review.

- There is a need to identify which patient groups are most likely to benefit from CVD & lung cancer death risk reduction while minimizing the harms resulting from increased risk of death from infectious causes.
- The response to therapy approach advocated by Ridker, et al.¹ (e.g., if response with hsCRP <2 mg/L then continue treatment; don't continue treatment if hsCRP > 2 mg/L after the first injection) is flawed on-treatment analysis. It fails to account for regression to the mean of hsCRP eligibility – hsCRP is an acute phase reactant. In the JUPITER trial², 25% had hsCRP <2 mg/L during follow-up. This means the low-risk patients (hsCRP <2 mg/L) who happened to have a cold (or some other acute insult) on the day of eligibility assessment (hsCRP >2 mg/L) were still low-risk after randomization, thereby inflating the apparent effect size for CVD/mortality risk reduction from canakinumab. A re-analysis, excluding those who regressed to the mean would address this issue.

(continued)

- The draft scoping document indicates that canakinumab will be compared to the standard of care, which includes high intensity statin therapy and aspirin in patients able to tolerate those therapies. And, that ICER does not expect to be able to assess the efficacy of canakinumab in patients who are receiving a PCSK9 inhibitor in addition to statin therapy. The Steering Committee and partners think that if a drug is being added to patient care, that it would be important to determine what provides the most value, canakinumab or a PCSK9i?
- Regarding low-value services used in the current management of ASCVD, the following have been identified as being those that could be reduced or eliminated to create additional resources in health care budgets for higher-value innovative services:
 - screening for atrial fibrillation with electrocardiography in asymptomatic and previously undiagnosed individuals aged ≥ 65 years.³
 - annual electrocardiograms or cardiac screenings in low-risk asymptomatic individuals; preoperative electrocardiograms prior to low-risk surgery, and cardiac stress testing and imaging for uncomplicated headache.⁴

Again, thank you for your consideration. We would like to have the opportunity to bring together representatives from the Steering Committee to meet with your team to further the conversation.

Sincerely,

Members of the Value & Access Steering Committee and Partners representing the following organizations:

National Forum for Heart Disease & Stroke Prevention (convener)
Alliance for Patient Access
American Association of Heart Failure Nurses
American Heart Association
American Pharmacists Association Foundation
Association of Black Cardiologists
Association of State and Territorial Health Officials
BallengeRx Consulting
Global Healthy Living Foundation
Independent Health
Mended Hearts
National Association of Chronic Disease Directors
National Lipid Association
Partnership to Advance Cardiovascular Health
Partnership to Improve Patient Care
Preventive Cardiovascular Nurses Association
WomenHeart

References

¹ Ridker PM, Everett BM, Thuren T, et al. Anti-inflammatory Therapy with Canakinumab for Atherosclerotic Disease. *The New England journal of medicine*. 2017;377(12):1119-1131

² Ridker, P., et al., Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *N Engl J Med*, 2008. 359: p. 2195 - 2207. <https://www.nejm.org/doi/full/10.1056/NEJMoa0807646>

³ US Preventive Services Task Force. Screening for Atrial Fibrillation With Electrocardiography: US Preventive Services Task Force Recommendation Statement. *JAMA* 2018;320:478-484

⁴ Brown D, Clement F. Calculating Health Care Waste in Washington State: First, Do No Harm. *JAMA Intern Med*. Published online August 06, 2018. doi:10.1001/jamainternmed.2018.3516