Sonpiretigene Isteparvovec for Advanced Retinitis Pigmentosa: Effectiveness and Value

Final Policy Recommendations

May 15, 2025

Policy Recommendations

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the April 11, 2025 New England CEPAC public meeting on the use of sonpiretigene for the treatment of advanced retinitis pigmentosa (RP). At the meeting, ICER presented the findings of its revised report on this treatment and the New England CEPAC voting council deliberated on key questions related to its comparative clinical effectiveness and potential other benefits and contextual considerations. Following the votes, ICER convened a Policy Roundtable of two patient experts, two clinical experts, two payers, and one representative from the pharmaceutical manufacturer to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed here, and a recording of the voting portion of the meeting can be accessed here. More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the Appendix of *this document.*

ICER's report on this treatment, which includes the same policy recommendations, can be found here. The roundtable discussion was facilitated by Sarah Emond, President and CEO, ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

General Recommendations

All Stakeholders

Recommendation 1

All stakeholders have a responsibility to make necessary accommodations for individuals with severe vision loss, including designing educational materials and signage suitable for low vision. Low vision should not undermine the tenets of fair access to medical care, to which all patients have a fundamental right.

There are many challenges for individuals with low vision to navigate the health care system, such as attending clinic visits, reviewing results and messages in electronic health records system, and learning about available clinical trials. All stakeholders emphasized the need to accommodate individuals with low vision to be able to access health care, such as better signage in offices, including in ophthalmology offices, and design of patient portals and other materials, such as the use of alternative text for figures and tables, compatibility with assistive technology, and adoption of electronic forms so that patients can complete them on their own to maintain privacy.

Recommendation 2

Researchers and regulators should partner with patients, clinical specialty societies, and manufacturers to validate and standardize patient-centered outcome measures that capture the full range of perceived visual function in individuals with advanced RP with severe vision loss. These measures should complement visual acuity in registries and future pivotal trials.

The primary outcome used in the pivotal trial of sonpiretigene was best corrected visual acuity (BCVA). However, individuals with severe vision loss may have no or some light perception and their vision cannot be assessed by BCVA. Furthermore, patients with advanced RP have a myriad of visual symptoms beyond central vision loss, such as loss of color perception, peripheral vision, and contrast sensitivity. To complement the primary outcome of BCVA, all stakeholders play a role in facilitating research and developing regulatory guidance to validate and standardize the use of patient-centered outcome measures for individuals with advanced RP with severe vision loss, including the newly developed tests for mobility (MLYMT) and shape discrimination (MLSDT) used by the manufacturers to evaluate the efficacy of sonpiretigene. Such outcomes may also be useful to evaluate treatments for other inherited retinal disorders with photoreceptor loss.

Health Equity

All Stakeholders

Recommendation 1

All stakeholders have a responsibility to increase awareness of and access to low vision aids and vision rehabilitation services for individuals with severe vision loss.

There is currently no cure or disease-modifying therapies for RP with severe vision loss. The best available treatment for advanced RP includes low vision aids and vision rehabilitation. However, patients and clinical experts highlighted low uptake of these services due to lack of awareness and access to these services, especially for individuals who live in more rural settings or from lower socioeconomic backgrounds who have more limited financial means, time flexibility, and social support. These inequities are driven in large part because they are paid for out-of-pocket since they are not traditionally covered by insurance the way durable medical equipment (i.e., wheelchairs) and physical rehabilitation are covered for medical conditions impairing mobility and physical functioning.

To address these concerns:

<u>Payers should take the following actions:</u>

- Expand the coverage of medically necessary services for individuals with low vision to include assistive devices, such as white canes and magnifiers, and vision rehabilitation services for training in the use of adaptive devices, orientation and mobility, and independent living skills, including vocational adaptations.

<u>Manufacturers should take the following actions:</u>

- Provide educational material to inform individuals with severe vision loss about low vision aids and vision rehabilitation services to successfully adapt to vision loss.

<u>Clinical specialty societies and patient organizations should take the following actions:</u>

- Educate retina specialists, optometrists, ophthalmologists, primary care providers, and patients about low vision services and available rehabilitation centers.

