REPORT AT A GLANCE: IGA NEPHROPATHY

KEY FINDINGS

Intervention	Comparators	Evidence Rating	US Price	Health-Benefit Price Benchmark
B-Cell Directed Therapies Compared with No Specific			Sibeprenlimab: $292,500 per year Atacicept: Not yet approved Nefecon: $133,741 for a single treatment course	Sibeprenlimab: $61,000 to $81,000 per year Atacicept: $60,000 to $80,000 per year Nefecon: $110,900 to $143,000 for a single treatment course
Sibeprenlimab	No specific immunomodulatory therapy	B+		
Atacicept	No specific immunomodulatory therapy	B+		
Nefecon	No specific immunomodulatory therapy	B+		
B-Cell Directed Therapies Compared to Systemic Glucocorticoids				
Sibeprenlimab	Systemic Glucocorticoids	P/I		
Atacicept	Systemic Glucocorticoids	P/I		
Nefecon	Systemic Glucocorticoids	P/I		
B-Cell Directed Therapies Compared to Each Other				
Sibeprenlimab	Atacicept	I		
Sibeprenlimab	Nefecon	I		
Nefecon	Nefecon	I		

"Even with greater recognition that IgA nephropathy often progresses to end-stage kidney disease, treatment options have been limited and have serious side effects. New non-glucocorticoid therapies targeted at B-cells appear likely to provide greater efficacy with fewer side effects, although longer term data are needed. Despite this, the very high price for sibeprenlimab led the independent appraisal council to conclude that it provides low value for money. We hope that the price of atacicept aligns better with the benefits it provides."

– ICER's Chief Medical Officer, David Rind, MD, MSc

THEMES AND RECOMMENDATIONS

- If the price of sibeprenlimab is reduced to a price aligned with value, and if the initial price of atacicept is aligned with value, payers should not require step therapy with systemic glucocorticoids or Nefecon before authorizing use of sibeprenlimab or atacicept for treatment of IgAN.
- Manufacturers should set prices that will foster affordability and good access for all patients by aligning prices with the patient-centered therapeutic value of their treatments. In the case of IgAN, substantial new hope with the availability of these therapies is diminished by the extremely high price of sibeprenlimab. Nefecon is also priced slightly above a value-based price.
- Research funding organizations should support pragmatic analyses assessing the feasibility and the effectiveness of large-scale screening for IgAN and other kidney diseases including among children, which would inform public health practices like school-based screening programs.

Clinical Analyses

KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

IgA nephropathy (IgAN) is a disorder that occurs when abnormal complexes of the antibody immunoglobulin A (IgA) are deposited in the kidneys, causing inflammation and damage. When the kidneys can no longer filter blood and clear toxins from the body, either kidney transplantation or dialysis is required to avoid death. There are uncertainties about how often this happens with IgAN: for many patients, either death or end-stage kidney disease (ESKD) occurs within 15-20 years after IgAN diagnosis, although other reports suggest more than two-thirds still have functioning kidneys at 25 years. In the United States (US), an estimated 200,000 individuals have IgAN. IgAN is more common in males than in than females in the US and many new diagnoses occur in young adults.

Patients have told us that their lives change substantially after IgAN diagnosis. By time of recognition, kidney damage has occurred for many. Current treatments have important toxicities and so far do not stop deterioration of kidney function, so patients are often faced with an uncertain tradeoff between drug toxicities in the short term to reduce the risk of kidney failure in the longer term. Since recognition of IgAN in the 1960s, the main treatment to reduce IgA deposition has been systemic oral glucocorticoids, which have substantial side effects.

Nefecon, an oral preparation of the glucocorticoid budesonide in a delayed-release formulation intended to target release to the distal ileum (Tarpeyo®, Calliditas Therapeutics AB; sometimes referred to as "delayed release" [FDA label] or "targeted release") is administered daily for nine months and was approved by the US Food and Drug Administration (FDA) in 2023. Nefecon has "first-pass" metabolism in the liver, and is thought to therefore have lower risk of systemic side effects. Sibeprenlimab (Voyxact®, Otsuka Holdings Co., Ltd.) is a monoclonal antibody that binds to and neutralizes a proliferation-inducing ligand (APRIL) that regulates immune cell activity and the production of IgA antibodies. The drug is administered subcutaneously every four weeks. Sibeprenlimab was approved by the FDA under accelerated approval on November 25, 2025. Atacicept (Vera Therapeutics, Inc.) is a recombinant fusion protein that can bind to and neutralize APRIL as well as B-cell Activating Factor (BAFF), another regulator of immune activity. The drug is administered subcutaneously and has a PDUFA date of July 7, 2026.

