THE LAST WORD:

Treatments for Atopic Dermatitis: Effectiveness and Value
ICER's Final Evidence Report
Issued August 17, 2021

On August 17, 2021, ICER issued a Final Evidence Report on the clinical and cost-effectiveness of new treatments for atopic dermatitis (more commonly referred to as eczema). After following its typical process for gathering and reviewing data, ICER concluded that the treatments are largely overpriced and recommended steep discounts for at least three of the five therapies. There is ample reason to question ICER's findings in this report.

Atopic dermatitis is a chronic condition that typically manifests in persistent or recurring lesions and patches of dry, inflamed, and itchy skin. It affects roughly 11-15% of children and 7-10% of adults in the United States. Severe cases can have an extremely negative impact on virtually every aspect of a patient's life. The condition can be quite painful and result in sleep loss, psychological distress, and an inability to perform at school or work. For some, the condition of their skin causes embarrassment and can severely impair their social lives.

In the U.S., the total cost of atopic dermatitis comes to about $5.3 billion a year, which includes about $1 billion in health care costs. And that is the first major problem with ICER's analysis of the new treatments. In the report, ICER and the CHOICE Institute in the College of Pharmacy, University of Washington, Seattle (as consultants building models used in the report) acknowledged that roughly 80% of the total economic burden of the atopic dermatitis comes from personal costs, lost productivity, and quality of life issues. Yet the report largely ignores these concerns and focuses almost exclusively on healthcare costs, which account for less than one-fifth of the economic impact of the disease.

The report considers the value and effectiveness of six specific therapies:

- **Abrocitinib** – Pfizer
- **Tralokinumab** – LEO Pharma
- **Baricitinib** (Olumiant®) – Eli Lilly, Incyte
- **Upadacitinib** (Rinvoq®) – AbbVie
- **Ruxolitinib** – Incyte
- **Dupilumab** (Dupixent®) – Regeneron, Sanofi

As always, the section grabbing the most attention is ICER's Health-Benefit Price Benchmarks (HBPB) – pricing ranges at which they claim a drug can be considered cost-effective – for the treatments. Not surprisingly, ICER's report concluded that the medicines are largely overpriced, and recommended the following HBPB ranges:

- **Abrocitinib:** $30,600-$41,800/year
- **Tralokinumab:** $25,700-$35,000/year

- **Baricitinib:** $24,400-$33,300/year (would require a 0-16% discount with current US list price)
- **Upadacitinib:** $30,400-$41,500/year (would require a 35-53% discount)
- **Dupilumab:** $29,000-$39,500/year (would require a 6-31% discount)

Unfortunately, the HBPB benchmarks fail to stand up to scrutiny. Just as the ICER framework – detailed below – is an analytical dead-end, the HBPB benchmarks that rely on the ICER modelling are essentially useless. Indeed, the report fails fully appreciate how atopic dermatitis can impact patients and their treatment choices beyond the faulty estimates and projections of the future cost of care. For example, the report mentions that eczema can significantly impair a patient's work and personal life, but it fails to capture the full impact of the embarrassment and social isolation that can result from the disease. According to a 2019 study, eczema patients were 44% more likely than the rest of the population to experience suicidal ideation and 36% more likely to attempt suicide. While the data does not definitively show the condition causes an increase in deaths from suicide, eczema can have a devastating impact on patients' mental, emotional, and behavioral health. Yet, the report does not explore any of these issues.

Put simply, ICER's analysis is woefully under-inclusive. It fails to even consider many factors that impact overall quality of life and the disease's impact on those it afflicts. These considerations are essential in determining the way patients consider the value of treatments.

On top of the report's severely limited perspective, there are fundamental problems with ICER's methodology. It has been widely acknowledged that ICER's modeling – and, in this case, that of the CHOICE Institute – fail to meet the standards of normal science, particularly when it comes to quantitative measurement. Following the lead of some European healthcare systems, ICER uses a "Quality Adjusted Life Year" (QALY) standard to make its cost determinations. Put simply, they assign a monetary value to the quality and duration of a patient's life to make assessments about a drug's value and effectiveness. One QALY equals one full year of life in perfect health.

However, the instruments ICER uses to produce its QALY measurements 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. The ordinal instruments also result in value ranges that do not have a true zero. Both of these factors – ratio values and the presence of a true zero – are prerequisites for objective scientific measurement of change over time.

Case in point, one of ICER's preferred scoring instruments – the EQ-5D-5L (measures 5 symptoms at 5 response levels) – results in 3125 possible health state values. Analysts have found that over 600 – roughly one in five – of those health states had negative scores. In fact, one study of atopic dermatitis that used the EQ-05D-5L reported negative preference scores in ranging from -0.003 to -0.53.

Does a negative score represent a health state worse than death? Likely not since we are talking about a non-fatal skin condition. Yet, applying these values to the CHOICE model used in ICER's report would result in negative QALYs, which suggests either that some eczema patients would be better off dead, or that the values produced by the model are imaginary and do not reflect anything resembling objective reality. The safe money is on the latter.

ICER tells us there are no credible alternatives to ordinal instruments like the EQ-5D-5L for most conditions. Yet, for atopic dermatitis, there is at least one more useful instrument: the Quality of Life Index for Atopic Dermatitis (QoLIAD), a disease-specific, patient-centric instrument that

focuses on need fulfillment as the appropriate measure of quality of life.
The QoLIAD was first developed in 2004 and has been used in several clinical trials and studies in multiple countries. ICER was undoubtedly aware of the existence of this instrument after it received public comments. ICER's reliance on its imaginary cost-per-QALY claims is absurd and nonsensical in all instances, but it is especially perplexing when there is a disease-specific quality of life instrument available that meets established standards for scientific evidence and measurement.

ICER did acknowledge the existence of some condition-specific metrics in the report's Supplemental Materials section. Yet, it only treats two of them with any seriousness, both of which focus on data collected by investigators, and not outcomes reported by patients. Neither of them measures factors directly related to quality of life, which is a problem when we are talking about a chronic disease that can cause severe pain and discomfort in a large patient population. Therefore, even if ICER's scoring methods met the measuring standards required by science, it is safe to assume that in the case of atopic dermatitis, they would still fail to capture the true value of effective treatments for patients suffering from this disease.

Ultimately, atopic dermatitis is a complex health condition with a wide range of presentations. As such, it requires a similarly wide range of treatment options. Because no two cases are the same, individualization of care and close consultation with clinicians is vital for effective treatment of this disease. As is all too often the case, ICER's report – with its myopic focus on dubious cost estimates over value – will likely end up limiting access to treatments and making it far more difficult for patients and doctors to effectively coordinate care.