



AMX0035 and Oral Edaravone for Amyotrophic Lateral Sclerosis: Final Policy Recommendations

September 13, 2022

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the August 19, 2022 Midwest CEPAC public meeting on the use of oral edaravone and AMX0035 for the treatment of Amyotrophic Lateral Sclerosis. 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, and long-term value for money at current prices. Following the votes, ICER convened a Policy Roundtable of one patient and one caregiver, two clinical experts, two payers, and one representative from a 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 these treatments, which includes the same policy recommendations, can be found [here](#).

The roundtable discussion was facilitated by Dr. Steven Pearson, MD, MSc, President of ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

All Stakeholders

Recommendation 1

To expand access and reduce health inequities, all stakeholders have a responsibility to facilitate the use of telehealth to deliver high-quality multidisciplinary care from specialized ALS clinics.

Specialized multidisciplinary ALS clinics are the standard of care in ALS.¹ By providing comprehensive care across a range of clinical disciplines, the multidisciplinary care approach in ALS increases the use of evidence-based therapies, improves quality of life, and may extend survival.²³ One particular challenge is access. There are over 200 ALS clinics in the US, 73 of which are Certified Treatment Centers of Excellence by the ALS Association.^{2,3} However, ALS multidisciplinary clinics are not evenly distributed—several states have only one or two clinics. Since travel to a multidisciplinary clinic is a major barrier for patients and families dealing with ALS,⁴⁵ clinical experts and patient and caregiver stakeholders told us that there were longer diagnostic delays for

racial/ethnic minorities, low-income households, and those living in geographic regions without these clinics. One potential solution to improve access to multidisciplinary ALS care is the use of telehealth, which is feasible and cost-effective.^{4,5} To enable telehealth during the COVID-19 pandemic, payers have relaxed geographic restrictions for state medical licensure and billing to allow doctors to see patients virtually from other states where they are not licensed.⁶ As the burden of the pandemic has eased, clinical experts have told us that many payers are reinstating these restrictions. The Veterans Health Administration and Kaiser Permanente were cited as model health systems providing broad access to ALS multidisciplinary care, in part through the use of telehealth.⁷ It should be noted that telehealth can promote access, but it can also exacerbate health inequities due to disparities in availability of devices, broadband connectivity, and digital health literacy. All stakeholders, therefore, should focus on not only improving access to telehealth, but also in evolving its use in a way that narrows instead of exacerbating the ‘digital divide.’

To address these concerns:

State and federal policy makers should take the following actions:

- Work together to break down ‘ALS care deserts’ by issuing legislation to promote telehealth for multidisciplinary ALS clinics, such as the Creating Opportunities Now for Necessary and Effective Care Technologies (CONNECT) for Health Act (H.R. 2903/S. 1512) that is being considered for Medicare beneficiaries which proposes to remove all geographic restrictions.
- Promote digital health equity through legislation, such as the Lifeline Program or the Emergency Broadband Benefit, that supports smartphone ownership and reduce broadband costs for low-income individuals.

Manufacturers should take the following actions:

- Consider the use of telehealth in clinical trial protocols to decrease in-person visit burden to include a more diverse patient population in clinical trials, including adequate number of patients with ethnic and racial backgrounds.

Payers should take the following actions:

- Ensure adequate payment for telehealth, including additional payment beyond synchronous and asynchronous telehealth visits to support digital navigators to screen for digital health readiness, train individuals and caregivers with low digital health literacy, and provide technical support.⁸

Clinical specialty societies should take the following actions:

- Create a separate certification that recognizes multidisciplinary ALS clinics that provide telehealth that meets acceptable standards.

Payers

Recommendation 1

Should AMX0035 be approved by the FDA, payers should use the FDA label as a guide to coverage policy and should engage clinical experts and diverse patient representatives in considering how to address coverage issues for which there is limited or no evidence at the current time. Coverage policies for oral edaravone should be developed through the same mechanism and reflect learnings from current coverage for IV edaravone.

Given the considerable uncertainty that remains about AMX0035 and oral edaravone, it is reasonable for payers to use prior authorization as a component of coverage, especially since the incremental cost effectiveness of oral edaravone and AMX0035 (if priced similarly to edaravone) far exceed typical cost-effectiveness thresholds. Prior authorization criteria for both drugs should be based on clinical evidence and input from clinical experts and patient groups. The process for authorization should also be clear, accessible, efficient, and timely for providers. Perspectives on specific elements of cost sharing and coverage criteria within insurance coverage policy are discussed below. Relevant [Fair Access Design Criteria](#) set out in ICER's previous work are included.

