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

Specialised Services Policy Position Statement PP156

Asfotase alfa for treating paediatric-onset hypophosphatasia in children aged under 16 years

November 2023
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Target audience	**For information** Chief Executives, Medical Directors, Directors of Finance, Directors of Planning, All Wales Medical Genetic Service
	For action Chief Pharmacists, Clinical Leads, Paediatric Nurse Specialists, Consultant paediatricians, Director of Nursing, Specialist Head of Finance and Commissioning, Health Board Commissioning Managers, Planning managers
Description	NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy
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Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission asfotase alfa for people with paediatric-onset hypophosphatasia in children aged under 16 years in accordance with the criteria outlined in this document.

Welsh Language

WHSSC is committed to treating the English and Welsh languages on the basis of equality, and endeavour to ensure commissioned services meet the requirements of the legislative framework for Welsh Language, including the Welsh Language Act (1993), the Welsh Language (Wales) Measure 2011 and the Welsh Language Standards (No.7) Regulations 2018.

Where a service is provided in a private facility or in a hospital outside of Wales, the provisions of the Welsh language standards do not directly apply but in recognition of its importance to the patient experience, the referring health board should ensure that wherever possible patients have access to their preferred language.

In order to facilitate this, WHSSC is committed to working closely with providers to ensure that in the absence of a Welsh speaker, written information will be offered and people have access to either a translator or 'Language-line' if requested. Where possible, links to local teams should be maintained during the period of care.

Decarbonisation

WHSSC is committed to taking assertive action to reducing the carbon footprint through mindful commissioning activities. Where possible and taking into account each individual patient's needs, services are provided closer to home, including via digital and virtual access, with a delivery chain for service provision and associated capital that reflects the WHSSC commitment.

Disclaimer

WHSSC assumes that healthcare professionals will use their clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply this policy position statement.

This policy may not be clinically appropriate for use in all situations and does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian, or Local Authority.

WHSSC disclaims any responsibility for damages arising out of the use or non-use of this policy position statement.

1. Introduction

This Policy Position Statement has been developed for the planning and delivery of asfotase alfa for treating paediatric-onset hypophosphatasia in children aged under 16 years and resident in Wales. This service will only be commissioned by the Welsh Health Specialised Services Committee (WHSSC) and applies to residents of all seven Health Boards in Wales.

In creating this document WHSSC has reviewed the relevant guidance issued by the National Institute of Health and Care Excellence (NICE)[1] and has concluded that asfotase alfa for treating paediatric-onset hypophosphatasia should be made available.

WHSSC only has commissioning responsibility for children aged under 16 years of age, therefore it will be for Health Boards to approve the use of asfotase alfa for paediatric-onset hypophosphatasia from 16 years of age.

1.1 Background

Paediatric-onset hypophosphatasia (HPP) is a rare disease that presents before the age of 18 years. Due the rarity of the disease, estimates of the prevalence and incidence for paediatric-onset HPP are limited. A 10-year study of 20 European countries reported an estimated birth prevalence of perinatal-/infantile-onset HPP of 1 in 300,000 live births[2]. Another study estimated an incidence of HPP of 0.8 per 1,000,000 for children under age 18 and 2.8 per 1,000,000 for children under age 1 using a survey method in 2003[3].

HPP 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).

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

[2] Mornet E, Yvard A, Taillandier A, et al. A Molecular-Based Estimation of the Prevalence of Hypophosphatasia in the European Population. Annals of Human Genetics. 2011; 75(3):439-45.

[3] Beck C, Morbach H, Stenzel M, et al. [Hypophosphatasia]. Klinische Padiatrie. 2009; 221(4):219-26.

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

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.

1.2 Equality Impact 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 subject to an Equality Impact Assessment in line with guidance contained in CPL-026[4].

The Assessment identifies the potential for adverse impact or missed opportunities to promote equality. A decision was made to proceed with the policy. In their submission to NICE, the company noted that if recommendations differ by age then there could be potential equality considerations. The NICE committee discussed this in light of its recommendations, which do differ by age at onset. However, the committee was clear that this is because the burdens of hypophosphatasia and the evidence it was presented with differ between perinatal- or infantile-onset and juvenile-onset hypophosphatasia. No other potential equality issues were identified by the committee. WHSSC have not identified any further potential equality issues beyond that included above.

An EQIA was also carried out by NICE during the evaluation of asfotase alfa. For further details, please refer to the NICE website at: https://www.nice.org.uk/guidance/hst23.

[4] https://whssc.nhs.wales/publications/corporate-policies-and-procedures/corp-026-eqia-policy/

2. Recommendations

The recommendations below represent the views of NICE, arrived at after careful consideration of the evidence available. Health professionals are expected to take into account the relevant NICE guidance[5], alongside the individual needs, preferences and values of the patient.

2.1 Inclusion Criteria

Asfotase alfa is recommended as an option for treating paediatric-onset hypophosphatasia if the person's symptoms started before or at birth (perinatal onset) or between the ages of 0 and 6 months (infantile onset). It is also recommended for people whose symptoms started between the ages of 6 months and 17 years (juvenile onset) only if:

- they are aged 1 year to 4 years and have:
    - not reached expected developmental gross motor milestones for their age or
    - continuing or recurring significant musculoskeletal pain that affects daily activities and quality of life, and has not improved after 2 different types of painkiller recommended by a national pain specialist
- they are aged 5 years to 18 years[6] and have:
    - limited mobility assessed by a specialist using the modified Bleck Ambulation Efficiency Score and a Bleck score between 1 and 6 or
    - continuing or recurring significant musculoskeletal pain that affects daily activities and quality of life, and has not improved after 2 different types of painkiller recommended by a national pain specialist

Asfotase alfa is only recommended if the company provides it according to the commercial arrangement.

