Therapies for Spinal Muscular Atrophy
Final Policy Recommendations

SEPTEMBER 2, 2025

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the August 1, 2025, Midwest CEPAC public meeting on therapies for spinal muscular atrophy (SMA). At the meeting, ICER presented the findings of its revised report on these treatments and the Midwest CEPAC voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations. Following the votes, ICER convened a Policy Roundtable of two patient representatives, two clinical experts and two payers 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 these treatments, which includes the same policy recommendations, can be found here.

The roundtable discussion was facilitated by Sarah Emond, President and Chief Executive Officer at ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

Health Equity

All Stakeholders

Recommendation 1

All stakeholders have a responsibility and an important role to play in ensuring that effective treatments for patients with SMA and persistent weakness are introduced in ways that will help reduce health inequities.

Muscle weakness remains a significant unmet healthcare need in patients with SMA even after SMN-directed therapy. This is particularly true for patients who were not diagnosed via newborn screening and so received treatment months to years after birth; lost motor neurons are never regained. Efforts are needed to ensure that the introduction of apitegromab does not aggravate existing health inequities. Concerns highlighted for this potentially expensive therapy, which requires IV infusion every four weeks, include the availability of specialists in SMA management, the costs of treatment, and the challenges faced by patients with limited mobility in traveling for care.

To address these concerns:

Manufacturers should take the following actions:

- **Set the price of apitegromab at launch to align with the value of added patient benefits.** The price for apitegromab has not been set, but analyst estimates are as high as $350,000 per year, which would likely lead to payers creating policies that might limit or delay patient access. ICER's analysis suggested that treatment would achieve common thresholds for cost-effectiveness if priced between $10,700 and $30,200 per year. The manufacturer should price apitegromab so that both individual patients and the health system will view the drug as fairly priced, leading to broader access in a way that will help reduce disparities.

Payers should take the following actions:

- **Ensure that benefit designs developed in conjunction with employers and other plan sponsors do not create requirements for out-of-pocket spending that create major barriers to appropriate access for vulnerable patients.**

- **Adopt standardized travel benefits or ensure access to home infusions of apitegromab for patients who have challenges traveling to an infusion center to receive therapy.** Patients in rural areas and those with severe muscle weakness and scoliosis often have challenges coming to medical centers for necessary services that are not available near their homes. Insurance plans variably cover the costs of travel and housing. Additionally, such coverage is commonly tied to specific diagnoses and therapies. Payers should develop standard coverage for travel for needed services to ensure equitable access to therapies like apitegromab, which requires IV infusions.

Clinicians and Clinical Specialty Societies

- **Expand the ability of Centers of Excellence to provide consultation and support for community neurologists.** Because of its rarity, many neurologists may not be up to date on the latest strategies for managing SMA. Patients and their treating neurologists would benefit from collaborative care through consultation with specialists at centers of excellence. Treatment plans can be designed by specialists working with the patient and then administered by community neurologists. Centers of Excellence need to have enough clinicians to meet the demand for consultation and ongoing remote management.

- **Collaborate with patient organizations to exercise their joint power to advocate for drug prices that do not exceed a fair value for added clinical benefit.**
  Patients often have significant co-pays for drugs like apitegromab that require IV infusions, with some commercial plans requiring a high coinsurance for infused therapies. Specialty societies have an opportunity and responsibility to reach out to patient groups to form a united front and advocate for fair insurance access linked to fair prices for drugs. Drug prices that align with analyses of added benefit will often be lower than those initially set by drug makers, and lower prices will lead to fewer restrictions on access to the drugs and less financial burden on patients. In addition, this will enhance more equitable access to effective therapies.

<u>Organizations representing patients</u>

- **Patient groups should seek relationships with clinical specialty societies to exercise their joint power to advocate for drug prices that do not exceed a fair value for added clinical benefit.**
  Patients often have significant co-pays for drugs like apitegromab that require IV infusions, with some commercial plans requiring a high coinsurance for infused therapies. Patient groups and specialty organizations have an opportunity and responsibility to advocate for fair insurance access linked to fair prices for drugs. Drug prices that align with analyses of added benefit will often be lower than those initially set by drug makers, and lower prices will lead to fewer restrictions on access to the drugs and less financial burden on patients. In addition, this will enhance more equitable access to effective therapies.