Recommendation 2

Given that ALS is a relentlessly progressive and fatal disease, payers should initiate the procedures needed to create formal coverage policies for new ALS treatments well in advance of likely FDA approval dates to minimize the use of “new-to-market blocks.”

In recent years payers have increased their use of “new-to-market-block” policies for up to six months after FDA approval of a new drug, ostensibly to provide additional time to review the evidence, negotiate pricing and payment terms, and ensure that coverage criteria and mechanisms for patient access are fully aligned.⁹ However, given that ALS progresses so rapidly, even waiting just a few months can lead to significant functional loss that could potentially be slowed by starting new medications to slow disease progression. Payers should consider scheduling their internal coverage criteria development in advance of FDA approval to formulate coverage policies that are operationally ready as soon as possible after market entry.

Recommendation 3

Payers should consider a benefit structure for ALS that covers necessary ancillary home health services, including assistive devices, home and vehicle modification, transportation, and caregiving.

As ALS progresses, patients develop mobility impairment and lose the ability to perform routine activity. Patients, caregivers, and clinical experts uniformly stressed the need for wraparound care at home in addition to high-quality medical therapy, but also noted that these services are inadequately covered by payers and result in high out-of-pocket costs. Payer representatives expressed that coverage is highly variable in the commercial insurance market, and if covered, are typically provided as a medical benefit in the form of a stipend to finance allowed categories of expenditures. The Department of Veterans Affairs was cited as a best practice for coverage benefits for ancillary care services.

Coverage Criteria: General

ICER has previously described general criteria for fair coverage policies that should be considered as cornerstones of any drug coverage policy:

<https://icer.org/wp-content/uploads/2020/11/Cornerstones-of-Fair-Drug-Coverage--September-28-2020.pdf>

Drug-Specific Considerations

The large number of patients with varying severity of ALS, combined with the high annual prices for newer treatments, 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.¹⁰ 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 AMX0035 and oral edaravone.

Coverage Criteria for AMX0035 – Assuming FDA Approval

- **Diagnosis:** There is tension between clinical experts and the diagnostic criteria used for clinical trial eligibility to identify a set of patients for whom the drug will have benefit. Clinical experts viewed the pivotal trial eligibility requirement of having a definite diagnosis of ALS per the El Escorial Criteria as being too restrictive, advising that these criteria were

only chosen to enrich the recruitment of patients in the trial to identify benefit in a very short timeframe. Clinical experts do not use the El Escorial Criteria to diagnose patients with ALS in practice and did not view any differences in the pathophysiology such that patients with ALS not meeting these diagnostic criteria would respond differently to AMX0035. There is also concern that the El Escorial Criteria do not sufficiently predict prognosis and can be misinterpreted as implying diagnostic uncertainty when there is none.¹¹ If the FDA approves AMX0035 for all patients with ALS but payers only cover the drug based on the trial criteria, then many patients who almost certainly have ALS will be excluded. Instead, it would be reasonable to consider coverage for all patients with ALS per the determination of a board-certified neurologist.

- **Age:** This treatment will likely be covered for adult patients, in line with clinical trial eligibility criteria.
- **Clinical eligibility for symptom onset and lung function:** Clinical experts advised that the pivotal trial eligibility criteria of symptom onset of 18 months or less and a slow vital capacity of greater than 60% were chosen to enroll a trial population that was not at risk for imminent death in order to detect a benefit in slowing functional decline over a very short timeframe, and these criteria do not represent clinically meaningful subpopulations in which coverage should be limited.
- **Exclusion criterion of tracheostomy:** Similarly, clinical experts advised that a tracheostomy does not correlate with symptom severity and should not be considered as a valid exclusion criterion for insurance coverage.
- **Duration of coverage and renewal criteria:** The ability to perform routine activities or other measure of function ability should not be used as a threshold for approving continuation of treatment, since the purpose of treatment is to slow functional decline. If renewal criteria are to be used in coverage decisions, clinical experts felt that it would be sufficient to require attestation by the doctor that the patient is receiving some benefit.
- **Provider restrictions:** Clinical experts agreed that it is reasonable to restrict prescribing to neurologists. Some payers may wish to consider restricting prescriptions to neurologists at designated ALS centers of excellence but this is likely to provide too narrow a network to adequately serve patients' needs.
- **Step therapy:** Clinical experts confirmed that there is no clinical rationale to justify requiring step therapy through riluzole and/or edaravone before gaining coverage for AMX0035. Mechanisms of action are complementary, side effects are very limited, and the clinical trial permitted background therapy of other FDA-approved therapies (riluzole and edaravone). Given the rapidly progressive and terminal nature of the disease, clinical

experts felt strongly that combining ALS medications that target different potential mechanisms of action is the best way to slow loss of motor neurons.

