NEW DRUGS

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Cerliponase alfa

Approved indication: neuronal ceroid lipofuscinosis type 2 disease

Brineura (BioMarin)
vials containing 150 mg/5 mL solution
Australian Medicines Handbook Appendix A

The lysosomal storage diseases result from inborn errors of metabolism. Enzyme deficiencies cause an accumulation of substrates inside lysosomes. Neuronal ceroid lipofuscinosis (Batten disease) results from the accumulation of lipofuscin. In the type 2 form of the disease there is a deficiency of the enzyme tripeptidyl peptidase due to an autosomal recessive genetic defect.

The disease causes developmental delay when children are 2–4 years old. This is followed by seizures and loss of vision with death usually occurring in adolescence.

Cerliponase alfa is a recombinant form of the deficient enzyme and is activated in the lysosomes. It has to be given by intracerebroventricular infusion. This requires the surgical implantation of a reservoir and catheter. The infusion is given over several hours every other week. After the infusion, the device is cleared with a flushing solution. The half-life of cerliponase alfa in cerebrospinal fluid is about seven hours and the enzyme is probably cleared by hydrolysis.

Neuronal ceroid lipofuscinosis type 2 is a rare disease so there is a limited number of children to participate in clinical trials. The main study of cerliponase alfa was an open-label trial of 23 patients with a mean age of five years. They were treated for up to 48 weeks and, depending on their response, could continue in an extension study. The mean duration of treatment at the recommended dose was 115 weeks.

There was no control group, so the outcomes of the trial had to be compared with historical cases. The main outcome was a 2-point decline in a clinical rating scale assessing motor and language skills (range 0–6 points). This decline occurred after a median of 49 weeks in the historical controls, but by that time only 9% of the intervention group had experienced this decline. Over 48 weeks the rate of decline was 2.12 points in the controls, but only 0.27 points with cerliponase alfa.[1]

Adverse events were very common, but some, such as seizures, could be due to the disease itself. No child stopped treatment because of adverse events. Several events, such as some infections, were related to the device or the infusion. As hypersensitivity is common, antihistamines are recommended 30–60 minutes before the infusion. Vomiting and fever are also common.[1]

The trial showed that children treated with cerliponase alfa are significantly less likely to have a decline in motor and language scores than historical controls. Although it is still significant, the difference in the rate of decline narrows (2.06 vs 0.38 points) once the results are adjusted for covariates such as age. Cerliponase alfa may slow the decline, but it does not stop the loss of brain cells as MRI showed decreasing grey matter in the treated children.[1] Longer term follow-up will be needed to see if cerliponase alfa prevents blindness or improves quality of life and survival.

T T manufacturer provided additional useful information

REFERENCE

1. Schulz A, Ajayi T, Specchio N, de Los Reyes E, Gissen P, Ballon D, et al. Study of intraventricular cerliponase alfa for CLN2 disease. N Engl J Med 2018;378:1898-907. https://doi.org/10.1056/NEJMoa1712649

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, and the European Medicines Agency.

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.