

Brineura treatment for CLN2 disease

The Managed Access Agreement

A guide for parents and caregivers
of children with CLN2 disease



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Disclaimer

The information contained in this booklet is intended as a guide to the Managed Access Agreement only and you should ensure that you understand the full content of the MAA Patient Agreement before signing it. This guide does not provide medical advice, always seek the advice of your child's consultant with any questions you may have regarding your child's medical condition.

Introduction

If you are reading this booklet it is likely your child has very recently been diagnosed with CLN2 disease.

Whilst being able to access a treatment can be very positive, the assessments and associated appointments can be stressful for families who are coming to terms with their child's condition and who are also new to the arrangements involved in receiving the treatment. The way Brineura is administered may also be distressing for patients and families.

We recognise that this is a life-changing and hugely emotional time and the Batten Disease Family Association (BDFA) is here to support you. We are also aware that this booklet may be daunting and official in places, but the guidance is taken from the National Institute for Health and Care Excellence (NICE)/ National Health Service (NHS) England official documentation, which is detailed and formal. If you have any concerns, or would just like to talk to a friendly voice, please do not hesitate to contact the BDFA. Via their support workers, they can put you in touch with other parents whose children are already accessing Brineura to discuss worries and concerns.



What is this guide for?

Brineura® (cerliponase alfa) is an enzyme replacement therapy for the treatment of CLN2 disease (Batten disease). It is the first disease-modifying treatment available for CLN2 disease, which was authorised for use in 2017. It is currently available in England through a **Managed Access Agreement (MAA)**.

This guide helps explain the MAA, the criteria set out in it to allow your child to start treatment with Brineura and how your child's treatment is monitored during the agreement.

Why do we have a MAA for Brineura?

In England, NICE recommended the collection of more information on treatment with Brineura before deciding if it should be available through the NHS.

As a result, the MAA was developed to make the treatment available for the next five years while more information is being collected. The MAA sets out criteria that your child will need to meet so they can start treatment with Brineura. It also details the assessments your child will need to take in order to continue treatment. If your child does not meet the assessments' criteria, their treatment may need to stop.

The MAA started in November 2019 and will end in November 2024. It is not known if the treatment will be available after this date. Availability will depend on a review of the information collected by the MAA and recommendation by NICE.

How to join the MAA

If you would like your child to join the MAA, you will need to **discuss this with your child's consultant**.

The consultant will complete assessments to check if your child meets the eligibility criteria for the Brineura MAA. If your child is not eligible, this will be discussed with you in more detail and your child's care will continue as usual at their local hospital with specialist input as needed.

Children already receiving treatment with Brineura prior to the start of the MAA, through the clinical trial or the expanded access programme, will be automatically eligible to join the MAA.



Eligibility Criteria

Treatment under the MAA can be started in children who:

- ✓ Have a **confirmed diagnosis** of CLN2 Batten disease
- ✓ Have a **CLN2 Rating Scale ML Score of 2 or above**
- ✓ **Do not have other serious, life-limiting conditions**
- ✓ **Patient, parent or carer to sign** the Managed Access Patient Agreement

Signing the Managed Access Patient Agreement

If your child meets the eligibility criteria, you will need to sign a Managed Access Patient Agreement at the hospital before treatment can start. The consultant at the hospital will go through the agreement with you and answer any questions you may have. By signing, you are agreeing to all the conditions set out in the MAA.

Ask your child's consultant about anything you are unsure about.

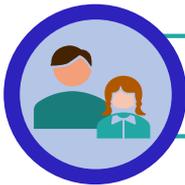


What is the CLN2 Rating Scale ML Score ?