Coverage Criteria for Oral Edaravone

- **Age:** This treatment will likely be covered for all adult patients, in line with the FDA label.
- **Clinical eligibility:** Although approved by the FDA for all patients with ALS, it would be reasonable for payers to limit coverage to the narrow Study 19 population criteria given that clinical trials in broader populations did not confirm clinical benefit. The Study 19 criteria included independent living status, progression of the disease of greater than 1 but less than 4 points on the ALSFRS-R scale during the 12 weeks preceding treatment, a score of 2 or more on each non-respiratory item of the ALSFRS-R scale, a score of 4 on the three respiratory items of the ALSFRS-R, a forced vital capacity of 80% or greater, symptom onset of 2 years or less, and a definite or probable diagnosis of ALS per the El Escorial Criteria. However, as noted in the discussion on AMX0035, clinical experts advised that the El Escorial Criteria are not used in clinical practice and are too narrow given that “misdiagnosis” of ALS is extremely uncommon.
- **Exclusion criteria of impaired renal function:** It is reasonable to include the exclusion criterion of renal dysfunction as defined according to the Study 19 trial, which is defined as a creatinine clearance of 50 mL/minute or below within 28 days of treatment.
- **Dose:** Although payers may include in coverage criteria the dosing as per the FDA label, clinical experts and payers advised that overuse of edaravone is not a problem, and that some flexibility in dosing the oral version may be of benefit to patients and families under the supervision of a neurologist.
- **Duration of coverage and renewal criteria:** The ability to perform routine activities or other measure of function ability should not be used as threshold for approving continuation of treatment, since the purpose of treatment is to slow functional decline. If renewal criteria are to be used in coverage decisions, clinical experts felt that it would be sufficient to require attestation of patient benefit by the treating neurologist for continuation of therapy.
- **Provider restrictions:** Clinical experts agreed that it is reasonable to restrict prescribing to neurologists. Some payers may wish to consider restricting prescriptions to neurologists at designated ALS centers of excellence but this is likely to provide too narrow a network to adequately serve patients’ needs.

- **Step therapy:** Clinical experts confirmed that there is no clinical rationale to justify requiring step therapy through riluzole and/or AMX0035 before gaining coverage for oral edaravone. Mechanisms of action are complementary, side effects are very limited, and the clinical trial permitted background therapy of other FDA-approved therapies (riluzole and edaravone). Given the rapidly progressive and terminal nature of the disease, clinical experts felt strongly that combining ALS medications that target different potential mechanisms of action is the best way to slow loss of motor neurons. In addition, payers should not create any barriers to switching from IV to oral edaravone given the notable benefit in ease of use of the oral version.

Manufacturers

Recommendation 1

Manufacturers should seek to set prices of new medications that will foster affordability and access for all patients by aligning prices with the patient-centered therapeutic value of their treatments, and not based on the price of existing ALS medications. This is especially important for ALS since new drugs are anticipated to be used in combination with other very expensive drugs, creating the highest risk for financial toxicity due to health care costs.

Drug prices that are set well beyond the cost-effective range cause not only financial toxicity for patients and families using the treatments, 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. Using the previous price of intravenous edaravone is not an appropriate justification for every new entrant for treatment. In general, more effective drugs should command greater price, and less effective drugs should be priced lower, rather than pegging the price of new drugs to the price of existing drugs on the market regardless of its value and innovation.

Recommendation 2

Manufacturers should consider moderating launch pricing in the context of significant uncertainty that will be addressed by clinical trials that are ongoing. One specific approach to consider is to set the launch price at a far lower price close to the cost of production until the benefits of treatment can be adequately evaluated.

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 clinical trial evidence on the efficacy 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 demonstrated benefit.

