AIMED ALLIANCE

August 19, 2019

Steven Pearson, MD
Institute for Clinical and Economic Review
2 Liberty Square, Ninth Floor
Boston, MA 02109

Dear Dr. Pearson:

Aimed Alliance is a 501(c)(3) non-profit health policy organization that seeks to protect and enhance the rights of health care consumers and providers. Aimed Alliance respectfully submits the following comment in response to the "Additive Therapies for Cardiovascular Disease: Effectiveness and Value Draft Evidence Report" ("Cardiovascular Draft Report") published by the Institute of Clinical and Economic Review (ICER) on July 30, 2019.

Cardiovascular disease ("CVD") is the leading cause of death in both men and women in the United States.[1] CVD refers to a number of conditions that affect the heart and blood vessels, including heart attack, stroke, heart failure, arrythmia, and heart valve problems.[2] Approximately 850,000 Americans die from CVD each year.[3] Moreover, about 735,000 Americans suffer from a heart attack each year. For roughly 525,000 individuals, this will be their first heart attack, while about 210,000 will have previously experienced one.[4] Depending on the particular condition, CVD is typically treated in one of three ways: lifestyle changes, medications, and medical procedures or surgery, such as coronary revascularization.[5] CVD also creates a significant financial burden on patients, their families, and the United States health system as a whole. Direct and indirect costs of CVD are estimated to be $330 billion each year.[6]

Because of the enormous prevalence of CVD in the United States and the numerous forms in which CVD can manifest, access to a variety of treatment and management options is critical.[7] Aimed Alliance appreciates that ICER has deemed icosapent ethyl and rivaroxaban cost effective, and we respectfully request that you consider the following information when developing your value-based price benchmarks.

I. Inappropriate to Compare Icosapent Ethyl and Rivaroxaban

Aimed Alliance cautions against comparing the effectiveness and value of icosapent ethyl and rivaroxaban because icosapent ethyl and rivaroxaban have different methods of action within the human body and are intended for different uses. Icosapent ethyl is indicated for use in adults as a supplement to "reduce triglyceride levels in patients with severe hypertriglyceridemia"[8] while rivaroxaban is indicated for "reducing the risk of stroke and systemic embolism in patients with

[1] https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_disease.htm
[2] https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_disease.htm, https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease
[3] https://www.ncbi.nlm.nih.gov/pubmed/30700139
[4] https://www.cdc.gov/heartdisease/facts.htm
[5] https://www.mayoclinic.org/diseases-conditions/heart-disease/diagnosis-treatment/drc-20353124
[6] https://www.mdmag.com/medical-news/heart-break-preventive-aspirin-use-physical-activity-on-the-decline
[7] https://www.heart.org/en/get-involved/advocate/federal-priorities/access-to-care
[8] https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202057s009lbl.pdf

nonvalvular atrial defibrillation,"[9] and for the treatment, prevention, and reduction of the recurrent risk of deep vein thrombosis and pulmonary embolism.[10] Therefore, we caution ICER against conducting a comparative effectiveness analysis of these two medications because they are not substitutes for each other.

II. ICER Must Consider Patients' Perspective

While ICER acknowledges the patient perspective, it should incorporate the direct and indirect costs to patients in its calculations. Patients with CVD who do not receive treatment have higher incidences of productivity loss, including days of work lost among employed individuals, home productivity lost, and work loss among individuals too sick to work.[11] Moreover, families of individuals who die prematurely incur the value of lost earnings.[12] Factors such as these should be considered in ICER's analysis.

III. Exclusion of Valuable Data

When determining the effectiveness of icosapent ethyl, the REDUCE-IT study considered five primary endpoints: cardiovascular-related death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, and hospitalization due to unstable angina. Yet, while ICER considered all five endpoints in its sensitivity testing, it excluded coronary revascularization and hospitalization due to unstable angina in its base case. Coronary revascularization, such as coronary artery bypass surgery (CABG), and hospitalization are both costly adverse events that should be considered in a cost-effectiveness analysis. The estimated costs of initial hospitalization for CABG has been estimated to be $34,467.[13] Moreover, patients who have had a secondary CVD-related hospitalization have been found to have annual costs associated with their treatment that are 4.5 times higher than patients who were not hospitalized.[14] Moreover, when conducting a cost-effectiveness analysis based on clinical trials, it is important to utilize all primary endpoints in those trials rather than selecting certain endpoints over others.

