Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)
Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Policy Position PP156

Asfotase alfa for treating paediatric-onset hypophosphatasia

Document information	
Document purpose	Policy Position
Document name	Asfotase alfa for treating paediatric-onset hypophosphatasia
Author	Welsh Health Specialised Services Committee
Published Date	June 2018
WHSSC Executive Lead:	Director of Planning
Target audience	Chief Executives, Medical Directors, Directors of Finance, Chief Pharmacists, Directors of Planning, Mark Francis
Description	NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy
Document No:	PP156

Policy Position Statement

Background	In August 2017 NICE published Highly Specialised Technologies (HST) guidance on Asfotase alfa for treating paediatric-onset hypophosphatasia (HST6)[1]. NICE HST are mandatory within NHS Wales and this policy position confirms the WHSSC commissioning position. WHSSC has developed this policy position to confirm the commissioning arrangements for patients paediatric-onset hypophosphatasia within Wales.
Summary of Policy Position	WHSSC will commission the use of Asfotase alfa for treating paediatric-onset hypophosphatasia (HPP) in-line with NICE Highly Specialised Technologies Guidance (HST6)[1]. Asfotase alfa is recommended as an option for treating paediatric-onset hypophosphatasia only: • for people who meet the criteria for treatment within the managed access arrangement (see section 4.18), and • for the duration of this arrangement and in line with the other conditions it specifies, and • when the company provides asfotase alfa with the confidential commercial terms agreed with NHS England. These recommendations are not intended to affect treatment with asfotase alfa that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. For children and young people, this decision should be made jointly by the clinician and the child or young person or the child or young person's parents or carers

[1] Asfotase alfa for treating paediatric-onset hypophosphatasia | Guidance and guidelines | NICE

	The criteria for treatment, and starting and stopping treatment can be found on page 11 of this policy.
Responsibilities	Treatment should be started by a physician experienced in the management of metabolic or bone disorders. The recommended dosage of asfotase alfa is 2 mg/ kg 3 times per week, or 1 mg/kg 6 times per week. For full details of the recommended dosage regimens of asfotase alfa, see the summary of product characteristics. Referrers should: • Inform the patient that this treatment is not routinely funded outside the criteria in this policy; and • Refer via the agreed pathway. Clinician considering treatment should: • Discuss all the alternative treatment with the patient; • Advise the patient of any side effect and risks of the potential treatment; • Inform the patient that treatment is not routinely funded outside of the criteria in the policy; and • Confirm that there is contractual agreement with WHSSC for the treatment. In all other circumstances an Individual Patient Funding Requests[2] (IPFR) should be submitted (see also section 3.3).

[2] Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

Contents

1. Aim

1.1 Introduction

This policy position describes the commissioning position within NHS Wales for the use of Asfotase alfa for treating paediatric-onset hypophosphatasia (HPP) based on the NICE HST guidance on Asfotase alfa for treating paediatric-onset hypophosphatasia (HST6)[3].

1.2 Plain language summary

Asfotase alfa is a targeted enzyme replacement therapy designed to restore the regulation of metabolic processes in the bones and teeth, and to reduce complications of dysregulated bone mineral metabolism.

Hypophosphatasia is a genetic disorder caused by mutations in the tissue non-specific alkaline phosphatase (TNSALP) gene, which reduce its activity. This causes disruption of mineralisation, a process in which calcium and phosphorous are deposited in developing bones and teeth. Several clinical forms of hypophosphatasia are currently recognised:

- perinatal onset (onset before or at birth)
- infantile onset (onset at 0–6 months)
- juvenile onset (also referred to as childhood-onset, onset between 6 months and 17 years)
- adult onset (onset at 18 years and over) and
- odontohypophosphatasia (only dental symptoms).

Paediatric-onset hypophosphatasia includes everyone with hypophosphatasia of perinatal, infantile, or juvenile onset.

1.3 Relationship with other Policies and Service Specifications

This document should be read in conjunction with the following documents:

- All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR)[4].
- NICE, Asfotase alfa for treating paediatric-onset hypophosphatasia HST6[3].

[3] Asfotase alfa for treating paediatric-onset hypophosphatasia | Guidance and guidelines | NICE
[4] Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

2. Scope

2.1 Definition

Hypophosphatasia is a genetic disorder caused by mutations in the TNSALP gene which reduce the activity of the enzyme tissue nonspecific alkaline phosphatase. Over 275 different mutations of this gene leading to hypophosphatasia have been identified. The reduction of this enzyme's activity disrupts mineralisation, a process in which calcium and phosphorous are deposited in developing bones and teeth. This leads to rickets, softening and weakening of the bones (osteomalacia), bone deformity and a greater incidence of fractures. Hypophosphatasia can also lead to vitamin B6 deficiency which can cause generalised seizures.

The signs and symptoms of hypophosphatasia vary widely and can appear anytime from before birth to adulthood. Six clinical forms are currently recognised:

- perinatal (lethal)
- perinatal (benign)
- infantile (where symptoms start within 6 months after birth)
- childhood
- adult
- Odontohypophosphatasia (which only affects the teeth).

Asfotase alfa (Strensiq, Alexion Pharma UK) is a targeted enzyme replacement therapy designed to restore the regulation of metabolic processes in the bones and teeth, and to reduce complications of dysregulated bone mineral metabolism. Asfotase alfa is administered by subcutaneous injection and has a marketing authorisation under exceptional circumstances in the UK 'for long-term enzyme replacement therapy in patients with paediatric-onset hypophosphatasia to treat the bone manifestations of the disease'.

2.2 Aims and objectives

This policy describes the commissioning position within NHS Wales for the use of Asfotase alfa for treating paediatric-onset hypophosphatasia based on published NICE HST guidance (HST6)[5].