- Explore and develop virtual options to provide vision rehabilitation to further increase access, particularly for individuals who do not have the financial means or ability to travel to attend in person.

Payers

Recommendation 1

Given that response to sonpiretigene appears to be widely variable across patients and that the durability of response is uncertain, payers that consider implementing outcomes-based contracts using best-corrected visual acuity should have a mechanism for judging meaningful responses that cannot be captured from BCVA. An outcomes-based contract that allows for patient and clinician reported outcomes and allows for refunds or rebates for treatment effects that are not maintained may be appropriate for a gene therapy that is expected to have a high price.

While variability in response makes an outcomes-based contract a consideration for payers, there are difficulties in developing such contracts for sonpiretigene. The most natural outcome to use for an outcomes-based contract is the best-corrected visual acuity (BCVA). However, this outcome will not be sufficient for everyone since individuals with severe vision loss who have unmeasurable visual acuity below the floor threshold of the BCVA may still have meaningful improvement (such as improvement from no light perception to some light perception). Additionally, advanced RP affects many visual symptoms beyond central vision, such as color vision and contrast sensitivity, which are not assessed by the BCVA. Thus, payers may wish to work with the manufacturer to develop patient-centered outcome measures that capture benefits that could be missed by the BCVA, such as the Michigan Retinal Degeneration Questionnaire, which assesses visual function across seven domains. Clinician and patient input will be important in developing any outcomes-based contracts in this space.

Recommendation 2

When designing coverage policies if sonpiretigene is approved by the FDA, payers should use the inclusion criteria from the pivotal trial as a guide to coverage policy.

There are no other curative or disease-modifying therapies for advanced RP. The potential alternative therapies to restore vision include photoreceptor transplantation and surgically implanted retinal "chips," which clinical experts we spoke to believe are both earlier in development with less robust evidence and are much more complicated therapies. Given the significant uncertainty that remains about sonpiretigene, it is reasonable for payers to use prior authorization as a component of coverage. Prior authorization criteria should be based on the ultimate FDA label, if the drug is approved, clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers and patients. Options for specific elements of coverage criteria within insurance coverage policy are discussed below.

Coverage Criteria: General

ICER has previously described general criteria for fair coverage policies that should be considered as cornerstones of any drug coverage policy in the report: Cornerstones of "Fair" Drug Coverage: Appropriate Cost-Sharing and Utilization Management Policies for Pharmaceuticals.

Drug-Specific Coverage Criteria: Sonpiretigene Isteparvovec

A one-time, likely costly treatment, combined with uncertain durability, long-term safety, and the potential to adversely interfere with intact visual pathways in the presence of sufficient photoreceptors, may lead payers to develop prior authorization criteria.

None of these criteria, however, should undermine the tenets of fair access to which all patients have a fundamental right.[1] Further, given the expected high cost of this therapy, and the lack of alternative treatments for this condition, patient cost-sharing is not expected to be an appropriate aspect of any coverage policy. To explore the appropriate application of evidence to coverage policy, and to reflect the views of patient experts and clinicians on specific ways that payers might appropriately use coverage policy to manage resources prudently, we present the following perspectives on specific elements of coverage criteria for sonpiretigene.

Coverage Criteria

- **Age:** Age criteria should follow the trial, which enrolled adults with severe vision loss, who comprise most individuals with advanced RP. While this treatment is not appropriate for young children since it requires appropriate cortical development to process vision, payers should have efficient mechanisms for clinicians to seek coverage exceptions for patients with serious unmet need who are near the cutoff for the age necessary for coverage.

- **Clinical eligibility**: There was consensus among policy roundtable participants to follow the trial criteria for determining eligibility. Specifically, clinical experts strongly recommended the reliance on a clinically defined diagnosis of advanced RP with severe vision loss. They did not recommend genetic testing be performed since the treatment is mutation agnostic, and because approximately 40% of cases have no identifiable genetic cause. As such, experts recommended a clinical diagnosis of advanced RP. This would entail a history, dilated fundus examination, and imaging (optical coherence tomography) to confirm the presence of an intact retinal inner layer. Eligibility based on trial criteria would require a BCVA worse than logarithmic minimum angle of resolution (LogMAR) 1.9 in the eye being considered for treatment, and a BCVA no better than LogMAR 1.6 in the contralateral eye. Given the potential for interference with the patient's intact visual system if administered at too early a stage, it would be reasonable for payers to require an attestation by a retinal specialist to confirm the diagnosis and eligibility prior to treatment.