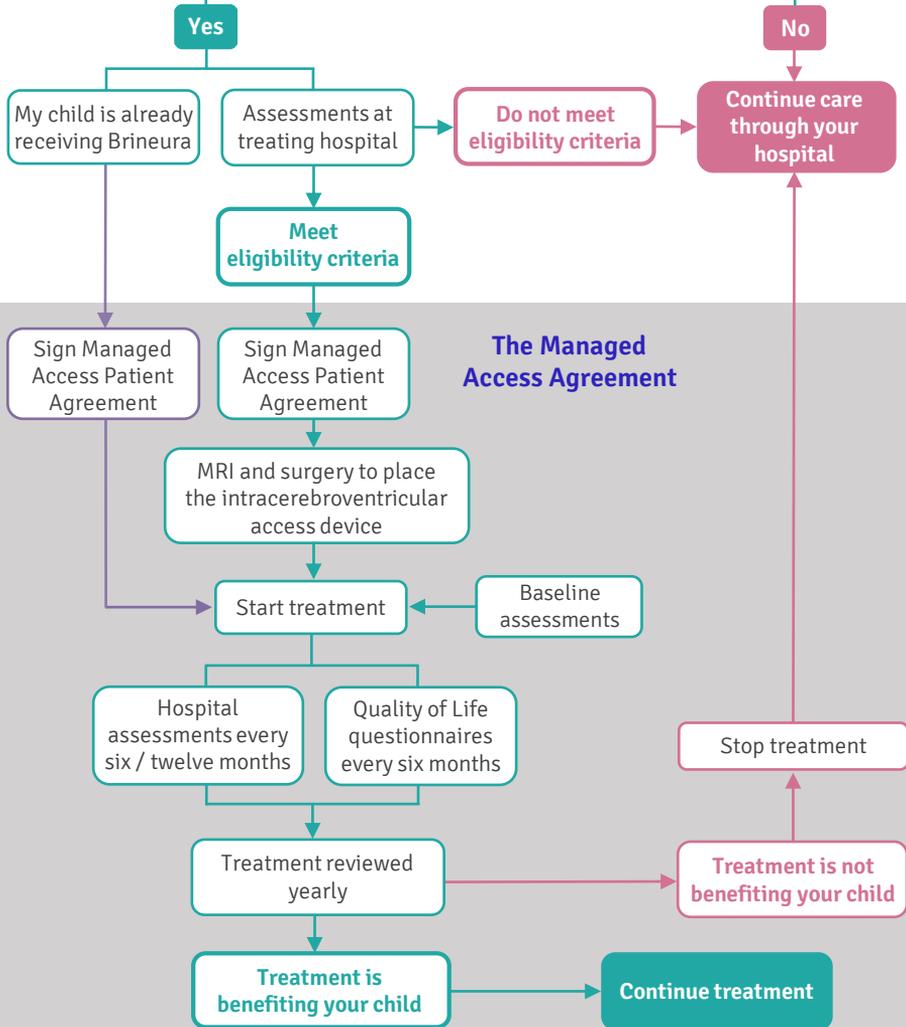
The CLN2 Rating Scale ML Score is a tool that measures the severity of the symptoms of CLN2 disease by assessing your child's motor and language (ML) skills. It is measured by assigning a score (0 to 3) to the different motor and language categories and calculating an overall score. The higher the score, the better the child's function. A description of the categories is available in the MAA document.

To be able to start treatment with Brineura, your child must have a score of 2 or above. This scale will also be used as part of the ongoing hospital assessments to determine whether treatment with Brineura can continue.

Read the agreement carefully so that you understand what you need to do. Treatment of eligible children may be stopped if they meet the stopping criteria (page 13).



Would you like treatment with Brineura for your child?



NICE review of information collected during the MAA and recommendation on future access to Brineura

Availability of Brineura after 2024 depends on NICE recommendation

The Managed Access Agreement: at a glance



To start treatment with Brineura your child must: (page 7)

- ✓ Have a confirmed diagnosis of CLN2 disease
- ✓ Have a CLN2 Rating Scale ML Score of 2 or above
- ✓ Not have other serious, life-limiting conditions
- ✓ Patient, parent or carer to sign the Managed Access Patient Agreement
- ✓ Undergo neurosurgery to implant an intracerebroventricular access device for infusions



To stay on treatment: (pages 7–12)