Additionally, ICER only considered the effect of icosapent ethyl on the time to first events rather than total ischemic events (first plus subsequent events). Yet, all adverse events directly and indirectly impact patients' lives. Subsequent events can be costly, and therefore, a proper cost-effectiveness analysis should take those expenses into account.

IV. Use of QALYs is Inappropriate

Aimed Alliance reiterates its longstanding recommendation against relying on quality-adjusted life year (QALY) measures to evaluate any treatment, including preventive CVD treatments. The use of QALY measures to evaluate cardiovascular disease raises significant ethical concerns. QALY measures put a price tag on the value of human life that merely reflects the

[9] https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/202057s009lbl.pdf
[10] https://www.xareltohcp.com/dvt-pe
[11] https://healthmetrics.heart.org/wp-content/uploads/2017/10/Cardiovascular-Disease-A-Costly-Burden.pdf
[12] https://healthmetrics.heart.org/wp-content/uploads/2017/10/Cardiovascular-Disease-A-Costly-Burden.pdf
[13] http://icer-review.org/wp-content/uploads/2016/01/Costs-PCI-CABG-DM-CAD-March-2013.pdf
[14] https://www.ajmc.com/journals/issue/2010/2010-03-vol16-n03/ajmc_10marnicholswebx_e86to93

individual's diagnosis and deems those with chronic, debilitating, and rare conditions as being worth less than those with common conditions. They treat individuals' lives and health as a commodity and ignore patients' and practitioners' individualized concept of the value of treatment.

Individuals with CVD may face challenges in obtaining consistent treatment due to barriers to health insurance coverage.[15] Health plans may impose high copays, prior authorization, or step therapy limits on coverage that result in a significant financial burden on patients.[16] As a result, patients ration their medications, and this lack of adherence to a treatment plan can result in higher rates of cardiovascular-related emergency room visits as well as preventable deaths.[17] The American Heart Association estimates that medication nonadherence results in approximately 125,000 preventable deaths each year.[18] A recent study found that 20.6 million people with cardiovascular disease and its risk factors still lacked health insurance.[19] QALYs are often used to justify coverage limitations that prevent individuals from obtaining treatments that are most appropriate for their individualized needs. For these reasons, we recommend against using QALYs.

V. A Value Assessment is Premature

While clinical trials have provided evidence of the safety, effectiveness, and value of icosapent ethyl for the treatment of hypertriglyceridemia, these treatments are still in their infancy. While icosapent ethyl was approved by the FDA in July 2012, the FDA is currently considering a new indication for reducing cardiovascular risk. Pending approval, valuable data will fully emerge in clinical practice. However, if icosapent ethyl is deemed inadequately cost-effective now, then the likelihood of third-party payers covering the treatment for new indications without imposing significant benefit utilization management policies increases, creating barriers to access for individuals who need them. Without market uptake, data cannot be collected and analyzed. Therefore, we recommend that ICER refrain from making a determination on the value of this treatment until mature data emerges.

VI. Conclusion

Thank you for the opportunity to comment on the Cardiovascular Draft Report. We offer our assistance in working closely with ICER to address our shared goals of improving access to high quality health care at a price that accurately reflects public and personal benefits.

Sincerely,

John Wylam
Staff Attorney

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[15] https://www.heart.org/-/media/files/about-us/policy-research/fact-sheets/access-to-care/fact-sheet-breaking-down-the-barriers-the-uninsured-with-heart-disease-and-stroke.pdf?la=en&hash=A789BC3E0158657CA4E47490EEF0528D6ED67CBB

[16] http://1yh21u3cjptv3xjder1dco9mx5s.wpengine.netdna-cdn.com/wp-content/uploads/2016/11/CWG-WhitePaper-Nov2016_FINAL.pdf; https://www.ahajournals.org/doi/10.1161/CIR.0000000000000652

[17] https://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_460769.pdf

[18] https://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_460769.pdf

[19] https://link.springer.com/article/10.1007/s11606-019-05108-1