Regulators

Recommendation 1

For conditions that are rapidly progressive and fatal, considering FDA approval of drugs on the basis of a single trial that shows benefit in clinically meaningful patient-centered outcomes is not unreasonable. However, there are known risks to approving drugs on the basis of such limited evidence, and if the FDA wishes to follow this course with AMX0035 and other drugs in similar circumstances, it should be more formal in creating a specific, well-defined pathway for conditional approval.

The Accelerated Approval pathway allows the FDA to grant approval for drugs that treat serious conditions with unmet need on the basis of promising trials using surrogate biomarkers that are reasonably likely to predict clinical benefit. Following accelerated approval, manufacturers are supposed to complete confirmatory trials to establish clinical benefit. But where does this leave drugs for serious conditions with tremendous unmet need that are supported by a single small clinical trial that shows clinical benefit, a low signal for serious harms, but does not show a response in a surrogate biomarker? Although uncertainty of benefit exists, there is currently no formalized process for the FDA to approve promising drugs which could improve meaningful patient-centered outcomes, like function and survival, in the absence of improving surrogate biomarkers, as is the case of AMX0035 for the treatment of ALS. The FDA should consider creating a specific, well-defined pathway for conditional approval to recognize the urgent unmet need for conditions like ALS that are rapidly progressive and fatal that is structured in a way to avoid the known pitfalls of the Accelerated Approval pathway. For example, such a new pathway could require timely completion of a confirmatory trial, and that the conditional approval should be removed if the confirmatory trial does not confirm benefit.

Clinicians and Clinical Societies

Recommendation 1

Clinical Societies should update guidelines for ALS regarding best practices for diagnosis and to reflect new treatment options in a way that is easy to interpret and use by clinicians, patients, and payers.

There is tension between expert clinicians and the diagnostic criteria used for clinical trial eligibility to identify a set of patients for whom the drug will have benefit. Clinical experts viewed the trial criterion of having a definite diagnosis of ALS per the El Escorial Criteria as being too restrictive and was only chosen to enrich recruitment of patients in the trial to identify benefit in a short timeframe. Clinical experts do not use the El Escorial Criteria to diagnose patients with ALS in practice and did not view any differences in the pathophysiology such that patients with ALS not meeting this diagnostic criterion would respond differently to AMX0035. There is also concern that the El Escorial Criteria do not sufficiently predict prognosis and imply diagnostic uncertainty for many ALS patients classified as not having definite ALS, when there is typically none.¹¹ However, the most up-to-date practice guidelines for ALS issued by the American Association of Neurology (AAN) does not identify evidenced-based best practices for the diagnosis of ALS.

Intravenous edaravone was approved in 2017 but has not had considerable uptake among patients and clinicians given the risky and burdensome nature of the therapy, as well as restrictions in coverage by payers. The AAN reaffirmed its practice guidelines for ALS in 2020 but did not discuss the use of intravenous edaravone for the treatment of ALS.

Payers base their coverage decisions and integration of utilization tools to a great extent on clinical guidelines. Therefore, it is important for the AAN to update their practice guidelines for ALS to include best practices for diagnosis to help resolve the tension between clinical trial eligibility criteria and standard of care among clinical experts, and to include recommendations for new drug therapies. Unlike before, there is greater urgency for updated practice guidelines now that there are two potentially novel medications for the treatment of ALS.

Patient Organizations

Recommendation 1

Patient organizations supporting ALS patients and their caregivers should continue to invest in the development and evaluation of new therapies through agreements including a repayment clause to recoup their initial investment which can then be reinvested in additional research to perpetuate the innovation cycle.

Supported by fundraising generated by the ALS Ice Bucket Challenge, The ALS Association committed \$750,000 to the manufacturer of AMX0035 and \$1.4 million to the consortium of ALS clinics who conducted the clinical trial. Through a standard repayment clause, the ALS Association could potentially recoup 150% of their investment, which they are planning on reinvesting in additional research. Patient organizations should continue this model of funding innovation which could help spur the development of new treatments for patients with tremendous unmet need.

Recommendation 2

Patient organizations should advocate for the best interest of their patients with ALS and their caregivers by including a focus on affordable drug prices in addition to access to care and new research. Patient groups have a powerful voice and should apply it to create significant pressure for fair pricing across all sectors of the health system.

