Australian Government
Department of Health and Aged Care

Life Saving Drugs Program (LSDP) 24-month Review Summary: Cerliponase alfa (Brineura®)

Introduction

Cerliponase alfa is an enzyme replacement therapy used for the treatment of Late Infantile Onset Batten Disease (CLN2 disease). It was listed on the LSDP on 1 May 2019.

Purpose of the 24-month review

Following a decision of Government in 2018, all new medicines made available on the LSDP are subject to reviews of usage and financial costs 24 months after listing.

The purpose of these 24-month reviews is to better understand the real-world use of a medicine by comparing the actual performance and use of the medicine to the recommendations and expectations at the time of listing. The reviews assess the clinical benefits achieved through the use of LSDP medicines, ensure the ongoing viability of the program, and ensure testing and access requirements for each medicine remain appropriate. The LSDP Expert Panel (the Expert Panel) is responsible for commissioning the reviews and making recommendations to the Chief Medical Officer.

This review aimed to undertake an assessment after 24 months listing on the LSDP to ensure that the listing of cerliponase alfa for the treatment of CLN2 disease remains appropriate. This review was considered by the Expert Panel at its October 2021 meeting.

Terms of Reference

The review considered five Terms of Reference (ToRs).

ToR 1 – Clinical effectiveness and Safety

This ToR aimed to review the available evidence, including evidence collected through the LSDP and outcomes from studies that were still in progress at, or have been performed since, the time of inclusion of cerliponase alfa on the LSDP, to inform judgements regarding the comparative clinical effectiveness and safety of cerliponase alfa. The new evidence was presented in the context of previous evidence.

ToR 2 – Test Validity and Utility

This ToR aimed to review the evidence of the validity and utility of the test to identify patients with CLN2 disease who are candidates for treatment with cerliponase alfa.

ToR 3 – Utilisation and Consumer Impact

This ToR aimed to review the utilisation of cerliponase alfa on the LSDP the impact on consumers.

ToR 4 – Financial Impact

This ToR aimed to review the value for money of cerliponase alfa under the current funding arrangements, including a review of the financial outcomes and future implications of the current listing of cerliponase alfa on the LSDP.

Main issues for consideration

ToR 1 – Clinical Effectiveness and Safety

The review found that additional evidence published about cerliponase alfa since 2018 is consistent with the evidence presented in the initial Pharmaceutical Benefits Advisory Council (PBAC) submission. No new safety signals were detected.

The majority of studies reviewed report the CLN2 motor-language (ML) scale as their measure of efficacy. Patients treated with cerliponase alfa had a significantly longer time to decline in their ML score, and a significantly smaller change from baseline in CLN2 Clinical Rating Scale Scores.

Potential additional outcomes included vision loss, use of palliative care, seizures (both frequency and use of antiepileptic medication) and neurofilament light (NF-L) assessment. However, the review did not propose including these outcome measures, due to a lack of evidence and because the sponsor's original LSDP application not propose their inclusion.

Treatment persistence and adherence was good, with reported adherence of 74 to 99 percent.

Based on the literature, adverse events and serious adverse events were common, occurring in almost all patients. The most common adverse events included convulsions, pyrexia, vomiting, hypersensitivity, nasopharyngitis and rhinitis. However, no adverse events were reported by patients on the LSDP, which is inconsistent with the literature. No deaths during cerliponase alfa treatment have been reported to date.

When cerliponase alfa was originally considered for LSDP listing, the Expert Panel considered that some uncertainty remained around the magnitude of any survival benefit from treatment with cerliponase alfa, and that the extrapolated survival benefit presented in the application was likely to be overestimated. The review found that if the CLN2 ML score is a proxy for death, then cerliponase alfa has been shown to slow the decline in CLN2 ML scores, and therefore is likely to extend survival.

The Expert Panel ultimately concluded cerliponase alfa should remain on the LSDP as a treatment for CLN2 disease with no changes to eligibility criteria.

ToR 2 – Test Validity and Utility

The review found that no studies published since 2018 have investigated the validity or reliability of tests used to diagnose CLN2 disease; however, there were 15 supportive publications that were identified during the literature searches.

Diagnosis of CLN2 disease was via tripeptidyl peptidase 1 (TPP1) enzyme activity assessment, confirmed by genotyping. This was consistent with the current recommendations place for LSDP. One study reported that all patients with deficient TPP1 enzyme were subsequently confirmed as having pathogenic mutations in their TPP1 gene.

Based on expert consensus, diagnosis of CLN2 disease during infancy was considered critical to optimise patient outcomes. Early diagnosis facilitates early initiation of disease specific care and is critical for family planning.

