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NICE National Institute for Health and Care Excellence

Cerliponase alfa for treating neuronal ceroid lipofuscinosis type 2

Chair's presentation

Highly Specialised Technologies, 29 August 2019
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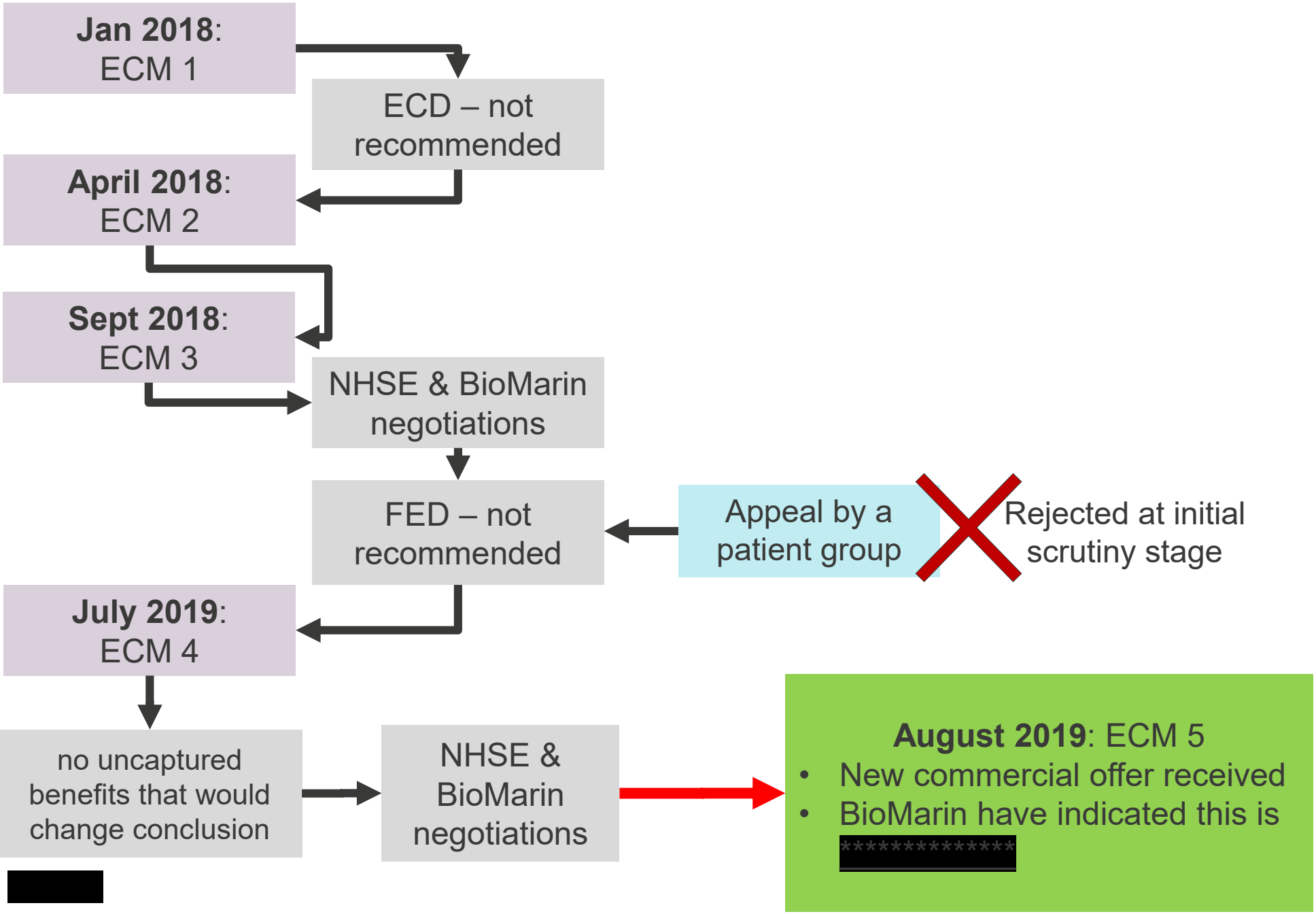
ERG: The University of York
NICE technical team: Orsolya Balogh, Thomas Strong, Sheela Upadhyaya
Company: BioMarin

Timeline of NICE evaluation of ID943



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Cerliponase alfa (BioMarin)

authorised under 'exceptional circumstances'