Drug prices that are set well beyond the cost-effective range cause financial toxicity for patients and caregivers using the treatments. This is especially important for ALS since new drugs are anticipated to be used in combination with other very expensive drugs, creating the highest risk for financial toxicity due to health care costs. Patient organizations have the opportunity to be vocal advocates for affordable drug pricing in line with the patient-centered therapeutic value of new treatments. Patient groups should additionally follow-up such statements with organized campaigns to advocate for fair pricing, for example, by encouraging patients and families to write to Congress or launch public relation campaigns with such messaging.

Researchers

Recommendation 1

Biomarker development will be critically important for the advancement of research in clinical care for ALS, but further work is also necessary to substantiate the use of existing functional measures since biomarkers will ultimately be validated against them.

Policy roundtable participants expressed that although the ALS functional rating scale is an imperfect outcome measure, it is likely to be used in future clinical trials since it has been

successfully used to secure FDA approval of several ALS drugs. Policy roundtable experts also emphasized the critical need for surrogate biomarkers to track progression of disease and response to therapy. Since biomarkers will ultimately need to be validated against existing functional measures before their use in practice and clinical trials, researchers should optimize the use and measurement of the ALS functional rating scale, including determining the minimal clinically important difference, which is currently unknown.

Recommendation 2

Future research should consider comparing sodium phenylbutyrate–taurursodiol versus pharmaceutical-grade taurursodiol monotherapy

It is unknown whether the combination of sodium phenylbutyrate and taurursodiol (TURSO) in AMX0035 is superior to TURSO alone. This is important because TURSO is the cheaper of the two components, currently available as a nutritional supplement, and is already used by some ALS patients. A pilot randomized controlled trial of TURSO in 34 ALS patients found the TURSO arm had less functional decline at 54 weeks.¹² A confirmatory multicenter RCT of TURSO versus placebo in Italy is underway and estimated to complete in 2023.¹³ And if effective, future head-to-head trials of pharmaceutical-grade TURSO monotherapy versus AMX0035 should be considered.

Recommendation 3

High prices are not the only way to incentivize new innovative treatments for patients with ALS. Future research should be funded amply by the federal government to help accelerate the development of new treatments for this population with tremendous unmet need.

References

1. Boylan K, Levine T, Lomen-Hoerth C, et al. Prospective study of cost of care at multidisciplinary ALS centers adhering to American Academy of Neurology (AAN) ALS practice parameters. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*. 2016;17(1-2):119-127.
2. I AM ALS. ALS Clinic Map. <https://iamals.org/get-help/find-your-als-clinic/>. Published 2022. Accessed.
3. ALS Association. ALS Certified Centers & Clinics. https://www.als.org/local-support/certified-centers-clinics?f%5B0%5D=certified_centers_clinics%3A101&search_api_fulltext=&f%5B0%5D=certified_centers_clinics%3A101&page=3. Published 2022. Accessed.
4. Haulman A, Geronimo A, Chahwala A, Simmons Z. The use of telehealth to enhance care in ALS and other neuromuscular disorders. *Muscle & nerve*. 2020;61(6):682-691.
5. Paganoni S, Van De Rijn M, Drake K, et al. Adjusted cost analysis of video televisits for the care of people with amyotrophic lateral sclerosis. *Muscle & Nerve*. 2019;60(2):147-154.
6. Medicare payment policies during COVID-19: Telehealth policy changes. <https://telehealth.hhs.gov/providers/billing-and-reimbursement/medicare-payment-policies-during-covid-19/>. Published 2022. Updated March 25, 2022. Accessed.
7. Matthews K. VHA DIRECTIVE 1101.07: AMYOTROPHIC LATERAL SCLEROSIS SYSTEM OF CARE. In: Administration VH, ed2021.
8. Davis T, Shore P, Lu M. Peer technical consultant: veteran-centric technical support model for VA home-based telehealth programs. *Federal Practitioner*. 2016;33(3):31.
9. *Trends in Drug Benefit Report*. Pharmaceutical Strategies Group, LLC;2022.
10. 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.
11. Traynor BJ, Codd MB, Corr B, Forde C, Frost E, Hardiman OM. Clinical features of amyotrophic lateral sclerosis according to the El Escorial and Airlie House diagnostic criteria: A population-based study. *Archives of neurology*. 2000;57(8):1171-1176.
12. Elia AE, Lalli S, Monsurrò MR, et al. Tauroursodeoxycholic acid in the treatment of patients with amyotrophic lateral sclerosis. *Eur J Neurol*. 2016;23(1):45-52.
13. ClinicalTrials.gov. Safety and Efficacy of TUDCA as add-on Treatment in Patients Affected by ALS (TUDCA-ALS). <https://clinicaltrials.gov/ct2/show/NCT03800524>. Published 2022. Accessed.