The review concluded no change in disease prevalence had occurred since the initial submission, and no increase in diagnosis of CLN2 disease through increased/improved screening, or as a consequence of cerliponase alfa being listed on the LSDP. Analysis of the LSDP data showed that [redacted] patients were prescribed cerliponase alfa soon after it was added to the LSDP. A further [redacted] patients were prescribed cerliponase alfa in the following 12-month period. Notably there had been no new patients admitted into the program in the 18 months prior to the review.

No new treatments have become available for the treatment of CLN2 disease since 2019.

The review found that the existing criteria for access to cerliponase alfa on the LSDP appeared to be fit for purpose.

ToR 3 – Utilisation and Consumer Impact

All patients who were accessing cerliponase alfa on the LSDP to date demonstrated deficient concentrations of TPP1 enzyme, except one patient for whom the date of TPP1 test was noted without a result. However, only one third of patients strictly met all diagnosis requirements of eligibility, which included having diagnosis supported by genetic testing of CLN2 mutation within 8 weeks of commencing treatment.

All patients complied with the clinical requirements for cerliponase alfa eligibility on the LSDP in terms of lack of complications or sequelae of CLN2 disease, and none recorded an ML score of zero. The review was unable to confirm the eligibility of reapplications from available recorded information.

The number of patients diagnosed with CLN2 disease and accessing cerliponase alfa on the LSDP was consistent with the expected incidence rate for the disease in the first year of the program.

The PBAC submission estimated the prevalence of CLN2 disease in Australia to be [redacted] patients. With no new patients in 18 months, nor any reported deaths or recorded cessation of treatment in the patient cohort to date, the review concluded that uptake is likely to be lower than expected.

The review identified that the cost to families of accessing cerliponase alfa principally related to travelling out of area to a particular hospital, and the time commitment required. Other

costs were relatively minor. Consumers emphasised that costs were very small relative to the benefit they received from accessing treatment.

ML score, survival and quality of life were considered very important outcomes for patients and their carers. Families described the changes in their children's quality of life as 'life saving', over and above any survival gains, surpassing expectations in terms of ability to retain mobility, forms of communication, independence (chewing, swallowing, eating by mouth) and socialisation (playing games, having friends and meaningful interaction with them, and attending school).

ToR 4 – Financial impact

Aside from slightly higher than expected expenditure in the initial six months, total costs were lower than anticipated at the time of listing on the LSDP.

Total recorded costs were:

- $[redacted] (excluding GST) in FY2019 compared to $[redacted] in the Drug Details Schedule
- $[redacted] (excluding GST) in FY2020 compared to an estimated $[redacted] in the Drug Details Schedule, and
- $[redacted] (excluding GST) in FY2021 compared to an estimated $[redacted] in the Drug Details Schedule.

In FY2022, the Drug Details Schedule anticipates costs of $[redacted] (excluding GST). With no new patients accessing cerliponase alfa on the LSDP by September 2021, expenditure in FY2022 is likely to again be lower than projected.

Expenditure below projections for cerliponase alfa appeared due to lower than expected uptake of treatment among the estimated eligible population, and less than full dosing for some patients. The review found a discrepancy in data between recorded total costs compared with number of administered doses and the cost per dose.

Price benchmarking was undertaken to compare the costs per patient of cerliponase alfa to other LSDP listed drugs. The results indicate that cerliponase alfa is close to the average price of all LSDP-listed drugs.

While there was insufficient data to recalculate the incremental cost effectiveness ratio (ICER) for LSDP patients, observations made in this review indicated that patients accessing the LSDP may well have performed better than expected, which would reduce the ICER for patients accessing the LSDP compared to that previously estimated.

No wastage of cerliponase alfa was identified due to the capacity of administration vials and patient needs, with all patients on the LSDP over two years of age and requiring the use of vials in full.

Two features of the agreement with the sponsor limit the Commonwealth's financial risk in subsidising cerliponase alfa:

- [redacted]

- [redacted]

The Panel recommended there should be reassessment of pricing of cerliponase alfa with the goal of improving value for money when the current deed of agreement with the sponsor expires.

Expert Panel Recommendations

The Expert Panel made the following recommendations in relation to cerliponase alfa:

1. That cerliponase alfa should remain on the LSDP as a treatment for CLN2 disease with no changes to eligibility criteria.
2. That the mechanisms of data collection and its management be reviewed by the Department with the aim of improving efficiency, completeness and stakeholder satisfaction. All data collected should have a defined purpose to ensure measures collected produce benefits and contribute to understanding of condition and its treatment effects without adding unnecessary burden to patients/families and clinicians.
3. That, in consultation with treating clinicians, data collection should be expanded to include a measure of quality of life and health function, adverse events and survival data.
4. That there should be reassessment of pricing of cerliponase alfa with the goal of improving value for money when the current deed of agreement with the sponsor expires.

Next Steps

The Minister for Health and Aged Care has agreed to these recommendations. The implementation of these recommendation is currently being considered and progressed by the Department in consultation with sponsors, treating physicians and patient advocacy groups.