- **Exclusion criteria**: It would be appropriate to follow the pivotal trial's criteria. Experts recommended that a clinical attestation alone would suffice for the exclusion of other mimickers of advanced RP, such as autoimmune disease or presence of ocular complications (i.e., cataracts).

- **Dose:** It would be reasonable for health plans to consider covering treatment of only a single eye, consistent with the available clinical trial evidence. If both eyes are considered for treatment, it would be reasonable to expect the same pricing from the manufacturer as the price for treating one eye in the absence of trial evidence demonstrating added benefit.

- **Provider restrictions**: While some payers may consider a requirement that sonpiretigene be administered by retinal specialists or at a center of excellence for retinal care, clinical experts agreed that most ophthalmologists could administer this treatment in their office given the intravitreal route of injection. While implementing provider restrictions is likely not clinically necessary, payers may prefer to approve therapy by general ophthalmologists only if done so in consultation with a retinal specialist to attest the diagnosis and eligibility for treatment. If payers choose to restrict administration to a retinal specialist or a center of excellence, then it would be incumbent on the health plans to work with the manufacturer to also cover costs related to travel for patients, including transportation and lodging.

Step Therapy

There are no other treatments that could be considered a first-line treatment prior to eligibility.

Manufacturers

Recommendation 1

Manufacturers should set prices that will foster affordability and access for all patients by aligning prices with the value of their treatments. In the setting of a new intervention for advanced RP, while there is considerable hope associated with the promise of sonpiretigene, there also remains substantial uncertainty regarding the durability of treatment effect and longer-term safety. Manufacturer pricing should also reflect these considerations in moderating launch pricing.

Drug prices that are set well beyond the cost-effective range cause not only financial toxicity for patients and families using the treatment but also contribute to general health care cost growth that pushes families out of the insurance pool, and that causes others to ration their own care in ways that can be harmful.

Manufacturers should therefore price novel treatments in accordance with the demonstrated benefits to patients for their specific therapies and should not benchmark prices to existing gene therapies. In settings of substantial uncertainty, initial pricing should err on the side of being more affordable. This would allow more patients access, while generating additional data on the real-world effectiveness of novel treatments that could be used in future assessment updates. With accumulation of evidence of substantial patient benefit, manufacturers should be allowed to increase pricing in accordance with demonstrating more benefits for patients.

We appreciate the commitment of the manufacturer during the policy roundtable to price their treatment based on value to ensure affordable access. Given that this treatment is mutation agnostic, there may be more patients eligible for treatment than the gene therapy for RP, including those with other inherited retinal diseases with photoreceptor degeneration (i.e., Stargardt disease). As more is learned about the real-world use of the therapy, the manufacturer should consider adjusting the price to reflect its value in a potentially larger population.

Recommendation 2

The manufacturer should follow all participants enrolled in ongoing clinical trials and establish registries that can be used to assess the long-term benefits and harms of all patients receiving this optogenetic therapy.

Concerns remain about the durability of treatment effect, potential benefits on other aspects of vision not measured in the clinical trial, and long-term harms that may be uncommon. Potential harms include ocular and retinal complications and transfection of cells outside of the injected eye as noted with other gene therapies for inherited retinal disorders. Whether these harms will be seen for this treatment requires larger, long-term follow-up studies, especially since the treatment

may be administered to younger adults with advanced RP. Experts emphasized the need to follow all patients currently enrolled in clinical trials to understand the safety profile and the durability of benefits. Additionally, registries of all patients receiving this therapy should collect standardized patient-reported outcome measures to assess benefits across all relevant domains of vision that could be affected by treatment, especially for individuals who have severe vision loss and are at or below the floor threshold for assessing visual acuity.

Recommendation 3

Support access to sonpiretigene by providing specialized delivery services of the therapy to ophthalmology clinics.

