GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Commissioning Policy: CP55

Drug Treatment for Lysosomal Storage Disorders (All ages)

January 2023
Version 2.0

PARCH - RESPECT

PARTNERIAETH - PARTNERSHIP

GWELLA AC ARLOESI - IMPROVEMENT & INNOVATION

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Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) commission drug treatments for lysosomal storage disorders (LSDs) for people of all ages and in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed this clinical condition and the associated treatment options. It has considered the place of each drug treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

Disclaimer

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

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.

1. Introduction

This document has been developed for the planning and delivery of drug treatments for lysosomal storage disorders (LSDs) for people of all ages 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.

1.1 Plain Language Summary

Lysosomal storage disorders (LSDs) are inherited metabolic diseases characterized by an abnormal build-up of harmful substances in the body which may affect different parts of the body; including the bones, brain, skin, heart, and central nervous system. The disorders occur as a result of a missing or damaged enzyme. There are nearly 50 of these disorders altogether and new disorders continue to be identified[1].

LSDs are progressive and the patient's symptoms can worsen over time. There is currently no cure for any of the LSDs. Medicines used to treat these disorders aim to reduce the build-up of harmful substance in the body, which results in a reduction in the speed at which the disease progresses, and over time leads to better outcomes for the patient[1].

Patients with these disorders, including those receiving drug treatments, need specialist medical care and regular review.

1.2 Treatments

Drug treatments given to manage LSDs are disease modifying and are widely used in the United Kingdom. The main aim of treatment is to reduce the severity of symptoms or delay the disease progression. Care for patients with LSDs is provided by specialist centres with experience of each condition and the medications used to treat them. Haematopoietic stem cell transplantation (HSCT) may be used as a therapeutic option in some LSD conditions. In addition, specialist centres provide supportive care to manage the symptoms and complications associated with the condition.

Patients are assessed according to current criteria for suitability of treatment. The criteria vary from disorder to disorder and are constantly reviewed.

Drugs used to treat some of the LSDs include:

- Enzyme replacement therapy (ERT) - given to people who suffer from chronic conditions resulting from enzyme deficiencies or malfunction.
- Substrate reduction therapy (SRT) - given to reduce the amount of harmful substances that the body has to break down.

[1] Lysosomal Storage Disorders - NORD (National Organization for Rare Disorders) (rarediseases.org)

- Molecular chaperone therapy - assist enzymes in becoming functional by helping them take the correct shape and stay stable.
- Gene therapy - the introduction of normal genes into the body in place of missing or defective ones in order to correct genetic disorders.

Despite there currently being no cure for any of the LSDs, new drug treatments continue to be developed in this rapidly advancing field.

1.3 Epidemiology

Although individual LSDs are considered very rare there are a large number of disorders (nearly 50) and thus the prevalence of the group as a whole is about 20 per 100,000 live births. Individually they are very rare with individual incidences ranging from 1:60,000 to 1:1,000,000[2].

1.4 Individual disorders

1.4.1 Fabry Disease

Fabry disease is an X-linked disorder which affects the way the body breaks down glycosphingolipids (lipids / fats). It is caused by the absent or marked deficient activity of the lysosomal enzyme alpha-galactosidase A. Early childhood symptoms include neuropathic pain. Without treatment the condition progresses throughout adult life to cause serious cardiac, neurological and renal disease.

Fabry disease is a pan-ethnic disorder with an estimated UK prevalence of 2:100,000 births[3]. There are three licensed medicines in the UK for treating Fabry disease; two ERT therapies, Agalsidase alfa (Replagal®)[4] and Agalsidase beta (Fabrazyme®)[5] and a chaperone therapy Migalastat (Galafold®)[6].

1.4.2 Gaucher Disease Types I, II, and III

Gaucher disease (GD) is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme Beta glucocerebrosidase. GD is the most common type of LSD.

There are three types of GD all of which occur in children, with symptoms sometimes not presenting until adulthood. The first, type I, is the most common and patients in this group usually present with enlargement of the

[2] Lysosomal Storage Disorders - NORD (National Organization for Rare Disorders) (rarediseases.org)
[3] Overview | Migalastat for treating Fabry disease | Guidance | NICE
[4] Replagal 1mg/ml concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[5] https://www.medicines.org.uk/emc/search?q=%22Fabrazyme%22
[6] Galafold 123 mg hard capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

liver and spleen and haematological problems. There are no signs of brain involvement but without treatment serious skeletal complications can occur. In type II GD, liver and spleen enlargement are apparent by three months of age and affected infants have central nervous system (CNS) damage and usually die before their second birthday. In the third category, called type III, liver and spleen enlargement is variable, respiratory disease is common and signs of brain involvement such as seizures become apparent over time. This type of GD is also associated with a specific eye movement abnormality.