- **Patient groups should help raise international awareness about the value of newborn screening.**

  Newborn screening and immediate treatment have transformed the lives of patients living with SMA in the United States. Unfortunately, newborn screening is not universally available in other countries. Disease-modifying treatments for SMA have the highest value when started before symptoms develop clinically, and there are cost savings inside and outside the health system compared with waiting for symptoms to become clinically apparent. Many patients with SMA identified with newborn screening are expected to meet all of their developmental motor milestones and live healthy lives.

Payers

Recommendation 1

When approval of a drug that represents a first-in-class therapy for an underserved population is anticipated, payers should be evaluating the evidence and preparing policies in advance to avoid a new-to-market block on insurance coverage.

Many payers now institute "new-to-market" policies that block routine insurance coverage for new drugs 180 days or longer after Food and Drug Administration (FDA) approval. Although these blocks can be justified to allow an insurer adequate time to review the clinical evidence, consult with clinical experts, and prepare special coverage policies, in practice, many insurers place new-to-market blocks on virtually any new specialty drug. Payers should recognize their responsibility to act prior to FDA approval to ensure that their coverage policies are ready at the time of approval. This preparation is facilitated when manufacturers share data in a timely and transparent way and engage with payers prior to the approval of their products to facilitate the establishment of payment policies. Since patients with SMA often suffer from severe disabilities, prompt access to a new therapy like apitegromab with the potential to improve motor functioning could improve their independence and reduce costs over the long term.

Recommendation 2

Payors should cover consultations between patients, their local neurologists, and Centers of Excellence.

SMA is a rare disease, and community neurologists have limited experience caring for patients with SMA. Expert consultation to establish a care plan will facilitate the use of the most up-to-date recommendations that optimize outcomes for patients.

Recommendation 3

Trial inclusion criteria are a reasonable starting point for developing coverage criteria for apitegromab, but payers should involve clinical experts and patient groups in designing flexible policies to account for the expected interest in the therapy for all SMA patients with muscle weakness.

Developing coverage policies for rare conditions can be challenging, given the evidence base. Since there are limited data from one small, randomized trial for apitegromab, and the cost is expected to be high, it would not be unreasonable for payers to use prior authorization as a component of coverage. Prior authorization criteria could be based on the inclusion and exclusion criteria from the SAPPHIRE trial, but will likely need to be sufficiently flexible to allow access for all SMA patients with muscle weakness, at least for a trial period. The process for authorization should be clear and

efficient for providers and patients. Perspectives on specific elements of cost sharing and coverage criteria within insurance coverage policy are discussed below. Relevant criteria set out in ICER's previous work, Cornerstones of "Fair" Drug Coverage: Appropriate Cost-Sharing and Utilization Management Policies for Pharmaceuticals, are included.

Drug-Specific Coverage Criteria: Apitegromab

The limited data on effectiveness, combined with the potential for serious adverse effects, and the high anticipated price for apitegromab, will lead payers to develop prior authorization criteria and to consider other limits on utilization.

None of these limits, however, should undermine the tenets of fair access to which all patients have a fundamental right. 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 cost sharing and coverage criteria for apitegromab.

Outcome-based agreements were briefly discussed, but there was general agreement that there was no role for them with apitegromab as they would be too cumbersome to administer.

Payors should be sensitive to the cumulative effects of cost-sharing on patients and set appropriate caps on the annual out-of-pocket expenditures for patients.

In addition, payers should ensure that their review team has a deep understanding of this rare and potentially devastating illness.

Step Therapy

Given that there is no alternative therapy available that increases motor function akin to apitegromab, step therapy is not appropriate.

Clinical Coverage Criteria

- **Age:** The primary endpoint in the pivotal SAPPHIRE trial of apitegromab was assessed in children aged 2 to 12 years. However, clinical experts told us that there is no biological reason why apitegromab should not help patients with SMA of other ages; in an exploratory group of 32 patients aged 13 to 21 years, the gains in the HFSME were similar to those observed in the younger patients. Payers could consider extending the covered age to all patients with SMA who have residual weakness.

- **Clinical eligibility**: The SAPPHIRE trial studied patients with Type 2 or Type 3 SMA who are non-ambulatory and are receiving either nusinersen or risdiplam, although the majority

(80%) were treated with nusinersen. Interestingly, the subgroup of patients treated with risdiplam and apitegromab saw almost no gain in the HSFME compared with placebo (change from baseline 0.5 points, 95% CI, -2.3 to +3.3).

