February 24, 2022

Public Comments
Institute for Clinical and Economic Review
14 Beacon Street, Suite 800
Boston, MA 02108

Re: **AMX0035 and Oral Edaravone for Amyotrophic Lateral Sclerosis (ALS) Draft Background and Scope**

Dear ICER Team,

On behalf of people living with ALS, their families and the ALS Association we appreciate the opportunity to comment on your Draft Background and Scope Document (Draft Scoping Document) for a cost-effectiveness evaluation of AMX0035 and oral edaravone.

We have several requests for revisions to the Draft Scoping Document.

1. **We ask that your primary analysis include the value of all ALS patient care, both medical and supportive, including the value of unpaid caregiving.**
2. **We ask that the Scoping Document define how you will measure quality of life and assign patients to health states, as well as document that the measure and the assignments align with ALS patients' self-assignments of their quality of life and health.**
3. **We also request that you make some specific, focused changes to the Scoping Document**.

We discuss each request in greater detail below.

Background

The ALS Association works with the ALS community members, stakeholders, and government policymakers to ensure pricing and coverage decisions reflect the urgent and unmet need for therapies for all people living with ALS. We reach this end by adhering to a core set of value principles assuring:

- All people with ALS are provided immediate, full coverage and affordable access to new therapies;
- Payors use methodologies that value the lives of all people with ALS;
- Health care utilization techniques and/or other administrative barriers that delay or decrease access to drugs for people with ALS and other neurodegenerative diseases are prohibited; and
- The use of arbitrary, discriminatory value assessments that limit access to ALS drugs, such as the use of metrics like Quality Adjusted Life Year (QALY) or the Equal Value Life Years Gained (evLYG) are prohibited.

As you state, ALS is a rare, progressive, debilitating, heterogenous, and deadly disease. Before the patient dies, he or she will lose most muscle function and will be dependent on people and technology for every aspect of daily life – a life that many ALS patients continue to have the cognitive ability to enjoy and value. The person with ALS also may experience various medical complications resulting from their paralysis and immobility, such as pressure ulcers or pneumonia, that require acute medical treatment.

Loss of muscle function and dependency are expensive. Depending on disease subtype and stage, as well as the patient's directives, home, and family support system, the patient will require extensive supportive care, including: paid and unpaid caregivers, mobility assistance, transportation assistance, home modification, mechanical ventilation, enteral nutrition, adaptive equipment and supplies, long-term care facility care, and hospice care.

At an advanced disease stage, patients require care twenty-four hours a day, seven days a week, sometimes by two caregivers. According to Genworth, a long-term care insurer, the 2021 medium cost for a home health aide was $27 per hour or $19,710 per month of 24-hour care.[1] While data show the total cost of caregivers and supportive care for those with ALS can easily exceed $10,000 per month, current documentation of this data is insufficient in capturing the true cost challenges associated with supportive care.[2,3]

These supportive costs are the direct result of ALS disease. Yet, you propose that your cost-effectiveness analysis will primarily focus on "direct medical care costs" and, data permitting, will consider "productivity impacts and other indirect costs" in a separate, secondary analysis (page 6 of the Draft Scoping Document).

Requests

1. We ask that your primary analysis include the value of all ALS patient care, both medical and supportive, including the value of unpaid caregiving. We firmly believe that all caregiving has value, including care provided by family members – care that often removes family members from paid employment.

We strongly object to you dividing the cost of care for ALS patients between medical and non-medical and including only medical care costs in your primary cost-effectiveness analysis. We also object to the apparent assertion that only medical costs are "direct" costs of the disease. We note that you do not define what constitutes a "medical care cost" and assume that your definition does not include the full array of medical and supportive care. For example, we suspect you do not intend to include all the costs of enteral feeding within your primary analysis. Enteral feeding costs include:

- Insertion of the gastrostomy tube;
- Gastrostomy tube supplies;
- Medical and nutritional supervision;
- Enteral nutrition; and
- Enteral feeding and non-medical supervision, often by family members.

While the last bullet is generally considered "non-medical," it is costly and absolutely essential. None of the other health care services or supplies listed above are effective if the patient is not actually fed. Similar examples can be provided for other medical and supportive care including but not limited to speech, swallowing and mobility challenges. People living with ALS also require paid and unpaid support for activities for daily living including personal hygiene, dressing, toileting, transferring or ambulating, and eating.

Relegating a portion of the costs of caring for an ALS patient to secondary status, and even possibly ignoring the costs due to lack of data, is improper from both a societal and a health insurer (payer) perspective. The above supportive care costs are real and direct costs of ALS. With the exception of unpaid caregiving, these costs are often paid for by health insurance plans, particularly Medicare, Medicaid, and Veterans Affairs (VA) plans – the payers for nearly all ALS patients who have progressed to the stage where they need supportive care. Medicaid

and VA plans pay family members to provide supportive care, thereby converting them from unpaid to paid status.