Both Type I and those with visceral symptoms with Type III GD respond favourably to ERT. Type II disease does not respond and ERT cannot prevent the neurological decline and is therefore not indicated in these patients. Two ERT products are currently licensed for use in the UK; Imiglucerase (Cerezyme®)[7] licensed for Type I and Type II GD and Velaglucerase alfa (VPRIV®)[8] licensed for Type I GD. Individualised therapeutic goals may be necessary in children especially those with type III disease. In addition to ERTs, there are two substrate inhibiting drugs licensed for Type I GD; Eliglustat (Cerdelga®)[9] indicated for long-term treatment of adults patients, and Miglustat (Zavesca®)[10] indicated for patients deemed unsuitable for treatment with ERT.

1.4.3 Mucopolysacharidoses

Mucopolysacharidoses (MPS) are a group of disorders associated with specific enzyme deficiencies. In individuals with MPS disorders, deficiency or malfunction of specific lysosomal enzymes leads to an abnormal accumulation of certain complex carbohydrates (mucopolysaccharides or glycosaminoglycans) in the arteries, skeleton, eyes, joints, ears, skin, and/or teeth. These accumulations may also be found in the respiratory system, liver, spleen, central nervous system, blood and bone marrow. All of the MPS diseases have certain characteristics in common, which include deformities of the bones and joints that interfere with mobility and often cause osteoarthritis, especially of the large, weight-bearing joints. All of the MPS diseases except MPS III disease interfere with growth, causing short stature**.** Most are inherited as autosomal recessive traits with the exception of MPS II (Hunter syndrome) which is X-linked[11].

[7] Cerezyme 400 Units Powder for concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[8] VPRIV 400 Units powder for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[9] Miglustat 100mg Hard Capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[10] Miglustat 100mg Hard Capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[11] Lysosomal Storage Disorders - NORD (National Organization for Rare Disorders) (rarediseases.org)

Haematopoietic stem cell transplantation (HSCT) is used as a treatment option for the severe form of MPS I (Hurler syndrome), and in some cases of MPSII and MPS VII. For those that require drug treatemnts, there are a number of ERT medicines licensed in the UK/Europe to treat MPS, Laronidase (Aldurazyme®)[12] is licensed for MPS I, Idursulfase (Elaprase®)[13] for MPS II, Galsulfase (Naglazyme®)[14] for MPS VI, Elosulfase alfa (Vimizim®) for MPS IVa[15] and Vestronidase alfa (Mepsevii®) for MPS VII (Sly syndrome)[16].

1.4.4 Glycogen Storage Disease II (Pompe Disease)

Pompe disease is caused by a deficiency of the lysosomal enzyme acid glucosidase (acid maltase) and is classified into two subtypes. The infantile onset presents within the first months of life and is the most severe form of the disease with a rapidly progressive cardiomyopathy, generalised skeletal muscle weakness and respiratory failure. If untreated, this form is fatal by one to two years of age. Late onset Pompe disease can present any time after birth and is characterised by a progressive muscle weakness (with little or no cardiac involvement) which can lead to severe morbidity, respiratory failure and early mortality.

Affected infants often require long periods of time in paediatric intensive care units and many require long term mechanical ventilation. ERT with Alglucosidase alfa (Myozyme®)[17] dramatically alters the natural history of the infantile disease but many patients still require long term follow up. Avalglucosidase alfa (Nexviadyme®)[18], a new ERT therapy licensed for use in Pompe disease, has recently been approved for use in the UK by NICE[19]

Pompe disease is estimated to affect approximately 0.3 in 10,000 people with a reported birth prevalence was 0.8 per 100,000 people for the infantile onset form and 1.75 per 100,000 for the late-onset form according to European Orphanet data[20].