- **Exclusion criteria**: The SAPPHIRE trial excluded patients with Hammersmith Functional Motor Scale Expanded (HFMSE) scores that were less than 10 or greater than 45. As with the age criteria, clinical experts suggested that there is no biological reason why patients with other scores could not benefit from apitegromab. It would be reasonable for payers to consider coverage for patients with a wider range of HFSME scores.

  In addition, the study excluded patients who had severe scoliosis, severe contractures, or the use of chronic daytime ventilator support.

  Finally, the study excluded patients who were previously treated with onasemnogene abeparvovec.

  Payers could consider flexible policies that require additional evidence generation (sometimes referred to as "coverage with evidence development") in the populations not studied in the SAPPHIRE trial to broaden access to other SMA patients with muscle weakness, and to further the clinical understanding of which patients would benefit from the new therapy.

- **Dose:** 10 or 20 mg/kg IV infusion every four weeks.

- **Duration of coverage and renewal criteria**: Initial coverage will likely be for a period of 4 to 6 months, which is long enough to assess response to therapy. Clinical experts and payers felt that it would be appropriate to require attestation alone for continuation of therapy.

  If payers decide to require documentation using some measure, they should recognize that there are significant challenges in assessing response with the HFMSE due to potential intercurrent illness leading to a short-term reduction in score and the small average increase in the HFMSE among treated patients. If stability or improvement in the HFMSE is required for renewal, then the trend over multiple assessments should be used rather than focusing on the most recent assessment.

- **Provider restrictions**: Clinical experts agreed that it is reasonable to restrict prescriptions for apitegromab to neurologists, ideally in consultation with an expert in the care of patients with SMA. Specialty clinicians are better suited to identify patients who are most likely to benefit, provide sufficient information for patients and families to make well-informed decisions, and monitor for response and side effects.

Site of Service Policies

Payors should establish site-of-service policies that cover home infusion or care at other low-cost sites when feasible.

Clinical experts did not suggest that there were risks of administration of apitegromab that would make it necessary to administer it in specialized clinical settings. Given the reduced cost and increased convenience for patients when infusions are delivered at home rather than at hospital-based infusion centers, payors should establish site-of-service policies that cover home infusion or care at other low-cost sites when feasible. Benefit design should enable patients to have lower cost sharing when lower-cost settings are used, and rapid, transparent procedures for exceptions should be universal.

Manufacturers

Recommendation 1

The manufacturer 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. Given the small average improvement in motor function for patients treated with apitegromab and the uncertainty about serious adverse events, manufacturer pricing should reflect ICER's value-based price range in moderating launch pricing.

Drug prices that are set well beyond the cost-effective range not only cause financial toxicity for patients and families using the treatments but also contribute to general healthcare cost growth that pushes families out of the insurance pool and 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. In settings of substantial uncertainty, initial pricing should err on the side of being more affordable. This would allow more patients access, generating additional data on the real-world effectiveness of novel treatments that could be used in future assessment updates. With the accumulation of evidence of substantial patient benefit, manufacturers should be allowed to increase pricing in accordance with clear evidence of significant net health benefits.

Clinicians and Clinical Societies

Recommendation 1

Update guidelines to move beyond SMA Type as the guidepost for therapy.

The use of SMA Type to describe patients and guide treatment recommendations is outdated in the era of newborn screening and early life intervention with SMN-directed therapy. Most patients in the US will appear to be asymptomatic when diagnosed as newborns. Research design and guideline development should focus instead on SMN2 copy number to characterize patients.

Patient Organizations

Recommendation 1

Cure SMA should continue to produce its annual State of SMA report.

The report was invaluable in the development of ICER's assessment. Given the rapidly evolving changes in the characteristics of patients since the advent of SMA-directed therapies and newborn screening, ongoing updates on the changing epidemiology of the community and their evolving needs are an irreplaceable service for all stakeholders.

Researchers/Regulators

Recommendation 1

Measure the impact of treatment on caregiver burden

The potential impact of effective therapy for SMA on caregiver burden was identified as an important potential benefit, but this is not explicitly measured in most clinical trials. Patient organizations have an important opportunity to partner with researchers in developing measures of caregiver burden and encounring pharmaceutical companies and the FDA to include them in future trials of therapies like apitegromab.

