GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

# Specialised Services
# Policy Position Statement PP257

## Atidarsagene autotemcel for treating metachromatic leukodystrophy in children

*April 2023*

*Version 0.6*

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| Document information | |
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| **Commissioning Team** | Women and Children |
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| | **For action**<br>Chief Pharmacists, Clinical Leads, Director of Operations for Specialist Services, Directorate Manager for Paediatrics, Specialist Head of Finance and Commissioning, Health Board Commissioning Managers |
| **Description** | NHS Wales propose to routinely commission this specialised service in accordance with the criteria described in this policy |
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## 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.

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

## 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.

# Contents

# 1. Introduction

This Policy Position Statement has been developed for the planning and delivery of antidarsagene autotemcel for treating metachromatic leukodystrophy for children aged 0-17 years old resident in Wales. This proposed service will only be commissioned by the Welsh 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 antidarsagene autotemcel for treating metachromatic leukodystrophy should be made available.

## 1.1 Background

Metachromatic leukodystrophy (MLD) is a rare genetic disorder caused by a deficiency in the enzyme arylsulphatase A (ARSA). The deficiency causes a build-up of a toxic substance (sulphatids), which affects the central nervous system causing neurological problems. MLD has a significant effect on the quality of life of children with the condition, and their families and carers. It progresses rapidly, with loss of mobility and cognitive function, and causes early death.

MLD can broadly be divided into a presymptomatic stage with normal motor and cognitive development, followed by a developmental plateau and early onset of first symptoms.

There are 3 main types based on genotype and age of symptom onset:

- The late infantile (LI) type is the most common (40% to 60% of children affected) and most aggressive form and usually starts before 30 months.

  Symptoms include peripheral neuropathy, muscle weakness, sight and hearing loss, difficulty walking, loss of speech, cognitive decline and seizures. The condition progresses rapidly so that children lose awareness of their surroundings over a few years. Death normally occurs within 5 to 8 years[1].

- The juvenile type is found in 20% to 35% of children affected. It can be subdivided into:
  - early juvenile (EJ) disease, starting between 30 months and 6 years
  - late juvenile disease, starting between 7 and 16 years.

  Symptoms include impaired fine motor skills and concentration, behavioural problems, difficulties with movement, slurred speech,

[1] Overview | Atidarsagene autotemcel for treating metachromatic leukodystrophy | Guidance | NICE

incontinence and seizures. Initial disease progression is slower than with the LI type but symptoms can progress rapidly. Death normally occurs within 10 to 20 years[1].

- The adult type (15% to 25% of people affected) is the rarest form and usually starts after 16 years.

  Symptoms include a decline in school or work performance, cognitive decline, personality changes and memory lapses. The decline can be slow and almost imperceptible. Death normally occurs within 25 years[2].

## 1.2 Current treatment

There are no national published guidelines on the treatment of MLD. There are no standard disease-modifying treatments available. Treatment options for early onset disease are limited to managing symptoms, disease complications and best supportive care[2].

This may include:

- physiotherapy (mobility and respiratory)
- management for pain and skeletal deformity
- dietary support
- drugs to reduce spasticity, seizures and psychiatric symptoms
- family and psychological counselling
- advanced care planning / end of life care.

## 1.3 Epidemiology

The prevalence of MLD is estimated as 1 in 147,000 live births in England and Wales, equating to about 4 to 5 children born with MLD per year[2].

## 1.4 Atidarsagene autotemcel

Atidarsagene autotemcel (Libmeldy, Orchard Therapeutics) is a gene therapy medicinal product that expresses the human arylsulphatase A (ARSA) gene. Ex vivo autologous CD34+ haematopoietic stem and progenitor cells are collected from the person's bone marrow or peripheral blood. These are then transduced with a lentiviral vector, which inserts copies of human ARSA complementary DNA into the cell genome, and transplanted into the person. When successfully engrafted, the genetically modified cells secrete functional ARSA enzyme, which is absorbed by surrounding cells and used to break down or prevent build-up of harmful sulphatides. The effects are potentially lifelong.

[2] Overview | Atidarsagene autotemcel for treating metachromatic leukodystrophy | Guidance | NICE

A myeloablative conditioning regimen is needed before infusing atidarsagene autotemcel, to promote engraftment of the genetically modified cells. Before starting myeloablative conditioning, the treating clinician should confirm that atidarsagene autotemcel is clinically appropriate for the patient. Atidarsagene autotemcel must be administered in a qualified treatment centre with experience in haematopoietic stem cell transplantation.

## 1.5 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[3].

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.

An EQIA was also carried out by NICE during the evaluation of antidarsagene autotemcel for treating metachromatic leukodystrophy. For further details, please refer to the NICE website[4].

[3] https://whssc.nhs.wales/publications/corporate-policies-and-procedures/corp-026-eqia-policy/
[4] History | Atidarsagene autotemcel for treating metachromatic leukodystrophy | Guidance | NICE

# 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

Atidarsagene autotemcel is recommended, within its marketing authorisation, as an option for treating metachromatic leukodystrophy with mutations in the arylsulphatase A (ARSA) gene:

- for children who have late infantile or early juvenile types, with no clinical signs or symptoms,
- for children who have the early juvenile type, with early clinical signs or symptoms, and who can still walk independently and have no cognitive decline[6].

Atidarsagene autotemcel should be delivered in a highly specialised service by a specialist multidisciplinary team. It is recommended only if the company provides atidarsagene autotemcel according to the commercial arrangement[1].

## 2.2 Exclusion criteria

- Late juvenile disease, starting between 7 and 16 years
- Adults (aged 18 years and over)

## 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.

## 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

[5] 1 Recommendations | Atidarsagene autotemcel for treating metachromatic leukodystrophy | Guidance | NICE

[6] Evidence of cognitive decline would include an IQ of <85

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-old. 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

MLD is managed in the NHS by local paediatric specialists who refer people to the paediatric lysosomal storage disease (LSD) specialist centre for multidisciplinary treatment led by a paediatric metabolic consultant.

There is one paediatric lysosomal storage disorder specialist centre in England providing this treatment:

- **St Mary's Hospital**
  Oxford Rd,
  Manchester
  M13 9WL

It is expected that atidarsagene autotemcel would be delivered within the current specialised services framework by a multidisciplinary team.

## 2.7 Blueteq and reimbursement

Antidarsagene autotemcel for treating metachromatic leukodystrophy 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 lysosomal storage disorders specialist centres.

Where the patient meets 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: wales.ipc@wales.nhs.uk). They will be asked to demonstrate they have an appropriate MDT in place.

Funding is approved on the basis that Antidarsagene autotemcel is prescribed and administered in accordance with its marketing authorisation[7].

The list price for atidarsagene autotemcel is £2,875,000 (excluding VAT; company submission). The company has a commercial arrangement. This makes atidarsagene autotemcel available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount. Health Boards in Wales should refer to the AWTTC Vault for further information on the Patient Access Scheme (PAS) 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 atidarsagene autotemcel at the agreed discounted price.
- Providers are to ensure the need to approve atidarsagene autotemcel 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] Libmeldy, INN-atidarsagene autotemcel (europa.eu)

# 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