Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

Proposed Project Scope

Cerliponase alfa (Brineura) for patients with neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency or Neuronal Ceroid Lipofuscinosis type 2

April 2025

Background

This review will focus on identifying and appraising any new clinical evidence that has emerged since the 2019 CDA-AMC review of cerliponase alfa (Brineura) for the treatment of pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency.

Full-text articles will be appraised using standardized, internationally recognized tools. The final report will summarize the evidence, study characteristics, and findings, with a brief statement on potential implications for decision- or policy-making. This review will not provide a Reimbursement Recommendation.

Table 1: Policy Question

Item	Policy Question
1	What new evidence exists to inform the discontinuation criteria for cerliponase alfa (Brineura) since the 2019 CDA-AMC review?

Project Description

Table 2: Project Scope

Criteria	Description
Population	Pediatric patients with CLN2 disease Subgroups of interest: • Disease severity at start of treatment (e.g., mild, moderate, severe) • Time of onset (e.g., later infantile versus juvenile) • Age group (e.g., younger versus older)
Intervention	Cerliponase alfa (Brineura)
Comparators	Best Supportive Care Placebo No Comparator
Outcomes	Efficacy outcomes: • Overall survival • Impact on symptoms, including neuropsychological (motor, cognitive, language), vision, seizures, and pain using validated scales • Health-related quality of life using validated scales • Caregiver burden using validated scales • MRI changes, if no other outcomes are identified Harms outcomes: SAEs, AEs, WDAEs, deaths due to AEs, and notable harms: administration-related (e.g., infection), cerebrospinal fluid pleocytosis, gastrointestinal (e.g., vomiting), fever, hypersensitivity
Study Design	This review will employ a hierarchical approach to evidence inclusion, prioritizing the most robust and current evidence. We will first seek recent, comprehensive,

	and high-quality Systematic Reviews (SRs), Meta-Analyses (MAs), or Network Meta-Analyses (NMAs). If we do not identify suitable SRs for the PICO question, or if supplementation is needed, we will include Randomized Controlled Trials (RCTs). If RCT evidence is insufficient to answer the PICO, we will consider non-randomized comparative intervention studies (e.g., cohort, case-control). Finally, we may include single-arm studies only if critical evidence gaps remain after considering comparative studies, particularly for assessing long-term benefits or harms. We will focus on the evidence-based guidelines for research question 2.

AE = adverse event; CLN2 = neuronal ceroid lipofuscinosis type 2; MA = meta-analyses; NMA = network meta-analyses; PICO = population, intervention, comparator, outcome; RCT = randomized controlled trials, SAE = serious adverse event; SR = systematic reviews, WDAE = withdrawal due to adverse event

* Note: A review is considered systematic if it includes the following elements: an objective and research question(s); indications that evidence was searched for in a systematic way (e.g., information on one or more of the following: names of databases, search platforms/engines, search date, keywords or search strategy); and inclusion and exclusion criteria. A guideline is considered evidence-based if a systematic search of the literature was undertaken and a guideline panel was involved in informing the recommendations.

Table 3: Research Questions

Item	Research Questions
1	What is the clinical effectiveness and safety of cerliponase alfa versus best supportive care, placebo or no comparator for pediatric patients with CLN2 disease?
2	What are the evidence-based recommendations regarding the use of cerliponase alfa for pediatric patients with CLN2 disease?

Status of Document

The proposed project scope document is being posted for input.