Since restricting prescribing to retinal specialists may not be necessary clinically, to improve availability and access of this treatment to patients with advanced RP, the manufacturer should consider providing "white glove" service which entails a dedicated case manager to oversee the delivery process, and customized logistics with temperature-controlled handling and a clear chain of custody to prevent contamination, mislabeling, or mishandling of this gene therapy that may deter clinicians from obtaining the treatment to administer to their patients.

Clinicians and Clinical Societies

Recommendation 1

Develop consensus recommendations for treatment of patients with RP.

Clinical societies should update their consensus recommendations or practice guidelines for managing patients with advanced RP to include newer therapies to help restore vision, such as sonpiretigene and more investigational therapies, such as photoreceptor transplantation and surgically-implanted "chips." Payers base their coverage decisions and utilization management policies to a great extent on clinical guidelines. The American Academy of Ophthalmology (AAO) last updated it guidance on the clinical assessment of patients with inherited retinal degenerations, which includes RP, in 2022. Current recommendations do not discuss treatment. After new therapies are approved by the FDA for the treatment of patients with RP, the AAO should consider issuing a consensus guideline to discuss and provide pragmatic advice as to how sonpiretigene and other FDA-approved therapies should be incorporated into practice. Guidelines should be easy to interpret by clinicians, payers, and patients with vision loss.

Patient Organizations

Recommendation 1

Patient organizations have a vital role to play to promote objective descriptions of the risks and benefits of new therapies in order to support shared decision-making for every patient. In addition, patient groups have a powerful voice and should apply it to create significant pressure for fair pricing and appropriate insurance coverage across all sectors of the health system.

Patient groups should endeavor to educate patients about the potential risks and benefits of new therapies, particularly those with uncertainty about durability of effect and long-term safety, and work with other stakeholders to develop and disseminate evidence-based, balanced materials that are accessible to all patients, including those with low health literacy. Patient groups should also accept responsibility to publicly promote access and fair pricing of new therapies.

Researchers and Regulators

Recommendation 1

Given that some patients did not appear to improve with sonpiretigene, and others had more dramatic responses in visual acuity, researchers should look for sources of heterogeneity in treatment response to optogenetic therapy.

Better understanding of the causes of heterogeneity in treatment response to optogenetic therapy would be immensely helpful to more precisely target which patients should be considered for treatment. Experts thought differences in the retinal biology were the key drivers of why patients may have differential treatment response to optogenetic therapy. Specifically, experts suspected that shorter duration of photoreceptor degeneration and having sufficient retinal thickness of the inner and middle layers might predict better response. Additionally, experts thought proteomics—the study of proteins produced by retinal cells—was another promising avenue to explore the heterogeneity in treatment response. They were less enthusiastic that differences in treatment response were driven by the underlying genetic mutation and noted that disentangling such heterogeneity would be implausible given the large number of genes and mutations involved in RP.

Recommendation 2

Researchers should study whether sonpiretigene improves vision for individuals with advanced RP who have severe vision loss better than the pivotal trial eligibility criteria.

The RESTORE trial eligibility was based upon BCVA inclusion criteria (LogMAR 1.9 or worse in treatment eye and BCVA not better than LogMAR 1.6 in the contralateral eye) which may be overly restrictive. To address the potential broader unmet need for other patients with advanced RP but better visual function, future studies should evaluate the efficacy and safety of sonpiretigene for individuals with better BCVA in the treatment eye than the trial criteria, better visual function in the non-treated eye than a LogMAR of 1.6, or have more preserved visual function but very narrow visual fields (less than 10 degrees).

Appendix

Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the April 11, 2025 public meeting of sonpiretigene isteparvovec for advanced retinitis pigmentosa.