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the August 19, 2022 Public meeting of Midwest CEPAC.

Appendix Table 1. ICER Staff and Consultants and COI Disclosures

ICER Staff and Consultants	
Josh Carlson, PhD, MPH,* Professor, University of Washington	Steven D. Pearson, MD, MSc,* President, ICER
Maggie Houle, BS,* Strategic Partnerships Associate, ICER	Marina Richardson, MSc,* Health Economist, ICER
Anil N. Makam, MD, MAS,* Assistant Professor of Medicine, University of California, San Francisco	David Rind, MD, MSc,* Chief Medical Officer, ICER
Avery McKenna, BS,* Senior Research Assistant, Evidence Synthesis, ICER	Liis Shea, MA,* Program Director, ICER
Dmitriy Nikitin, MSPH,* Research Lead Evidence Synthesis, ICER	Kangho Suh, PharmD, PhD,* Assistant Professor, School of Pharmacy, University of Pittsburgh

*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.

Appendix Table 2. Midwest CEPAC Panel Member Participants and COI Disclosures

Participating Members of CEPAC	
Eric Armbrrecht, PhD,* Associate Professor, Saint Louis University Center for Health Outcomes Research, School of Medicine and College for Public Health and Social Justice	Angela Fleming Brown, MPH,* CEO, St. Louis Regional Health Commission
Alan Balch, PhD,* CEO, Patient Advocate Foundation	Heather Guidone, BCPA,* Program Director, Center for Endometriosis Care
Bijan Borah, PhD,* Professor of Health Services Research, Mayo Clinic College of Medicine and Science	Jill Johnson, PharmD,* Professor, Department of Pharmacy Practice, University of Arkansas for Medical Sciences College of Pharmacy
Aaron Carroll, MD, MS,* Professor of Pediatrics, Chief Health Officer, Indiana University School of Medicine	Bradley Martin, PharmD, PhD,* Professor, University of Arkansas for Medical Sciences
Donald Casey, MD, MPH, MBA,* Associate Professor of Internal Medicine, Rush Medical College	Timothy McBride, PhD,* Professor, Washington University in St. Louis
Gregory Curfman, MD,* Deputy Editor, JAMA	Reem A. Mustafa, MD, PhD, MPH* (Chair), Professor of Medicine, University of Kansas Health System
Sneha Dave, BA,* Executive Director, Generation Patient	Timothy Wilt, MD, MPH,* Professor of Medicine and Public Health, University of Minnesota
Stacie B. Dusetzina, PhD,* Associate Professor, Vanderbilt University School of Medicine	

*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.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Participant	Conflict of Interest
Stephen Apple, MD , Executive Medical Director, Medical Affairs, Mitsubishi Tanabe Pharma America, Inc.	Dr. Apple is a full-time employee of Mitsubishi Tanabe Pharma America, Inc.
Richard Bedlack, MD, PhD , Professor of Neurology, Director of ALS Clinic, Duke University School of Medicine	Dr. Bedlack has received consulting support in excess of \$5,000 and research support from the ALS Association and Amylyx.
Mary Catherine Collet, MS , ALS Patient Advocate	No conflicts of interest to disclose.
Aaron Lewis, MD , Neurologist, Neuromuscular Medical Director, ALS Multidisciplinary Clinic, Kaiser Permanente	Dr. Lewis has received a grant from the ALS Association in support of patient care.
Michelle Rogers, PharmD, BCPS , Director of Clinical Pharmacy, IPD Analytics	Dr. Rogers is a full-time employee of IPD Analytics.
Joel Shamaskin, MD , Person with ALS; Professor Emeritus of Medicine (Retired), University of Rochester School of Medicine and Dentistry	No relevant conflicts of interest to disclose, defined as more than \$10,000 in health care company stock or more than \$5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers. Dr. Shamaskin serves on the ALS Association research committee.
Emily Tsiao, PharmD , Clinical Pharmacist, Utilization Management, Premera Blue Cross	Dr. Tsiao is a full-time employee of Premera Blue Cross.