[12] Aldurazyme 100 U/ml concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[13] Elaprase 2 mg/ml concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[14] Naglazyme | European Medicines Agency (europa.eu)
[15] Vimizim, INN-elosulfase alfa (europa.eu)
[16] Mepsevii | European Medicines Agency (europa.eu)
[17] Myozyme 50 mg, powder for concentrate for solution for infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
[18] Nexviadyme, INN-avalglucosidase alfa (europa.eu)
[19] Final draft guidance | Project documents | Avalglucosidase alfa for treating Pompe disease [ID3737] | Guidance | NICE
[20] Prevalence_of_rare_diseases_by_decreasing_prevalence_or_cases.pdf (orpha.net)

1.4.5 Niemann-Pick Disease

Niemann-Pick type C (NPC) is a progressive neurodegenerative disorder. It is an autosomal recessive LSD that affects infants, children and adults. It is characterised by a defect in the handling of cholesterol and other fats inside cells. Mutations in the NPC genes cause the accumulation of fats in the liver, brain and spleen. There are two subtypes (NPC1 and NPC2) caused by mutations in either the NPC1 or NPC2 gene. NPC1 is the most prevalent: approximately 95% of cases are caused by genetic mutations in the NPC1 gene. The incidence of NPC is currently estimated at 1 in 100,000 live births[21].

Accumulation of lipids lead to a variety of symptoms, including liver and spleen enlargement, liver dysfunction and neurological abnormalities. Children frequently have lack of muscle coordination, loss of muscle tone, spasticity, increased sensitivity to touch and learning difficulties. Young people and adults have psychiatric illness, dementia and progressive neurological deterioration. Most people also have difficulties with swallowing. The age of onset and severity of symptoms varies substantially from person to person. Patients with neurological onset early in life deteriorate faster and have a shorter life expectancy than those with adult onset. Most people with NPC die between the ages of ten and twenty five.

Treatment options for NPC include substrate reduction therapy and management of symptoms and complications. Miglustat[22] is a substrate reduction therapy with a marketing authorisation for treating progressive neurological deterioration in children and adults with NPC. Supportive care is directed toward the specific symptoms apparent in each individual. This may include palliative care.

1.4.6 Metachromatic Leukodystrophy (MLD) Disease

Treatment for Metochromatic Leukdystrophy is covered in a separate WHSSC Policy Position Statement (PP257) (In development).

1.4.7 Neuronal ceroid lipofuscinosis type 2

Treatment for Neuronal ceroid lipofuscinosis type 2 is covered in a separate WHSSC Policy Position Statement (PP262) (In development).

[21] Consensus clinical management guidelines for Niemann-Pick disease type C (nih.gov)
[22] Miglustat 100mg Hard Capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

1.5 Aims and Objectives

This policy aims to define the commissioning position of WHSSC on the use of the medicines listed within this policy, for people with the respective LSD.

The objectives of this policy are to:

- ensure commissioning for the use of the medicines listed for LSDs is evidence based.
- ensure equitable access to drug treatments for LSDs.
- define criteria for people with LSDs to access drug treatments.
- improve outcomes for people with LSD.

1.6 What NHS Wales has decided

WHSSC has carefully reviewed the evidence for the drug treatments listed within this policy for each LSD and concluded that:

- There is sufficient evidence to fund the use of drug treatments for LSDs in accordance with the criteria set out in section 2.1.
- There is insufficient evidence to support the routine commissioning of drug treatments for LSDs as listed in section 2.4.

1.7 Relationship with other documents

This document should be read in conjunction with the following documents

- **NHS Wales**
  - All Wales Policy: Making Decisions in Individual Patient Funding requests (IPFR).

- **National Institute of Health and Care Excellence (NICE) guidance**
  Individual and up to date drug policies are available on:
  www.nice.org.uk/guidance/.

- **All Wales Medicine Strategy Group (AWMSG) guidance**
  Individual and up to date drug policies are available at:
  www.awmsg.nhs.wales/medicines-appraisals-and-guidance/.

- **Other Relevant Documents**
  - NHS Standard Contract for Lysosomal Storage Disorders Service (Children). Service Specification. 2013/2014. B (england.nhs.uk) [accessed 26/04/2022].
  - Transition from children's to adults' services for young people using health or social care services (2016) NICE guideline NG43
  - Welsh Government - The Transition and Handover Guidance (February 2022)

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of drug treatments for lysosomal storage disorders (LSDs) for people of all ages, in line with the criteria identified in this policy.

2.1. Inclusion Criteria

2.1.1. Commissioned drug treatments

WHSSC will only approve funding of drug treatments for lysosomal storage disorders (LSDs) as listed in Table 1.

