



THE LAST WORD:
Aducanumab for Alzheimer's Disease: Effectiveness and Value
ICER's Final Evidence Report
Issued August 5, 2021

On August 5, 2021, ICER issued its [Final Evidence Report](#) on aducanumab, a first-of-its-kind medication created to treat Alzheimer's disease. Following its typical process for gathering information – which included the solicitation of public comments and a public meeting – ICER determined the available evidence was “insufficient to conclude that the clinical benefits of aducanumab outweigh its harms or, indeed, that it reduces progression” of Alzheimer's disease. As a result, they found that the manufacturer's proposed pricing would “not be in alignment with its clinical benefits.” These findings are questionable for several reasons.

Aducanumab – manufactured by Biogen and sold under the brand name Aduhelm – was approved by the Food and Drug Administration (FDA) for medical use in the US for Alzheimer's disease under somewhat unusual circumstances. Clinical trials for the drug were halted when the initial data suggested it was not having a positive impact. However, subsequent reviews indicated the treatment showed at least some clinical benefits for patients, though those benefits were not consistent across separate trials.

The FDA's approval of the treatment was controversial and there was strong disagreement between the FDA's outside experts and patient advocacy groups over the decision. Because aducanumab was approved under the FDA's accelerated approval pathway, the manufacturer is required to perform follow-on studies to determine the drug's clinical benefit over a longer period.

While that means more data is coming, and with it (ideally) more clarity, for the time being,

aducanumab's future remains murky and indeterminate. It would be premature to make final, definitive conclusions about the clinical and economic value of aducanumab – however, with this report, ICER attempts to do just that.

In addition to that procedural context, it is important to consider the almost unspeakable burdens Alzheimer's places on patients, families, caregivers, and society. ICER pays lip service to these burdens in its report but fails to adequately reflect and incorporate them into its conclusions.

On top of this refusal to consider the complete picture on pricing, ICER's analyses in the report – if taken to their logical end – suggest some conclusions that are almost nonsensical. Most notably, ICER's cost-effectiveness methodology assumes that higher prices can be justified as treatments are shown to be more clinically effective. Yet, ICER's budgetary impact analysis essentially mandates that treatments with higher prices be given to fewer people in order to stay under arbitrary spending limits. In other words,

as a treatment is shown to be more effective, ICER will recommend that fewer patients get access to it.

Most parties would agree with the assertion that the societal impact of a truly effective treatment for Alzheimer's would be massive. Yet, ICER's valuation approach would severely limit patient access to any such treatment just to avoid exceeding an entirely artificial budget threshold that ICER set for itself.

Useful pricing and value determinations must also factor in the treatment landscape for the relevant illnesses. For some conditions – like HIV or rheumatoid arthritis – effective treatments have been developed over many years, often beginning with therapies that solely relieved symptoms, and shifting to treatments that could slow or halt progression of the disease. Over time, subsequent options are developed to accomplish that same goal more effectively with reduced side-effects.

In this type of environment, pricing decisions for early treatment options can determine whether more and better treatments are developed at all. Drug developers need some indication that patients will actually have access to new and improved treatments. If the price ICER or any other party determines is "fair" for a particular treatment is too low, there is very little reason for those companies to continue pursuing those innovations and improvements at all. Aducanumab is a first-of-its kind treatment, and is the first new FDA-approved treatment for Alzheimer's in nearly two decades. Patients, caregivers, and society need more innovation and more treatments for this devastating disease. ICER predictably ignores these facts in its analysis, and disregards the potential chilling effect its conclusions may have on investments to develop new treatments in the future.

Finally, as we have noted repeatedly, ICER's methodology fails to meet the demands of

normal science. Its conclusions are not based on hard data, but on a series of assumptions and simulated outcomes among hypothetical patient populations. The approach is absurd, especially when you consider the number of actual real-life Alzheimer's patients who live in the United States, and the fact that additional data on this drug will be forthcoming.

Moreover, ICER's assumption-driven models rely on measurement standards that have been widely discredited for this type of analysis. In making a value determination on a new drug or therapy, ICER's goal is to divine a cost-per-QALY (Quality Adjusted Life Year) estimate and match it to a baseline "willingness to pay" threshold. Yet, the instruments ICER uses to measure patient outcomes and quality of life produce scores that are ordinal – not ratio – in nature. In other words, they can tell us whether a patient improved in specified areas, but they cannot tell us by how much. More important, the QALY is purportedly determined by multiplying these scores by time. Yet, by definition, ordinal scores cannot be multiplied, which means ICER's use of the QALY is a mathematically impossible construct. This is not science. It is pseudoscience.

Many questions remain about the effectiveness, safety, and value of aducanumab as a treatment option for patients with Alzheimer's disease. Those uncertainties have been acknowledged by the manufacturer, the FDA, and most informed patient advocates and other stakeholders. Yet rather than acknowledge this uncertainty and await further information, ICER has attempted to render a final verdict about the drug's value and efficacy. Its analysis and conclusions can provide little practical value at this stage. At the same time, they may very well limit patients' access to life-altering medications and discourage further investment in better treatment options in the future. As always, patients stand to lose the most when ICER acts as a self-appointed arbiter of drug pricing in the United States.