Marketing authorisation	Indicated for treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency
Mechanism of action	Recombinant human tripeptidyl peptidase 1, which is an enzyme replacement therapy
Administration & dose	Cerliponase alfa is supplied as a sterile solution (30 mg/ml) for intracerebroventricular (ICV) infusion to the cerebrospinal fluid (CSF). The ICV access device must be implanted prior to the first infusion. The recommended dose of cerliponase alfa for children over the age of 2 is 300mg administered every other week, given by ICV over approximately 4.5 hours
Price	The list price of a pack of cerliponase alfa (consisting of two 150mg vials) is £20,107. The company has proposed a confidential commercial access agreement
Treatment length	Lifetime treatment duration, subject to clinical judgement

Decision problem

	Final Scope
Population	People with a confirmed diagnosis of CLN2
Intervention	Cerliponase alfa
Comparator	Established clinical management without cerliponase alfa
Outcomes	• Symptoms of CLN2 (vision, seizures, myoclonus, dystonia, spasming, pain and feeding) • Disease progression (Hamburg scale, CLN2 rating scale, Weill Cornell LINCL score) • Need for medical care • Mortality • Adverse effects of treatment • HRQoL (patients and carers)

Considerations in FED – Recap

Nature of the condition	• CLN2 is a **progressive and devastating condition**, associated with very poor quality of life and a very short life expectancy which **severely affects the lives of families, carers and siblings** • There is currently no cure or life-extending treatment • **Significant unmet need**
Clinical effectiveness	• **Short term:** cerliponase alfa **improves quality of life**, and slows the deterioration of motor and language function • **Long-term**: only 96 weeks follow-up, assumptions about disease stabilisation and mortality are **associated with substantial uncertainty**
Value for money	• Cerliponase alfa **met the criteria for a QALY weight** of 3.0 • ICERs, with the QALY weighting applied, were **above the range NICE normally considers acceptable** • MAA (risk-sharing agreement) to address uncertainties appropriate • Company and NHS England were **unable to agree a commercial arrangement**
Impact beyond direct health benefits	• **Substantial financial impact on families** and costs incurred by non-NHS government departments • **Full effect of benefits beyond direct health benefits not captured** in the economic model • Uncaptured benefits **not sufficient to affect its conclusions** on the value for money

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Managed access agreement

Managed access agreement – Recap

- The committee previously concluded that the starting and stopping criteria presented were relevant, and could be incorporated in the proposed managed access agreement.
- Previously committee have been satisfied with the data collection proposal and considered it could address the key clinical uncertainties that the committee had identified
- Committee noted that the Managed Access Agreement would only be implemented if a commercial agreement is considered sufficient by both NHS England and Committee
- If at an MAA review a negative recommendation were made, NHS England funding would cease to be available and the treatment would cease for existing and new patients

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Managed access agreement (I)

- The committee identified two key areas for which there is currently no available evidence: improvements in earlier diagnosis and long-term clinical outcomes
  - ICER is sensitive to assumptions on the expected starting distribution of Motor and Language (ML) scores and the expected long-term stabilisation of disease
- The committee considered a data collection proposal which includes collection of:
  - CLN2 clinical rating scores over time;
  - the frequency and severity of tonic-clonic seizures;
  - myoclonus and dystonia control;
  - visual acuity;
  - extra-neurological symptoms;
  - cause of mortality;
  - trends in earlier diagnosis resulting from the proposed initiatives;
  - measures of quality of life
- Committee has not previously considered what period of time would be required to collect enough meaningful data for a potential guidance review

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How long would the Managed Access period need to be to ensure it could provide meaningful data on the key uncertainties identified by committee?

Managed access agreement (II)

The Batten Disease Family Association (BDFA) consider:

- Clinicians and families recognise it would not be in the child's best interests to be on treatment if they did not meet the eligibility criteria
- not all patients would chose to have treatment with cerliponase alfa, particularly if a gene therapy became available in the future
- families are fully aware and committed to the collection of long term data, and would be wiling to submit supplementary data, such as school reports

The BDFA would be able to provide support for:

- education of professionals to assist with earlier diagnosis
- help explore the suitability of real world evidence from a variety of sources to demonstrate quality of life and supplement clinical data collected as part of the MA. This could include school reports, photographs, videos, and patient diaries.
- input into the creation of NICE guidelines and/or be consulted on draft guidelines
- assisting with the implementation of any Managed Access Agreement

- What are the expected numbers that would choose to have cerliponase?
- Are stakeholders in agreement with the suitability and feasibility of an MAA?
- Any additions or amendments required to the MAA?