2.2 Exclusion criteria

- People aged 16 years and older[6].

2.3 Continuation of Treatment

Healthcare professionals are expected to review a patient's health at regular intervals to ensure they are demonstrating an improvement to their health due to the treatment being given.

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

[6] Health Boards have the commissioning responsibility of asfotase alfa for people aged 16 years and older

If no improvement to a patient's health has been recorded then clinical judgement on the continuation of treatment must be made by the treating healthcare professional.

2.4 Acceptance Criteria

The service outlined in this specification is for patients ordinarily resident in Wales, or otherwise the commissioning responsibility of the NHS in Wales. This excludes patients who whilst resident in Wales, are registered with a GP practice in England, but includes patients resident in England who are registered with a GP Practice in Wales.

2.5 Transition arrangements

Transition arrangements should be in line with Transition from children's to adults' services for young people using health or social care services NICE guidance NG43 and the Welsh Government Transition and Handover Guidance.

Transition involves a process of preparation for young people and their families for their transition to adulthood and their transition to adult services. This preparation should start from early adolescence 12-13 year olds. The exact timing of this will ideally be dependent on the wishes of the young person but will need to comply with local resources and arrangements.

The transition process should be a flexible and collaborative process involving the young person and their family as appropriate and the service.

The manner in which this process is managed will vary on an individual case basis with multidisciplinary input often required and patient and family choice taken into account together with individual health board and environmental circumstances factored in.

2.6 Designated Providers

Birmingham Women and Children's hospital
Steelhouse Lane
Birmingham
B4 6NH

Sheffield Teaching Hospital
Herries Road
Sheffield
S5 7AT

University Hospitals Birmingham
Queen Elizabeth Hospital Birmingham,
Mindelsohn Way
Edgbaston
Birmingham
B15 2GW

University Hospitals Manchester
Cobbett House
Oxford Road
Manchester
M13 9WL

2.7 Blueteq and reimbursement

Asfotase alfa for paediatric-onset hypophosphatasia in children under 16 years old will only be funded for patients registered via the Blueteq system and where an appropriately constructed MDT has approved its use within highly specialised paediatric endocrinology centres.

Where the patient meet the criteria in this policy and the referral is received by an agreed centre, a Blueteq form should be completed for approval. For further information on accessing and completing the Blueteq form please contact WHSSC using the following e-mail address: WHSSC.blueteq@wales.nhs.uk

If a non-contracted provider wishes to treat a patient that meets the criteria, they should contact WHSSC (e-mail: WHSSC.IPC@Wales.nhs.uk). They will be asked to demonstrate they have an appropriate MDT in place.

The neonatal dose is 2 mg/kg by subcutaneous injection 3 times a week, alternatively 1 mg/kg by subcutaneous injection 6 times a week, dosing frequency depends on body-weight - consult SmPC for further information.

Dosing for a child is 2 mg/kg by subcutaneous injection 3 times a week, alternatively 1 mg/kg by subcutaneous injection 6 times a week, dosing frequency depends on body-weight - consult SmPC for further information.

The list prices for asfotase alfa are:

- £12,700.80 per 12-injection vial, which contains 18 mg/0.45 ml of asfotase alfa
- £19,756.80 per 12-injection vial, which contains 28 mg/0.7 ml of asfotase alfa
- £28,224.00 per 12-injection vial, which contains 40 mg/1 ml of asfotase alfa
- £56,448.00 per 12-injection vial, which contains 80 mg/0.8 ml of asfotase alfa[7]

The company has a commercial access agreement (CAA) which makes asfotase alfa available to the NHS with a discount. The size of the discount is commercial in confidence. Health Boards in Wales should refer to the AWTTC vault for further information on the CAA price.

2.8 Action to be taken

- Health Boards and WHSSC are to circulate this Policy Position Statement to all Hospitals/MDTs to inform them of the conditions under which the technology will be commissioned.

- WHSSC are to ensure that all providers are purchasing asfotase alfa at the agreed discounted price.

- Providers are to ensure the need to approve asfotase alfa at the appropriate MDT and are registering use on the Blueteq system, and the treatment will only be funded where the Blueteq minimum dataset is fully and accurately populated.

- Providers are to determine estimated patient numbers and the current dose of any patient(s) who will transfer from any company compassionate use scheme or EAMS.

- The Provider should work to written quality standards and provide monitoring information to WHSSC on request.

[7] Medicinal forms | Asfotase alfa | Drugs | BNF | NICE

3. Putting Things Right

3.1 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.

If 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.

3.2 Individual Patient Funding Request (IPFR)

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The All Wales IPFR Panel will then consider the request.

If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent review of the process to be undertaken by the patient's Local Health Board. The ground for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated

If the patient wishes to be referred to a provider outside of the agreed pathway, an IPFR should be submitted.

Further information on making IPFR requests can be found at Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

Annex i Codes

Code Category	Code	Description
	E83.9	Disorder of mineral metabolism, unspecified