- ✓ Attend infusion appointments every two weeks
- ✓ Attend clinic appointments for assessments every six months
- ✓ Complete Quality of Life questionnaires every six months
- ✓ Assessments must show that Brineura is benefiting your child



Treatment may stop if: (page 13)

- ✓ Your child misses more than two infusions in any 14-month period*
- ✓ You or your child have not completed at least two hospital assessments or two Quality of Life questionnaires appointments in any 14-month period
- ✓ Brineura is not shown to be benefiting your child
- ✓ You wish for your child to stop the treatment with Brineura
- ✓ There is a medical reason for your child to stop treatment



After the MAA: (page 14)

- ✓ The MAA ends in November 2024
- ✓ The National Institute for Health and Care Excellence (NICE) will decide if treatment with Brineura will be available after this date

* Excluding for medical reasons or public health emergency situations, e.g. COVID-19.

Starting treatment with Brineura



Surgery to implant an intracerebroventricular access device

About 10–14 days before the first infusion

Brineura is infused directly into the cerebrospinal fluid (CSF) so, before treatment can begin, your child will have a brain scan (MRI) at the hospital and, as soon as there is availability, they will undergo a surgical procedure to implant an intracerebroventricular access device to be able to administer the infusions.

The reason Brineura needs to be administered directly into the CSF is because the brain is protected by a barrier separating the blood from the CSF, which means the treatment would not be able to reach the central nervous system in the body if using another method of administration (e.g. infused into the blood flow).

The device allows Brineura to reach the fluid cavity in the brain so your child can gain the maximum benefit from the treatment.

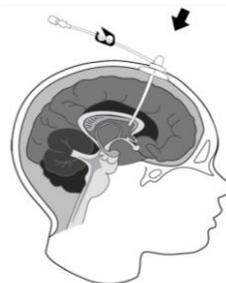
As a parent, you may find this surgical procedure upsetting, but this device has been used successfully for many years in children with various diseases and it is a well-established method to deliver treatment into the CSF.

The device can be accessed around 10–14 days after the surgery. Your child's specialist team will inform you of when the first infusion will be.

The hospital team will always be on hand to answer any questions you may have. Please discuss any doubts and concerns with your child's consultant as soon as they arise.

? What is cerebrospinal fluid (CSF)?

CSF is a watery liquid that surrounds the brain and spinal cord, acting as a 'cushion'. It also supplies nutrients to the brain.



Implanted intracerebroventricular access device[†]

Continuing treatment with Brineura

To stay on treatment with Brineura, you must **meet the conditions** set out in the MAA. Throughout the duration of the MAA, your child will be expected to:

- ✓ Attend **all infusion appointments***
- ✓ Attend **all appointments** for hospital assessments*
- ✓ Parent/carer to **complete the Quality of Life (QoL) questionnaires** over the telephone

Treatment will only continue if the assessments show Brineura is benefiting your child.

* Excluding for medical reasons or public health emergency situations, e.g. COVID-19; † Image used with permission of BioMarin.



Infusions with Brineura

Once every 2 weeks

Brineura infusions are administered once every two weeks and you and your child will need to attend the hospital to receive the infusion. Brineura can only be given at specific centres and, for your child to receive the infusion, you will need to travel to a particular centre. The infusion will be given by a healthcare professional trained in the administration of this specific type of infusion.

The MAA requires that your child does not miss more than two infusions in a 14-month period.*



If you feel that Brineura is not benefiting your child, you must notify your child's consultant in the first instance. Communicating with your child's consultant is imperative to your child's care. Remember that the hospital team welcomes any feedback you may have on your child's health and treatment.



How long does it take to administer the Brineura infusion?

The time it takes to complete a full administration of Brineura can vary depending on the dose and volume of the infusion. In general, it takes approximately four and a half hours. For children under 2 years of age on a lower dose, the time may be shorter.



Why is it important not to miss infusions?

To gain the maximum benefit from the treatment, it is essential that infusions are not missed.

The frequency of the dosing is based on clinical studies that recommend Brineura to be administered once every two weeks.



What happens if my child misses an infusion due to medical reasons?