2.3 Codes

E83.9, Disorder of mineral metabolism, unspecified

[5] Asfotase alfa for treating paediatric-onset hypophosphatasia | Guidance and guidelines | NICE

3. Access Criteria

3.1 Clinical Indications – general principles

Hypophosphatasia is a rare, serious and heterogeneous genetic condition associated with considerable mortbidiy that serverly affects the quality of life of people with the condition and their families.

To be considered for Asfotase alfa treatment, patients must agree to the terms of the arrangement. This includes attending regular follow-up clinics and inclusion in date collection.

3.2 Criteria for Treatment

Asfotase alfa is recommended as an option for treating paediatric-onset hypophosphatasia only:

- for people who meet the criteria for treatment within the managed access arrangement (see section 4.18, NICE HST guidance on asfotase alfa),and
- for the duration of this arrangement and in line with the other conditions it specifies, and
- when the company provides asfotase alfa with the confidential commercial terms agreed with NHS England.

Full details of the managed access agreement are available here: https://www.nice.org.uk/guidance/hst6/resources/managed-access-agreement-august-2017-pdf-4543781149

3.2.1 Starting criteria (as defined in the managed access arrangement)

All people with perinatal- and infantile-onset hypophosphatasia, regardless of current age, can start treatment with asfotase alfa. Asfotase alfa can be considered for children (aged 1–4 years and 5–18 years) with juvenile-onset disease if they do not reach motor milestones, have pain with significant disability or have restricted mobility.

The drug can also be considered for adults (18 years and over) with juvenile-onset disease if they have 2 of the following:

- current fractures or a history of fractures characteristic of hypophosphatasia
- persistent or recurrent pain with disability
- restriction of mobility.

3.2.2 Stopping criteria (as defined in the managed access arrangement)

Babies under 1 year with respiratory problems can continue treatment for the duration of the managed access arrangement unless they develop serious adverse events, other life-limiting conditions or remain ventilator dependent after 2 years.

Children with juvenile-onset disease will stop treatment if 2 of the 3 following stopping criteria are met:

- loss of height or growth impairment
- no improvement in physical function or fall in mobility score, and
- no reduction in pain.

Adults with juvenile-onset disease will stop treatment if 1of the following criteria are met:

- no improvement in physical function or fall in mobility score;
- continued fractures over a 3-year period, and
- no reduction in pain.

3.3.3 Monitoring and data collection (as defined in the managed access arrangement)

Data will be collected from everyone who has asfotase alfa within the managed access arrangement, and will be recorded in a dedicated database. The company stated that NHS England will have access to this database for audit and analysis of individual-level data, and will also be provided with relevant data extracts from the global hypophosphatasia registry database to assist in assessing asfotase alfa.

3.3 Exceptions

This policy is not intended to affect treatment with asfotase alfa that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. For children and young people, this decision should be made jointly by the clinician and the child or young person or the child or young person's parents or carers.

If the patient does not meet the criteria for treatment, but the referring clinician believes that there are exceptional grounds for treatment, an Individual Patient Funding Request (IPFR) can be made to WHSSC under the *All Wales Policy for Making Decisions on Individual Patient Funding Requests (IPFR).*

If the patient wishes to be referred to a provider out of the agreed pathway and the referring clinician believes that there are exceptional grounds for treatment at an alternative provider, an Individual Patient Funding Request (IPFR) can be made to WHSSC under the *All Wales Policy for Making Decisions on Individual Patient Funding Requests (IPFR).*

Guidance on the IPFR process is available at:
www.whssc.wales.nhs.uk

3.4 Responsibilities

Referrers should:

- Inform the patient that this treatment is not routinely funded outside the criteria in this policy, and
- Refer via the agreed pathway.

Clinician considering treatment should:

- Discuss all the alternative treatment with the patient
- Advise the patient of any side effect and risks of the potential treatment
- Inform the patient that treatment is not routinely funded outside of the criteria in the policy, and
- Confirm that there is contractual agreement with WHSSC for the treatment.

In all other circumstances an IPFR should be submitted[6].

[6] Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

4. Putting Things Right: Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided. The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern:

- When a patient or their representative is unhappy with the decision that the patient does not meet the criteria for treatment further information can be provided demonstrating exceptionality. The request will then be considered by the All Wales IPFR Panel.
- If the patient or their representative is not happy with the decision of the All Wales IPFR Panel the patient and/or their representative has a right to ask for this decision to be reviewed. The grounds for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated. The review should be undertaken, by the patient's Local Health Board;
- When a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for NHS Putting Things Right. For services provided outside NHS Wales the patient or their representative should be guided to the NHS Trust Concerns Procedure, with a copy of the concern being sent to WHSSC.

5. Equality Impact and Assessment

The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (Welsh).

This policy has been subjected to an Equality Impact Assessment.

The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

Annex (ii) Checklist

Asfotase alfa for treating paediatric-onset hypophosphatasia

The following checklist should be completed for every patient to whom the policy applies:

i) Where the patient meets the criteria **AND** the procedure is included in the contract **AND** the referral is received by an agreed centre, the form should be completed and retained by the receiving centre for audit purposes.
ii) The patient meets the criteria **AND** is received at an agreed centre, but the procedure is not included in the contract. The checklist must be completed and submitted to WHSSC for prior approval to treatment.
iii) The patient meets the criteria but wishes to be referred to a non contracted provider. An Individual Patient Funding Request (IPFR) Form must be completed and submitted to WHSSC for consideration.
iv) The patient does not meet criteria, but there is evidence of exceptionality. An Individual Patient Funding Request (IPFR) Form must be completed and submitted to WHSSC for consideration for treatment.