Furthermore, a lack of quality supportive care very often moves care into the more expensive acute care and medical facility settings. The patient who is not well cared for at home by unpaid caregivers is more likely to end up in a hospital with pressure ulcers or pneumonia. A patient with ALS who does not have a supportive family will ultimately need to have care in a long-term acute care facility.

A successful ALS treatment will extend lives, improve quality of lives, and reduce acute and supportive care costs. All cost savings should be included in a cost-benefit analysis of the treatment – irrespective of whether the costs are arbitrarily classified as medical or non-medical.

2. We ask that the Scoping Document define how you will measure quality of life and assign patients to health states, as well as document that the measure and the assignments align with ALS patients' self-assignments of their quality of life and health.

While we recognize that quality adjusted life years (QALYs) as the primary outcome and equal value life years gained (evLYGs) are integral to your cost-effectiveness analysis framework, we wish to record our objection to the use of QALYs as the primary outcome and evLYGs as an alternative outcome for the cost-effectiveness analysis. Neither measure captures the value of life from the perspective of a patient disabled by ALS. Of particular importance to people living with ALS is the ability to maintain level of function for as long as possible and to slow the progression of the disease.

QALYs are inherently discriminatory against people with disabilities, as their lives are assigned a lower quality score and are therefore implicitly deemed less worthy of being extended. We strongly endorse the positions and findings within the National Council on Disability's 2019 Report to the President, "Quality-Adjusted Life Years and the Devaluation of Life with Disability".[4]

Furthermore, while we appreciate that you have tried to address objections to QALYs by introducing evLYGs, evLYGs, by virtue of being quality-neutral, do not address the quality of life that is highly valued by ALS patients. If you use QALYs, a major gap in the Scope of Comparative Value Analyses section of the Draft Scoping Document (page 6) is that you do not define how you will measure quality of life and assign patients to declining "health states".

We suspect you will rely, at least in part, on mapping the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) measurements to quality of life. In our experience, however, ALSFRS-R's 48-point scale, which was developed as a tool to assess functional status and the disease progression in ALS patients, is an ineffective method for describing ALS quality of life. For example, while patients highly value their ability to communicate with loved ones and caregivers, including with assistive technology, communication is dwarfed by physical function measures within ALSFRS-R and does not consider assistive technologies. As noted by Goldstein and colleagues twenty years ago, "*Quality of life (QOL) in patients with ALS does not correlate with physical function. Unfortunately, many quality of life (QOL) instruments which have been used to assess individuals with ALS are heavily weighted toward strength and physical function, and therefore fail to capture other important non-health related factors*."[5]

We are also concerned with the possibility of people without ALS assessing the quality of ALS patients' lives. In our experience, the utility assigned to an ALS patient's life is much lower when the assessment is made by people without ALS.

3. Finally, we also request that you make the following specific, focused changes to the Scoping Document.

- Strengthen the first paragraph (page 1) to include a more comprehensive list of the supportive care often required by ALS patients.
- Restate the ALS gender ratio (page 1, paragraph 3). The assertion that males are twice as likely to develop sporadic ALS as females is inaccurate. The average gender difference is a factor of about 1.3 – higher at younger ages and lower at older ages.[6]
- Call out the increased relative risk of ALS incidence among veterans and consider veterans as a potential subgroup.[7]

*****

We look forward to reviewing the Revised Scoping Document.

Sincerely,

Neil Thakur, Ph.D. | Chief Mission Officer
The ALS Association

---

[1] https://www.genworth.com/aging-and-you/finances/cost-of-care.html
[2]Nonoyama, et al, "Healthcare utilisation and costs of home mechanical ventilation", Thorax, 2018, doi:10.1136/thoraxjnl-2017-211138.
[3] Schönfelder, et al, "Costs of illness in amyotrophic lateral sclerosis (ALS): a cross-sectional survey in Germany", Orphanet Journal of Rare Diseases, 2020, doi:10.1186/s13023-020-01413-9
[4] https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf
[5] Goldstein, Atkins, and Leigh, "Correlates of Quality of Life in people with motor neuron disease (MND)", Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders, doi: 10.1080/146608202760834120.
[6] McCombe and Henderson, "Effects of Gender in Amyotrophic Lateral Sclerosis", Gender Medicine, 2010, doi:10.1016/j.genm.2010.11.010.
[7] McKay, Smith, Smertinaite, et al, "Military service and related risk factors for amyotrophic lateral sclerosis", Acta Neurologica Scandinavica, 2020, doi: 10.1111/ane.13345.