Recommendation 2

Expand research on apitegromab to populations not included in SAPPHIRE

There are currently no data on the utility of apitegromab in patients who did not meet the eligibility criteria for the study. Ambulatory patients with residual weakness may benefit, as may patients with Types 1 or 4 SMA. Finally, the drug should be studied in patients who have received gene therapy.

Recommendation 3

Expand research on measuring the clinical impact of therapies for SMA

Patients, caregivers, advocates, and clinicians agreed that changes in the HFMSE are insensitive to some meaningful benefits experienced by patients and their caregivers. Attention should be given to the development of instruments to capture the marginal gains reported by caregivers. In addition, more attention should be paid to the experience of young patients, whose voice is often not considered when assessing response to therapies. The International Consortium for Health Outcomes Measurement (ICHOM) is currently developing a new set of Patient-Centered Outcomes for patients with SMA, which may address some of these needs: https://www.ichom.org/patient-centered-outcome-measure/spinal-muscular-atrophy/

Recommendation 4

The use of SMN-directed therapy after gene therapy or in combination should only be done in the context of research studies.

Experts expressed significant skepticism about whether patients who had been treated with onasemnogene abeparvovec received any further benefit from treatment with either nusinersen or risdiplam. Adding extremely expensive therapies on top of an ideally curative therapy is not warranted without higher-quality evidence of benefit. If manufacturers will not perform such a trial, organizations like PCORI (Patient Centered Outcomes Research Institute) should consider funding a trial with regulatory requirements for medications to be provided at the cost of production. Payers could also potentially contribute to funding such a trial through a coverage with evidence development mechanism. Uncertainties also exist for combination treatment with nusinersen with risdiplam, though this is rarely covered.

Recommendation 5

A randomized trial should be performed of first-line therapy in asymptomatic patients identified through newborn screening to better understand the comparative advantages and disadvantages of each of the three SMN-directed therapies.

Experts highlighted the possibility that all three of the SMN-directed therapies (nusinersen, onasemnogene abeparvovec, and risdiplam) may maximize the protection of motor neurons. However, they have different mechanisms of action and distinct adverse events. Only randomized trials can provide an unbiased estimate of the relative benefits and harms between the three therapies. Without randomized trial data, parents making the ultimate decision in consultation with specialists must base their decision on results coming from case series with different entry criteria. If manufacturers will not collaborate to perform such a trial, organizations like PCORI should

consider funding a trial with regulatory requirements for medications to be provided at the cost of production.

Recommendation 6

Remove barriers across state lines to facilitate consultations between patients, their local neurologists, and Centers of Excellence.

Eliminating barriers to expert collaboration and care coordination allows patients with SMA to access the most knowledgeable centers of excellence, regardless of geographic location.

Recommendation 7

Explore biomarkers that will help predict response to treatments for SMA

We heard preliminary evidence that neurofilament (NfL, PNF-H) levels may identify patient groups with ongoing motor neuron loss who may benefit from additional therapy. Furthermore, these markers could be used as a surrogate marker for treatment efficacy if well validated, thus improving the ability of clinicians to appropriately prescribe therapies.

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the August 1, 2025 Public meeting of the Midwest CEPAC.

Appendix Table 1. ICER Staff and External Collaborators Conflict of Interest Disclosures

ICER Staff and External Collaborators	Conflict of Interest
Josh Carlson, PhD, MPH	Josh Carlson has received consulting fees from Genentech that are not related to SMA.
Hui-Hsuan Chan, MHS	No conflicts to disclose.
Sarah Emond, MPP	No conflicts to disclose.
Anna Geiger, BS	No conflicts to disclose.
Kelsey Gosselin, MA	No conflicts to disclose.
Grace Ham, MSc	No conflicts to disclose.
Max Lee, PharmD	No conflicts to disclose.
Woojung Lee, PharmD, PhD	No conflicts to disclose.
Linda Luu, MSc	No conflicts to disclose.
Dmitriy Nikitin, MSPH	No conflicts to disclose.
Marie Philips, BA	No conflicts to disclose.
David M. Rind, MD, MSc	No conflicts to disclose.
Sol Sanchez, BA	No conflicts to disclose.
Temiwunmi Shobanke, MS	No conflicts to disclose.
Jeffrey A. Tice, MD	No conflicts to disclose.