Clinical evidence includes high-quality Phase II and Phase III randomized comparisons of systemic glucocorticoids, Nefecon, atacicept, and sibeprenlimab against no specific immunomodulatory therapy. All these treatments appear to slow the deterioration in kidney function in IgAN, although interim Phase III results for atacicept and sibeprenlimab focus on reduction in urine protein (proteinuria) rather than loss of kidney function; final Phase III results will present data on kidney function. The trajectory of placebo arms differ across the various trials, showing that enrolled trial populations differ. As such, effect estimates from interventions in trials have limited ability to be compared against each another. The harms of systemic glucocorticoids are well known. Atacicept and sibeprenlimab appear well tolerated but have a new mechanism of action and so rare and/or longer-term harms could emerge. Nefecon produces systemic glucocorticoid side effects in at least some patients, and it is unclear how effective a single nine-month course is over a lifetime; repeated courses of treatment are being evaluated. Given the strengths and limitations of these data, we have high confidence of at least a small net health benefit for all these interventions and the comparator relative to no specific immunomodulatory therapy but less confidence about the comparative effectiveness of the intervention and comparator against one another.

Economic Analyses

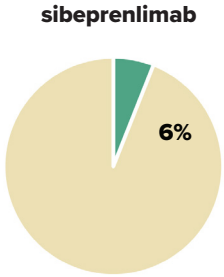
LONG-TERM COST EFFECTIVENESS

To estimate the cost-effectiveness of these new therapies, we developed a de novo Markov model with a cycle length of one month, informed by key clinical trials and prior relevant economic models.

Our analysis has substantial uncertainties given that IgAN can progress over many years while available data on new therapies are short-term. Our best estimates suggest that at its current price, a single course of Nefecon is more expensive but more effective than systemic glucocorticoids with base-case findings meeting the upper bound of commonly cited cost-effectiveness thresholds. However, in probabilistic sensitivity analyses, there was uncertainty in whether Nefecon would meet commonly cited cost-effectiveness thresholds. For example, varying inputs related to adverse effects from systemic glucocorticoids led to either increases in the incremental cost-effectiveness ratios or decreases to a point where Nefecon may be more effective and less costly. We also estimate that sibeprenlimab compared to systemic glucocorticoids leads to extensions to life and improvements in quality of life but, at the current estimated net price, far exceeds commonly used cost-effectiveness thresholds. The cost-effectiveness of atacicept will depend on its actual price, though would also far exceed commonly used cost-effectiveness thresholds if atacicept is priced similarly to sibeprenlimab. The annual Health Benefit Price Benchmark (HBPB) is $61,000 to $81,000 for sibeprenlimab, $60,000 to $80,000 for atacicept, $110,900 to $143,000 for a single treatment course of Nefecon.

POTENTIAL BUDGET IMPACT

At the current net price of sibeprenlimab ($292,500 per year), 6% of the eligible population could be treated before reaching the ICER potential budget impact threshold of $821 million. Therefore, ICER is issuing an access and affordability alert for sibeprenlimab. For atacicept, ICER is issuing an alert based on a placeholder price of $292,500 per year, but no alert would be needed if atacicept is actually priced within the HBPB range. ICER is not issuing an alert for Nefecon.



Percent of eligible IgAN patients that could be treated in a given year before crossing the ICER potential budget impact threshold.

Public Meeting Deliberations

VOTING RESULTS

ICER's Public Meeting: Voting Results on Clinical Effectiveness and Benefits Beyond Health

ICER assessed, and the independent appraisal committee voted on the evidence for the net health benefit of sibeprenlimab, atacicept, and Nefecon:

- The panelists unanimously found (14-0) that current evidence is **adequate** to demonstrate a net health benefit for sibeprenlimab when compared to no specific immunomodulatory therapy.
- A majority of panelists (13-1) found that current evidence is **adequate** to demonstrate a net health benefit for atacicept when compared to no specific immunomodulatory therapy.
- The panelists unanimously found (14-0) that current evidence is **adequate** to demonstrate a net health benefit for Nefecon when compared to no specific immunomodulatory therapy.
- A majority of panelists (9-5) found that current evidence is **adequate** to demonstrate a net health benefit for sibeprenlimab and for atacicept when each is compared to systemic glucocorticoids.
- A majority of panelists (9-5) found that current evidence is **not adequate** to demonstrate a net health benefit for Nefecon when compared to systemic glucocorticoids.

Panel members also weighed potential benefits and disadvantages beyond the direct health effects and weighed special ethical obligations. Voting highlighted the following as particularly important for payers and other policymakers to note:

- Sibeprenlimab and atacicept are likely to **substantially improve** caregivers' quality of life and/or ability to pursue their own education, work, and family life; Nefecon would likely provide a **small** improvement.

ICER's Public Meeting: Voting Results on Long-Term Value for Money

- A majority of panelists (12) found that at current pricing, sibeprenlimab represents "low" long-term value for money; 2 panelists found that sibeprenlimab represents **"intermediate"** long-term value for money.
- A majority of panelists (11) found that at current pricing, Nefecon represents **"intermediate"** long-term value for money; 3 panelists found that Nefecon represents "low" long-term value for money.

About ICER

The Institute for Clinical and Economic Review (ICER) is an independent, non-profit research institute that conducts evidence-based reviews of health care interventions, including prescription drugs, other treatments, and diagnostic tests. In collaboration with patients, clinical experts, and other key stakeholders, ICER analyzes the available evidence on the benefits and risks of these interventions to measure their value and suggest fair prices. ICER also regularly reports on the barriers to care for patients and recommends solutions to ensure fair access to prescription drugs. For more information about ICER, please visit www.icer.org.