Hon. Josie Osborne
Minister of Health
Government of British Columbia

A BDSRA Foundation Designation
Center of Excellence

July 16, 2025

Re: B.C. Health Ministry's Decision to Terminate Coverage of Cerliponase Alfa in CLN2 Disease

Dear Hon. Josie Osborne,

We write to you as clinicians and researchers from the U.S.-based Batten Disease Centers of Excellence Program and U.S. Batten Disease Clinical Research Consortium. Collectively, we have cared for the majority of U.S. patients with CLN2 disease treated with enzyme replacement therapy (ERT) cerliponase alfa (Brineura).

Our international colleagues and collaborators Angela Schulz MD and Miriam Nickel MD at the NCL Specialty Clinic, University Children's Hospital Hamburg-Eppendorf, Germany, were instrumental in developing the clinical outcome measures used to track disease progression in CLN2 disease. Together, our organizations played critical roles in the processes and the pivotal trial that led to regulatory approval of this therapy.

Drawing from our collective and unparalleled expertise in CLN2 disease, ***we strongly oppose the decision to withdraw funding for life-sustaining ERT from Charleigh Pollock and call for a review of the current discontinuation criteria.***

Prior to 2017, the late-infantile form of CLN2 disease was universally fatal, with no disease-modifying treatment available. The introduction of intracerebroventricular ERT has fundamentally altered the disease trajectory. ERT has demonstrably prolonged survival, slowed progression, improved seizure control, and enhanced quality of life.[1] In a multi-year longitudinal study directly comparing ERT-treated children to matched natural history controls, 29% of the natural history (untreated) cohort died compared to ***none*** of the ERT-treated cohort.[2] In our ongoing discussions and collaboration with our colleagues at University Children's Hospital Hamburg-Eppendorf, it is clear that our growing clinical understanding and real-world experience with treated CLN2 patients in the U.S. is closely aligned.

We are concerned by the clinical and scientific justification employed by the B.C. Ministry in their decision to terminate treatment coverage,[3] for the following reasons:

(1) The clinical trial endpoint of a combined Motor/Language (M/L) score of zero or a decrease of 2 or more points was used narrowly to analyze treatment efficacy in a research setting.[4] It was never intended to be used an endpoint for decision-making regarding treatment discontinuation.[5, 6] **It does not account for complete cognitive, feeding, or breathing functions. It does not measure therapeutic response in critical domains such as seizure burden, hospitalization frequency, comfort, and family-reported quality of life.**

(2) ***Equating an M/L score of zero with end-of-life is inaccurate.*** The M/L score was developed well before the advent of ERT and before the emergence of new, more stable

phenotypes now observed in treated patients. Based upon our clinical experience, treated children with CLN2 disease with severely limited mobility and language may continue to meaningfully interact with their environment and communicate nonverbally for years without the need for nutritional or respiratory support. These treated children are far from imminent death, even if their M/L score may be zero. In contrast, cessation of cerliponase alfa is likely to hasten death as seen in untreated historical controls.[1]

(3) It is therefore essential to look beyond narrowly defined motor and language functions to assess efficacy. For instance, without ERT, seizures in CLN2 disease are often difficult to control despite multiple antiseizure medications. Observational studies—as well as our day-to-day clinical experience—demonstrate that ERT can significantly reduce seizure frequency and severity in CLN2 disease.[1] **These are not minor benefits, but critical outcomes that directly impact hospitalization risk, need for ICU-level care, and quality of life.**

(4) Rather than over-indexing on the M/L score, we strongly agree with existing guidance from the Canadian Agency for Drugs and Technologies in Health (CADTH) that states that **"decisions to stop treatment would be made in the context of the child's symptoms, treatment goals of the family, and the physician's professional judgment."**[5] This point was emphasized in your recently published evidence review, recommending use of a shared decision-making model specific for each patient.[3, 6]

The question of when to discontinue life-sustaining therapy is a profoundly difficult one. We urge an evidence-based approach, acknowledging the lack of data on the use of M/L scores to discontinue cerliponase alfa,[3] as well as the existing data on the long-term benefit of cerliponase alfa on seizures, survival, and quality of life.[1] The clinical judgment of the treating physician is essential, as previously voiced by clinical experts and caregivers.[5] Integrating all of this requires patient-centered dialogue, grounded in up-to-date science and medical practice.

We welcome the opportunity to discuss these concerns further with you.

Sincerely,

The Directors of the Batten Disease Clinical Centers of Excellence and Affiliates

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