Table 1. ICER Staff and Consultants and COI Disclosures

ICER Staff and Consultants*	
Madeline Booth, BA, Program Manager, ICER	**Sarah Emond, MPP,** President and CEO, ICER
Grace Ham, MSc, Senior Program and Events Coordinator, ICER	**Belén Herce-Hagiwara, BA**, Research Assistant, ICER
Woojung Lee, PharmD, PhD, Associate Director of Health Economics and Decision Modeling, ICER	**Anil Makam, MD, MAS**, Assistant Professor of Medicine, University of California San Francisco
Avery McKenna, BS, Research Lead, ICER	**Marie Phillips, BA**, Health Economics Research Assistant, ICER
Marina Richardson, PhD, MSc, Associate Director of HTA Methods and Health Economics, ICER	**David Rind, MD, MSc,** Chief Medical Officer, ICER
Sol Sanchez, BS, Research Assistant, ICER	

*No conflicts of interest to disclose, defined as individual health care stock ownership (including anyone in the member's household) in any company with a product under study, including comparators, at the meeting in excess of $10,000 during the previous year, or any health care consultancy income from the manufacturer of the product or comparators being evaluated.

Table 2. New England CEPAC Panel Member Participants and COI Disclosures

New England CEPAC Member	Conflict of Interest
Austin Frakt, PhD, Principal Research Scientist, Harvard T.H. Chan School of Public Health	No conflicts to disclose.
Megan Golden, JD, Co-Founder and CEO, Mission: Cure	No conflicts to disclose.
Rebecca Kirch, JD, EVP, Policy and Programs, National Patient Advocate Foundation	No conflicts to disclose.
Stephen Kogut, PhD, Professor, University of RI	No conflicts to disclose.
Donald M. Kreis, MS, JD, Consumer Advocate, New Hampshire Office of the Consumer Advocate	No conflicts to disclose.
Julie Kueppers, PhD, NP, Clinical VP, Alera Group	No conflicts to disclose.
Tara Lavelle, PhD, Assistant Professor, Tufts Medical Center	No conflicts to disclose.
Aaron Mitchell, MD, MPH, Assistant Attending, Memorial Sloan Kettering Cancer Center	No conflicts to disclose.
Brian O'Sullivan, MD, Professor of Pediatrics, Geisel School of Medicine	No conflicts to disclose.
Jo Porter, MPH, Chief Strategy Officer, NH Center for Justice and Equity	No conflicts to disclose.
Rishi Wadhera, MD, MPP, MPhil, Associate Professor, Harvard Medical School	No conflicts to disclose.
Jason Wasfy, MD, MPhil, Associate Professor, Harvard Medical School	No conflicts to disclose.

Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Participant	Conflict of Interest
Todd Durham, PhD, Senior Vice President, Clinical and Outcomes Research, Foundation Fighting Blindness	Foundation Fighting Blindness (FFB) has received sponsorships from various health care companies, including Nanoscope Therapeutics, for their scientific conferences, accounting for<25% of their funding. A member of Dr. Durham's household works in the life sciences industry and receives ≥25% of income from the industry. Additionally, the RD Fund, a venture philanthropy subsidiary of the FFB, has equity interests in several life science companies in its portfolio.
Julie Grutzmacher, MSW, MPH, Director of Patient Advocacy and Population Health Initiatives, Prevent Blindness	Prevent Blindness receives >25% of funding from health care companies, including Nanoscope Therapeutics.
Hemant Hora, MD, FACP, Vice President, Medical Affairs, Senior Medical Director, Point32Health	Dr. Hora is a full-time employee of Point32Health.
Vinit B. Mahajan, MD, PhD, Professor of Ophthalmology, Stanford University	Dr. Mahajan has received funds from Nanoscope Therapeutics, Chigenovo, and Kerna Labs.
Samarendra Mohanty, PhD, Co-Founder and President, Nanoscope Therapeutics	Dr. Mohanty is a full-time employee of Nanoscope Therapeutics.
Lindsay Rippelmeyer, PharmD, Senior Director, Supply Chain Finance, Express Scripts by Evernorth	Dr. Rippelmeyer is a full-time employee of Express Scripts.
Stephen Russell, MD, Professor of Ophthalmology, University of Iowa	Dr. Russell has received funds from Spark Therapeutics, ProQR Therapeutics, Novartis, Digital Diagnostics (IDx, LLC) and has stock ownership in Digital Diagnostics (IDx, LLC).

References

1. Pearson SD, Towse A, Lowe M, Segel CS, Henshall C. Cornerstones of 'fair'drug coverage: appropriate cost sharing and utilization management policies for pharmaceuticals. *Journal of Comparative Effectiveness Research*. 2021;10(7):537-547.