Table 1: WHSSC commissioned LSD drug treatments

Lysosomal Storage Disorder	Drug Treatment
Fabry	**Agalsidase alfa** (Replagal®) **Agalsidase beta** (Fabrazyme®) **Migalastat** (Galafold®)
Gaucher type I	**Eliglustat** (Cerdelga®) **Velaglucerase alfa** (VPRIV®)
MPS I (Hurler/Hurler-Scheie syndrome)	**Laronidase** (Aldurazyme®)
MPS IVa (Morquio syndrome)	**Elosulfase alfa** (Vimizim®)
Glycogen Storage Disease Type II (Pompe)	**Alglucosidase alfa** (Myozyme®) **Avalglucosidase alfa** (Nexviadyme®)

2.1.2. Criteria for Commencing Treatment

To commence drug treatment for LSDs the following criteria should be met:

- A confirmed genetic or enzymatic diagnosis of the relevant LSD, based upon the full assessment of clinical signs and symptoms and a documented deficiency of the relevant enzyme, and DNA variant analysis undertaken where appropriate.
- The patient is under the care of a specialised centre, and treatment is initiated and supervised by specialist physicians experienced in the diagnosis and treatment of LSDs.
- The relevant gatekeeper at Cardiff and the Vale University Health Board has given approval for treatment to commence. (See annex i)
- The drug has marketing authorisation for the condition being treated and is prescribed and administered in accordance with its marketing authorisation.
- The drug is listed as approved for funding within Table 1.

- Drug treatment is prescribed and administered according to agreed local guidelines at the designated centres.
- A Blueteq form is completed prior to commencing treatment (see section 2.6 Blueteq and reimbursement)
- Drugs are purchased by the provider in according to the commercial arrangement where applicable.
- A homecare service provider is used where available and appropriate.

2.1.3. Individual Disorders and Treatment Options

WHSSC approve funding for drug treatments in line with the specific recommendations made by NICE or AWMSG as defined in Table 3.

Prior to commencement of drug treatment people should be counselled that if their condition deteriorates during treatment, then drug treatment will be stopped.

Table 3: Individual Disorders and Treatment Options[23]

Fabry Disease	
Drug treatment	**Recommendations**
Agalsidase alfa (Replagal®)	**AWMSG advice 1107: Agalsidase alfa (Replagal®)** • Agalsidase alfa (Replagal®) should be recommended for use within NHS Wales as a long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease. • Patients receiving agalsidase alfa (Replagal®) will be entered into the Fabry Outcomes Survey. • Treatment will be administered under the supervision of a physician experienced in the management of Fabry disease or other inherited metabolic diseases. • Treatment will be administered according to agreed guidelines at appropriate designated centres.
Agalsidase beta (Fabrazyme®)	**AWMSG advice 12: Use of agalsidase beta (Fabrazyme®) within NHS Wales** Agalsidase beta (Fabrazyme®) should be endorsed within NHS Wales for the treatment of

[23] All treatment options are to be used within their licensed indication and/or marketing authorisation

	Fabry disease in accordance with the licensed indication with the following restrictions: AWMSG recommends: • Patients receiving agalsidase beta (Fabrazyme®) will be entered into the Fabry registry. • Treatment will be administered under the supervision of a physician experiences in the management of Fabry disease or other inherited metabolic disease. • Treatment will be administered according to agreed guidelines at appropriate centres**.**

Migalastat (Galafold®)	**NICE HST4: Migalastat for treating Fabry disease**
	
	• Migalastat is recommended, within its marketing authorisation, as an option for treating Fabry disease in people over 16 years of age with an amenable mutation, only if:
	  ○ Migalastat is provided with the discount agreed in the patient access scheme, and
	  ○ only if enzyme replacement therapy (ERT) would otherwise be offered.

Migalastat (Galafold®)	**AWMSG Advice 4268: Migalastat For the long-term treatment of adolescents aged 12 years to 16 years with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation** • Migalastat hydrochloride (Galafold®) is recommended as an option for restricted use within NHS Wales. • Migalastat hydrochloride (Galafold®) is licensed for the long-term treatment of adolescents aged 12 years to 16 years with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation. • Migalastat hydrochloride (Galafold®) is restricted for use for the treatment of Fabry disease in adolescents aged 12 years to 16 years with an amenable mutation, only if enzyme replacement therapy (ERT) would otherwise be offered.

