Asfotase alfa (Strensiq) Managed Access Agreement for treating Hypophosphatasia

What is Hypophosphatasia?

Hypophosphatasia (HPP) is a rare inherited bone disorder which affects the development of bones and teeth. The signs and symptoms can appear any time from before birth to adulthood. The most severe forms usually occur before birth and in early infancy. In babies it is often fatal, and in older children and adults it can be debilitating. If your bones have not formed properly it can cause symptoms including:

- delayed walking
- limb weaknesses
- bone pain
- recurrent fractures

Additional complications in early infancy include:

- poor feeding
- failure to gain weight and height
- respiratory problems
- high levels of calcium in the blood causing recurrent vomiting and kidney problems
- seizures

What is asfotase alfa?

You may know asfotase alfa by its brand name Strensiq®. Hypophosphatasia is caused by a problem in a gene which provides instructions for the alkaline phosphatase (ALP) enzyme. This is needed to develop and maintain your bones and to manage the amounts of calcium and phosphate in your body. If you have Hypophosphatasia your body does not make enough of this enzyme. Asfotase Alfa is a man-made version of this enzyme and is used to replace the one that does not work properly.

Asfotase alfa has been recommended for use in patients with paediatric onset HPP by NICE in accordance with a Managed Access Agreement (MAA).

Who are NICE?

NICE stands for The National Institute for Health and Care Excellence. It is an independent organisation and was set up by the Government. NICE's role is to:

- assess any new drugs and treatments to decide which should be available on the NHS in England
- provide guidelines and advice to health, public health and social care providers
- develop quality standards and ensure services are providing the best support and care
- provide information services for health and social care providers
- ensure everyone has access to treatment regardless of where they live

The Department of Health and NHS England decide which topics NICE should review. These topics fall under different categories. The asfotase alfa treatment is classed as a "Highly Specialised Technology". You can learn more about this on the NICE or Metabolic Support

UK websites (links to these are included at the end of this information).

As part of the Highly Specialised Technology treatment evaluation process, an independent committee will hear input from nominated experts, patients and carers who will discuss:

- the severity and natural development of the disorder
- research Study / Trial outcomes
- the impact of the disorder on patient's and carers
- the effectiveness of the treatment on the patient
- the patient population / who it affects? / How many?
- other treatment alternatives
- treatment cost / value for money

Following this, NICE offers draft recommendations and invites comments from health professionals and members of the public. These will be considered and if there are no appeals upheld, NICE will issue the recommendations as NICE final guidance.

What is a Managed Access Agreement?

When the NICE appraisal committee evaluate a treatment for an ultra-rare disease they can make one of the following 3 recommendations:

1. YES- NICE recommend the drug and it will enter routine commissioning and become available on the NHS.

2. NO- NICE do not recommend the drug, and the NHS is therefore not obligated to make this drug available.

3. The drug is recommended for use only within a Managed Access Agreement (MAA). This option is used when the committee believe the drug has promising potential to be effective, but there are remaining uncertainties about how well the drug performs and whether it is value for money for the NHS. These uncertainties need more investigation before a final funding decision can be made.

A Managed Access Agreement is an arrangement between NICE, the drug company (who makes the treatment), and NHS England. The purpose of the agreement is:

1. To enable patients in England access to promising treatments for a specified length of time.

2. To collect new information on patients receiving a treatment to address the clinical uncertainties that were identified when the drug was originally evaluated by NICE. This may be long term follow up on patients already receiving the treatment (possibly in a clinical trial) or information on new patients starting the treatment.

3. To help the NICE appraisal committee make a better-informed decision on whether a treatment is appropriate for patients and whether it is a good use of NHS money.

It can be difficult to collect enough data on new treatments for ultra-rare diseases during research trials because of the small numbers of patients. Although a new drug may show promise, there sometimes simply isn't enough information available for NICE to be able to decide whether to make a positive recommendation for the treatment to be made available via the NHS.

When NICE evaluated asfotase alfa they issued guidance recommending asfotase alfa for use as an option for treating paediatric-onset Hypophosphatasia for people who meet the criteria for treatment within the Managed Access Agreement (MAA).

The MAA will allow new data to be collected on how effective the drug is, and to help answer the uncertainties that were found during the first evaluation of the treatment by NICE. At the end of the Managed Access Agreement, NICE will use the new data collected on

patients who have received asfotase alfa to re-review and issue new guidance.

How long is the MAA for?

The MAA lasts for five years. It began on the 2nd August 2017 and will finish on the 2nd August 2022. During this period patients that meet the "start" criteria outlined in the MAA will be able to access asfotase alfa. Towards the end of the MAA period, NICE will review all the patient data that has been collected and will make a new recommendation before 2nd August 2022. If NICE does not recommend asfotase alfa for NHS funding, NHS England funded treatment may stop for all patients. If NICE recommends asfotase alfa for further NHS funding, then asfotase alfa will continue to be funded in England according to the arrangements between NICE and NHS England at that time.

Can anyone access asfotase alfa?

During the MAA, only those patients with paediatric-onset HPP who meet certain clinical 'Start' criteria will have access to asfotase alfa.

You or your child may be eligible for treatment if a diagnosis of paediatric-onset HPP has been confirmed.

The diagnosis must be confirmed in a HPP centre and your case will then be assessed by the National Authorisation Panel (NAP). This panel consists of key decision makers from NHS England, NICE representatives, an adult and a paediatric specialist and a pain expert.

What if my baby has HPP and needs urgent treatment?

