THE LAST WORD:

Treatments for Hereditary Angioedema: Effectiveness and Value
ICER's Final Evidence Report
Issued August 24, 2021

In April 2021 ICER announced plans to update its final evidence reviews to create a further final evidence review with revised assumptions drawn from real-world data on assumptions data where previous assumptions had been guesswork. A revised assumption-driven simulation for prophylactic treatments for hereditary angioedema was released on August 24. The results were further imaginary recommendations for discounts in the pricing of Takhzyro, Haegarda and Clinryze. As ICER's claims rest upon modeled assumptions, these recommendations have, as in the initial report, no credibility. They fail to meet the required standards of normal science.

Hereditary angioedema (HAE) is a rare genetic condition that causes attacks of swelling of the patient's face, hands, feet, and stomach. Worst of all, attacks can also cause swelling of the throat, which can be life-threatening. Most HAE diagnoses result from a deficiency or dysfunction of C1 inhibitor.

The recent reassessment, prepared in partnership with the modelling group at the University of Washington College of Pharmacy, aims to update ICER's findings on three specific HAE therapies:

- **Takhzyro®** – Takeda
- **Haegarda®** – CSL Behring
- **Cinryze®** – Lev Pharmaceuticals

As with the initial report, ICER believes its primary value added to the discussion of HAE treatment is its Health-Benefit Price Benchmark (HBPB). These are imaginary pricing ranges at which ICER claims a drug can be considered cost-effective, based on their assumption that the "threshold" value a year in perfect health – expressed as a cost per quality-adjusted life year (QALY) – ranges from $100,000 to $150,000.

Using its typical approach, ICER recommended the following maximum HBPBs for the reassessed HAE treatments:

- **Takhzyro®**: $219,844/year (would require a discount of more than 52% off the current US list price)
- **Haegarda®**: $248,779/year (would require a discount of more than 53%)
- **Cinryze®**: $140,550/year (would require a discount of roughly 75%)

To update its previous assessment, ICER purportedly sought to incorporate new inputs into its modeling via an updated review of the randomized controlled trials for each of the treatments. Next, they claimed to analyze real-world data to "provide new inputs for model assumptions regarding baseline attack frequency and utilization costs related to the severity of attack."

After modifying its initial assumptions regarding the frequency of acute attacks in HAE, ICER was able to dramatically increase its imaginary cost-per-QALY estimates for each of the three medications. Meanwhile, the HBPBs remained nearly the same between the two reports. As a result, the biggest change between 2018 and 2021 is the size of the discounts ICER recommended for the HAE treatments.

Of course, access to real-world data to select further assumptions for a simulation model is a waste of time as ICER's intent is still to invent evidence to support claims for price discounting. The claims still lack any credibility. Not surprisingly, ICER's reference case framework – centered around an assumption-driven simulation model to support cost-per-QALY claims for threshold pricing recommendations – remains an analytical dead end. By design, any claims produced by this framework are not empirically evaluable. That being the case, ICER's methods fail to meet even the most basic standards of normal science.

The outcomes are inevitable. Every ICER model is essentially a placeholder for a succession of future models, all of which remain subject to alterations based on new assumptions. Ongoing observations or research simply become part of a mining operation for real-world data to drive a new set of assumptions. These real-world data do not need to meet the standards for fundamental measurement – they can be "new" ordinal preferences or new patient-reported outcomes. They can be based on scientifically useless instruments – like the widely used EQ-5D-5L – that assign negative scores for health states, suggesting a patient's condition is worse than death.

Anyone hoping to refute – or even scientifically confirm – ICER's work can only try to challenge the assumptions in the models and its data points. However, ICER's models are not based on hard data, but on selected scoring instruments taken from the available literature. As a result, anyone could create or even reverse engineer a competing model for pricing recommendations for virtually any treatment regimen.

Ultimately, ICER's reassessment of HAE therapies follows its normal pattern of creating – and then re-creating – imaginary claims by revisiting assumptions. It maintains the tradition – well entrenched in practice of assessing health technology – to reject hypothesis testing and the discovery of new data in favor of imagined simulations of a hypothetical patient population.

It is also worth noting that in reassessing its work from years past, ICER made no additional effort to factor in the perspective of patients. Questions such as whether the treatments meet the needs of the real-world patient population and what value those suffering from HAE might place on therapies with significant clinical benefits go completely unaddressed. This is a major omission – one that is unfortunately commonplace in ICER's publications – given the organization's stated belief that pricing should reflect value. Once again, ICER's gaze is myopically focused on value from a clinical perspective, which leaves out important pieces of the value puzzle.

As we have noted in the past, the biggest problem with ICER's flawed assessments is the weight they carry with various government health programs and private healthcare payers. Put simply, ICER's recommendations – particularly its touted HBPB benchmark – should not be the basis for the denial or approval of care for HAE patients.