If your child misses an infusion due to medical reasons, they may still be able to continue treatment with Brineura once the medical issue has been resolved. Your child's consultant will be able to advise you.



Can I stop my child's treatment and restart it again later on?

Once you have decided to stop treatment, you will not be allowed to restart again at a later date while the MAA is running. Please discuss your decision to stop treatment with your child's consultant.

* Excluding for medical reasons or public health emergency situations, e.g. COVID-19.



Hospital assessments

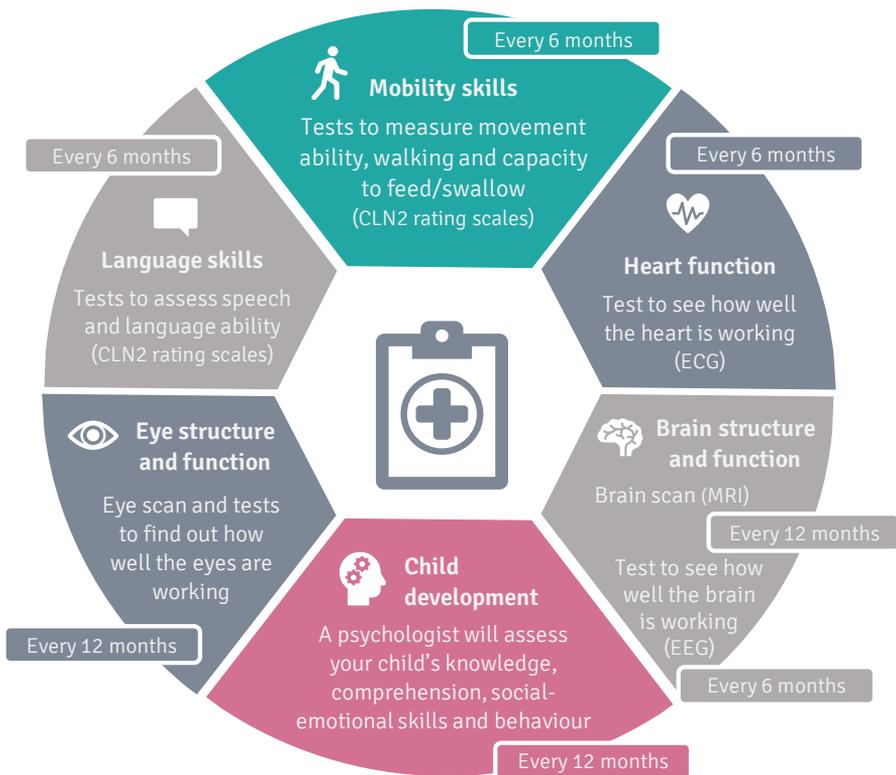
Every 6 or 12 months

As part of the MAA, you and your child will need to attend the hospital every six months to complete the hospital assessments.

These assessments are an important part of the MAA and the results will be used to determine if the treatment is providing benefit to your child.

What are the hospital assessments?

The hospital will do various clinical and developmental assessments to evaluate your child and to find out if the treatment is working:



ECG: electrocardiogram

EEG: electroencephalogram

MRI: Magnetic resonance imaging



Quality of Life (QoL) assessment questionnaires

Every 6 months

As part of the MAA, you will need to complete QoL questionnaires on behalf of your child every six months. Questionnaires will be completed over the telephone with a member of the MAA team at Rare Disease Research Partners (RDRP). It will take approximately 30 minutes to complete all three questionnaires.

These questionnaires will measure the effect Brineura has on the quality of life of your child and on their family and caregivers.

These assessments are an important part of the MAA and they will be used to determine if Brineura is providing benefit to your child. These results are never used on their own and will be reviewed in conjunction with your child's hospital assessments.

What are the QoL questionnaires?