If your newborn baby has been diagnosed with HPP by a specialist and is in emergency care they will not need to be assessed by the NAP before starting treatment and will be allowed access to asfotase alfa immediately.

What are the Start Criteria?

All perinatal- and infantile-onset HPP cases up to one year of age, who meet the start criteria below will be initiated on asfotase alfa as soon as practical.

Other Patients with Childhood-Onset HPP who meet the starting rules for asfotase alfa therapy include:

Children aged 1-4 with **ONE** of the following:

- Have not achieved expected developmental gross motor milestones for age as demonstrated by the BAMF-Scale (Brief Assessment of Motor Function); **OR**

- Continuing or recurring musculoskeletal pain where there is significant pain that affects daily activities which:
  - Affects quality of life
  - Hasn't got better with 2 different types of painkiller which have been recommended by a national pain specialist

Children aged 5-18 with **ONE** of the following:

- Continuing or recurring musculoskeletal pain where there is significant pain that affects daily activities which:
  - Affects quality of life
  - Hasn't got better with 2 different types of painkiller which have been recommended by a national pain specialist

OR

- Limited mobility assessed by a specialist according to the modified Bleck Ambulation Efficiency Scoring and with a Bleck score between 1-6*

Patients over the age of 18 years old with childhood-onset HPP who have **TWO** or more of the following:

- Current fractures (commonly affected areas include feet, hip, spine, wrist and thigh bone) with a history of non-traumatic, recurrent or non-/ poorly-healing fractures (e.g. inability to remove fixation devices due to risk of recurrent fracture.
- Continuing or recurring musculoskeletal pain where there is significant pain that affects daily activities which:
  - Affects quality of life
  - Hasn't got better with 2 different types of painkillers which have been recommended by a national pain specialist
- Limited mobility assessed by a specialist according to the modified Bleck Ambulation Efficiency Scoring and with a Bleck score between 1-6*.

What happens after I get approval?

Once your case has been approved, you will be asked to sign consent forms to allow your data which is needed for the MAA to be collected and stored. This allows eligible patients to start being treated while at the same time allowing more data on the drug's efficacy and safety to be collected. By signing the relevant consent forms you confirm that you accept the terms and will comply with the requirements of the MAA (including attending all the clinical assessments outlined in the MAA).

A full set of tests will be carried out to measure how you or your child is doing before treatment. The doctor at the treatment centre may call this a 'baseline assessment'.

Those under the age of 5 may not be able to complete all these tests, but the doctors will try every 12 months until they reach the age of 5, at which point all tests become compulsory.

How often will I need to come to clinic?

After your first assessment you will need to attend clinic at months 3, 6 and 12 in the first year. After this you will need to attend a minimum of every 6 months. These clinic appointments will allow your doctor to assess your progress.

Will there be home visits?

Yes, in the first year, you will be asked to take part in 4 Quality of Life questionnaires. This short survey allows you to say how you feel the treatment is helping you. These will be arranged prior to your clinic appointments. After the first year, this will reduce to a minimum of 2 questionnaires.

During the first year your you will also be allocated up to 15 home visits by a nurse who will support you and help you to administer the drug at home. Your doctor will help you to organise when these will be.

Are there any reasons why my treatment with asfotase alfa might be stopped during the MAA?

Yes. If you do not keep to the agreed terms of the MAA then your treatment may be discontinued. There may be an unavoidable circumstance where you are unable to make your clinic appointment. In such cases, you **must** let your doctor (or your child's doctor) know and reschedule the appointment.

You may also be taken off the treatment if you, or your child, are:

- showing less than the expected rate of improvement
- if there is a severe adverse reaction, or
- if another condition is diagnosed which means that asfotase alfa is unlikely to benefit you.

You will have a review every 12 months. Your doctor will discuss this with you and answer any questions and concerns you may have about the rate of improvement and if this is not met. Full details of the 'stop criteria' are in the MAA.

Treatment will also discontinue if NICE do not recommend asfotase alfa at the end of the MAA period. See the full MAA for further information.

I've improved a lot on the treatment but I'm now showing no further progress. Should I be worried about being taken off the treatment?

All the information gathered throughout your assessments will be reviewed. The National Authorisation Panel will look at how you are now compared to your first assessment. After improving on the drug, it is expected that you will reach a period where your disorder remains the same (a plateau in improvement). Your doctor will be able to offer any reassurances and advice.

Where can I get further information?

Your doctor at clinic will be able to talk you through what to expect at clinic appointments and answer any questions you have about the MAA. It is a good idea to make a note of any questions you have and take them to your next clinic visit. If you need to feedback any issues about the treatment service (i.e. homecare issues) please contact your doctor. For further information and for support and advice about HPP you can contact Metabolic Support UK www.metabolicsupportuk.org or Soft Bones UK www.softbonesuk.co.uk

References

https://www.nice.org.uk/guidance/hst6

https://www.nice.org.uk/about/what-we-do

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003794/human_med_001901.jsp&mid=WC0b01ac058001d124

https://www.england.nhs.uk/2017/07/nhs-patients-with-rare-bone-disease-to-benefit-from-potentially-life-transforming-drug/

https://ghr.nlm.nih.gov/condition/hypophosphatasia

*Bleck Score Description (1-6)

1 Non-walker older than 2 years of age
2 Therapy walker with the use of crutches or sticks
3 Therapy walker without the use of crutches or sticks
4 Household walker with the use of crutches or sticks
5 Household walker without the use of crutches or sticks
6 Neighbourhood* walker with the use of crutches or sticks (Neighbourhood walker defined as one who can walk less than 300m)

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