Appendix Table 2. Midwest CEPAC Panel Member Participants and Conflict of Interest Disclosures

Midwest CEPAC Member	Conflict of Interest
Bijan Borah, PhD Professor of Health Services Research, Mayo Clinic College of Medicine and Science	Dr. Borah has received a consulting fee of <$5K from Boehringer Ingelheim in 2025.
Kurt Vanden Bosch, PharmD System Formulary Lead, St. Luke's Health System	No conflicts to disclose.
Donald Casey, MD, MPH, MBA, MACP, FAHA Associate Professor of Internal Medicine, Rush Medical College	No conflicts to disclose.
Sneha Dave Executive Director, Generation Patient	No conflicts to disclose.
Stacie Dusetzina, PhD Professor of Health Policy, Vanderbilt University Medical Center	No conflicts to disclose.
Jayani Jayawardhana, PhD Associate Professor, University of Kentucky	No conflicts to disclose.
Jill Johnson, PharmD Professor, Pharmacy Practice, University of Arkansas for Medical Sciences, College of Pharmacy	Dr. Johnson receives royalties from UAMS Bioventures for intellectual property generated as part of the Evidence-based Prescription Drug program (EBRx), a service division of the UAMS College of Pharmacy. She

	leads a Pharmacy & Therapeutics Committee to discover the peer-reviewed, published evidence with emerging and existing drugs and to report these findings to our committee who votes on which drugs to recommend coverage for using the lowest net cost approach. Through this service arm, part of her salary is covered in addition to the IP income (about $450/month) which comes from RxResults, a private pharmacy risk management company. Additionally, she serves as a consultant to Stephens Insurance and receives $25,000 per year. However, she does not take part in the drug selection process.
David Kim, PhD Assistant Professor, University of Chicago	No conflicts to disclose.
Bradley C. Martin, PharmD, PhD Professor, University of Arkansas for Medical Sciences	Dr. Martin receives royalties of approximately $7,500/year from Trestle Tree for the commercialization of an opioid risk prediction tool. He has no other potential conflicts to disclose.
Timothy McBride, PhD Washington University in St. Louis	No conflicts to disclose.
Reem Mustafa, MD, MPH, PhD, FACP Professor of Medicine, Division of Nephrology & Hypertension, Director of Evidence based Practice and Impact Center(EPIC), The University of Kansas Medical Center	No conflicts to disclose.
Rachel Sachs, JD, MPH Professor of Law, Washington University in St. Louis School of Law	No conflicts to disclose.
Stuart Winston, DO Patient Experience Consultant, Trinity Health IHA Medical Group	No conflicts to disclose.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Participant	Conflict of Interest
Thomas Crawford, MD, Professor of Neurology and Pediatrics, Johns Hopkins Hospital	Dr. Crawford has served as consultant on advisory panels to Biogen, Avexis, Scholar Rock, Muscular Dystrophy Association, SMA Foundation and CureSMA. Dr Crawford has received compensation for continued conductance of clinical trials by Biogen, Novartis/Avexis, Sarepta, and Scholar Rock, as well as monetary support for participation in advisory boards by Biogen and Scholar Rock in the last 36 months.
Giles Lomax, CEO, Spinal Muscular Atrophy UK	SMA UK received 15.6% of income from pharmaceutical companies including Scholar Rock, Biogen, Novartis, and Roche in 2024/2025.
Hugh McMillan, Professor of Pediatrics/Pediatric Neurologist, University of Ottawa/Children's Hospital of Eastern Ontario	Dr. McMillan serves as a consultant for Novartis, Roche, and Biogen. He also serves as the Principal Investigator for clinical trials for Novartis, Roche, and Biogen, with funds provided to the institution.

Portia Thorman, Head of Advocacy and Community, Spinal Muscular Atrophy UK	SMA UK received 15.6% of income from pharmaceutical companies including Scholar Rock, Biogen, Novartis and Roche in 2024/2025.
Lindsey Samera, PharmD, Associate Director, PDL Strategy, UnitedHealthcare	Dr. Samera is a full-time employee of United Healthcare.
Emily Tsiao, PharmD, BCPS, Medical Policies Clinical Pharmacist, Premera Blue Cross	Dr. Tsiao is a full-time employee of Premera Blue Cross.