These questionnaires are known as 'Quality of Life questionnaires' because they gather information to understand the ability of your child and their family/caregivers to enjoy normal life activities. You can find more details of the three questionnaires on page 11. You will be asked questions on the following topics:



Feeding



Pain



Participating in society
(e.g. nursery, school)



Self-care



Fatigue



Psychological impact



Seizures



Disrupted sleep



Mobility



Digestion
issues



Speech or
communication



Impact on family
and caregivers



How do I complete the QoL questionnaires?

A member of the MAA team at Rare Disease Research Partners (RDRP) will contact you to arrange a convenient time to complete the questionnaires with you. They will contact you every six months to go through the three questionnaires that need to be completed (see page 11).

RDRP can provide an interpreter for these calls where English is not the first language of the parent/carer.



What happens if I miss my phone appointment?

If you miss the call, RDRP will try to contact you at a later time to re-arrange the appointment. If they are unable to make contact with you to re-arrange the call, they will notify your child's consultant and it will be logged as a missed assessment.

Please contact RDRP if you know you will be unable to make the appointment and need to re-schedule the call. Their details are on the back of this booklet.

Three assessment questionnaires

To be answered by parents or caregivers of children treated under the Brineura MAA



PAST
MONTH

Peds QL

A short questionnaire to find out **how much of a problem** certain things have been for your child over the **past one month**.

Questions will cover your child's physical, emotional, social and school functioning. You will be given these five answer options to choose from:

- It is **never** a problem
- It is **almost never** a problem
- It is **sometimes** a problem
- It is **often** a problem
- It is **almost always** a problem



PAST
MONTH

CLN2QoL

A questionnaire to find out how some **issues related to your child's disease** may have been a problem for you, your family and your child in the **past one month**.

The questions include issues related to seizures, feeding, sleep, behaviour and daily activities. You will be given these five answer options to choose from:

- It is **never** a problem
- It is **almost never** a problem
- It is **sometimes** a problem
- It is **often** a problem
- It is **almost always** a problem



TODAY

EQ-5D-5L

A short questionnaire used to measure your **child's quality of life today**.

Questions will be related to their mobility, self-care, usual activities, pain/discomfort and emotional well-being and you will be given five answer options to choose from.

There are no right or wrong answers to any of these questions.



Review of your child's treatment with Brineura

Every 12 months

To continue treatment with Brineura on the MAA, the assessments completed as part of the MAA need to show evidence that Brineura is benefiting your child.

Your child's consultant, along with a team of consultants specialising in lysosomal storage disorders, will undertake a review each year of the results of the hospital and QoL assessments.

Your child's consultant will discuss the measures with you and explain whether they suggest that treatment with Brineura is of benefit to your child.



How is it determined that Brineura is of benefit to my child?

Benefit is determined through the hospital and QoL assessments completed during the MAA. If a significant decline in the results of these assessments is observed, a decision will be made by the child's consultant, and discussed with you, about stopping treatment with Brineura.

As long as the results of the assessments do not meet the stopping criteria set out in the MAA, then the treatment is deemed to be of benefit to your child and they will remain on treatment.

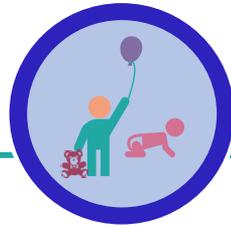
A full description of what is required to meet the assessments' criteria to remain on treatment with Brineura is available in the MAA document.



What can I do if I am unhappy about the assessment results?

If you feel the assessments were performed incorrectly, or the information was not gathered appropriately, please discuss this with your child's consultant.

If you are still unsure, you have the right to ask for a second opinion at your child's hospital. You can also ask for the assessments to be repeated at another hospital of your own choosing but all associated costs will be at your own expense.



Allowances for children under three years of age

Some children may be too young to be able to complete all of the assessments.

If your child is under the age of three, they will automatically meet the eligibility criteria on the assessments that they cannot perform. These assessments will then be conducted within six months of their third birthday.



What if my child was unwell when the assessments took place?

If your child was temporarily unwell before undergoing an assessment, they will be reassessed within 12 weeks.

Reassessing your child will ensure that results are not affected by any temporary circumstances, which will also be taken into consideration when deciding if treatment may continue or not.

Stopping treatment

Treatment may be stopped if the conditions set out in the MAA are not met, or the results of the hospital and QoL assessments suggest Brineura is not benefiting your child.

Below are some of the reasons why treatment may be stopped for your child:



Assessments show your child is not benefiting from treatment with Brineura



Your child has missed more than two infusions in any 14-month period



Medical reasons, such as reactions to Brineura or another serious condition



Your child has not completed at least two hospital assessments in any 14-month period



You wish to stop your child's treatment



You have not completed at least two QoL questionnaire assessments in any 14-month period



What happens if treatment with Brineura is stopped?

Your child's consultant will discuss with you what the next steps are. Your child will continue to receive care and support from the hospital.

The UK Batten Disease Family Association (BDFA) is able to provide support for your child and family whether your child is receiving treatment with Brineura or not. Their details are on the back of this booklet.



What other medical reasons may stop treatment?

If your child is unable to tolerate infusions despite attempts to reduce reactions with medication, treatment with Brineura may need to be stopped either temporarily or permanently.

If another serious or life-limiting condition is diagnosed, it may need to take priority and treatment with Brineura will be reviewed to consider the new diagnosis.

Be reassured that your child's consultant will discuss with you any modifications to your child's treatment before any changes take place.



Can I appeal if my child is taken off treatment?

You can appeal a decision to stop treatment with Brineura if you feel that treatment was discontinued as a result of assessments being performed incorrectly or information not being collected properly.

You can ask for a second opinion at your child's hospital. If you ask for the assessments to be repeated at another hospital of your own choosing, all associated costs will be at your own expense.



After the MAA



Brineura will be available to children with CLN2 disease until the end of the MAA in November 2024, provided that the conditions for staying on treatment are met. It is not known if Brineura will be available after this date.

Availability beyond November 2024 will depend on a review of the information collected during the MAA on the effects of Brineura treatment. This review will be undertaken by NICE and a recommendation will be issued by the end of the MAA, in 2024.



Additional questions



Can we go on holiday during the MAA?

You may be able to take a short holiday if it means your child is not missing more than two infusions in a 14-month period.

Any break needs to be discussed with your child's consultant to make sure you will not break the conditions of the MAA, as this could lead to the treatment being stopped.



I feel my child's symptoms are getting worse

If you feel that your child's symptoms are worsening while receiving treatment with Brineura, please discuss this with your child's consultant.



I feel my child is not benefiting from the treatment

If you feel treatment with Brineura is not providing benefit to your child, please discuss this with your child's consultant.

If you decide not to continue with treatment, you can withdraw your child from the MAA at any time.



Can my child join the MAA at a later date?

If you are unsure whether to start your child on treatment with Brineura, please discuss your concerns with your child's consultant.

If you decide you would like your child to start treatment at a later date, the assessments will need to be performed again. This is because your child's condition may have changed and they may no longer meet the eligibility criteria at that time. If this is the case, your child will not be able to start treatment.



What happens if my child misses a hospital assessment?

Sometimes, your child may miss an appointment due to medical reasons or other unforeseen circumstances that prevent you from reaching the hospital.

Get in touch with the hospital as soon as you can to let them know you are unable to attend and to reschedule your appointment. To be compliant with the MAA, your child must attend at least two assessments in any 14-month period.



Will I be informed of the final decision made by NICE on access to treatment with Brineura after the MAA?

Your child's consultant will let you know of any decisions that may change your access to treatment.

Where to find more information and support

Your child's consultant

Talk to your child's consultant if you are unsure of anything concerning your child's health, the treatment or the MAA.

The MAA

The full text of the MAA is available at: www.nice.org.uk/guidance/hst12/resources/managed-access-agreement-pdf-6968825245

Batten Disease Family Association

You can contact the Batten Disease Family Association (BDFA) for support and advice.

General: 07876 682 589; admin@bdfa-uk.org.uk
Support: 0800 046 9832; support@bdfa-uk.org.uk
Web: www.bdfa-uk.org.uk



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Rare Disease
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