	This recommendation applies only in circumstances where the approved Patient Access Scheme (PAS) is utilised or where the list/contract price is equivalent or lower than the PAS price.
Gaucher Disease	
Drug Treatment	**Recommendation**
Eliglustat (Cerdelga®)	**NICE HST5: Eliglustat for treating type 1 Gaucher disease** • Eliglustat is recommended within its marketing authorisation for treating type 1 Gaucher disease, that is for long-term treatment in adults who are cytochrome P450 2D6 poor, intermediate or extensive metabolisers. • Eliglustat is only recommended when the company provides it with the discount agreed in the patient access scheme.
Velaglucerase alfa (VPRIV®)	**AWMSG advice no 1214: Velaglucerase alfa (VPRIV®)** • Velaglucerase alfa (VPRIV®) is recommended as an option for use within NHS Wales for long-term enzyme replacement therapy in patients with type 1 Gaucher disease. • This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.
Mucopolysacharidoses (MPS)	
Drug Treatment	**Recommendation**
Laronidase (Aldurazyme®)	**AWMSG advice: Laronidase (Aldurazyme®)** AWMSG would support the use of laronidase (Aldurazyme®) within NHS Wales subject to the following restrictions: **1.** Use of laronidase will be in accordance with: • the drug's Summary of Product Characteristics (SPC), subject to paragraph 2 below, and • agreed uniform service standards and clinical guidelines. **2.** AWMSG recognises that some current uses of laronidase fall outside the drug's SPC (such as its short term use before and after Bone

	Marrow Transplantation). Any use which falls outside the SPC will only be supported if part of an approved clinical trial. Patients from Wales will be treated at either: • the specialist centre for the treatment of lysosomal storage disorders at the University Hospital of Wales, Cardiff, or • one of the six centres which will be nationally designated and funded by the Department of Health under the auspices of the National Specialised Commissioning Advisory Group to provide a service for patients with lysosomal storage disorders. **3.** Having received appropriate consent, details of patients receiving treatment will be entered into the Registry for MPS1 held by the Society for Mucopolysaccharide Diseases (the MPS Society)
Elosulfase alfa (Vimizim®)	**NICE HST19: Elosulfase alfa for treating mucopolysaccharidosis type 4A** • Elosulfase alfa is recommended, within its marketing authorisation, as an option for treating mucopolysaccharidosis type 4A (MPS 4A) for people of all ages. It is only recommended if the company provides elosulfase alfa according to the commercial arrangement.

Glycogen Storage Disease II (Pompe Disease)	
Drug Treatment	**Recommendation**
Alglucosidase alfa (Myozyme®)	**AWMSG advice: Use of alglucosidase alfa (Myozyme™) within NHS Wales** Alglucosidase alfa (Myozyme™) is recommended, within its marketing authorisation, for the treatment of Pompe disease in accordance with the licensed indication but with the specific restriction: • That there is presently insufficient evidence of clinical effectiveness in late-onset disease and AWMSG does not endorse its use in this group of patients at this stage AWMSG endorsed the use of alglucosidase alfa (Myozyme™), but with the specific exclusions of alglucosidase alfa (Myozyme™) in Late Onset Pompe disease of the adult Onset form (Adult Onset disease) because of insufficient evidence of clinical effectiveness. AWMSG recommends that: • Patients receiving alglucosidase alfa (Myozyme™) will be entered into the Pompe registry. • Treatment will be administered under the supervision of a physician experienced in the management of Pompe disease or other neuromuscular disorders. • Treatment will be administered according to agreed guidelines at appropriate centres.
Avalglucosidase alfa (Nexviadyme®)	**NICE TA821: Avalglucosidase alfa for treating Pompe disease** Avalglucosidase alfa (AVAL) is recommended, within its marketing authorisation, as an option for treating Pompe disease in babies, children, young people and adults, only if the company provides AVAL according to the commercial arrangement.

2.2. Continuation of Treatment

Healthcare professionals are expected to review a patient's health at regular intervals to ensure they are demonstrating an improvement or stabilisation of their health due to the treatment being given. This includes optimisation of medicine doses recognising any changes in weight. The patient will continue to receive treatment if they are demonstrating an improvement or stabilisation of their health.

2.3. Stopping Criteria

The prescribing clinician should discontinue drug treatment for LSDs if:

- The patient's condition deteriorates whilst receiving drug treatment following maximum escalation of care.
- The patient will not, or cannot comply with the treatment regime after suitable support has been provided by the prescribing clinician, including homecare service provision where applicable.

If treatment is discontinued, the prescribing team will be responsible for stopping the Blueteq form (see section 2.6 Blueteq and reimbursement).

2.4. Exclusion Criteria

WHSSC do not approve funding of drug treatments for lysosomal storage disorders (LSDs) as listed in Table 2 as they have either not been subject to a Health Technology Appraisal (HTA) by NICE/AWMSG or have been previously reviewed and did not receive a positive recommendation.

Table 2: **WHSSC non-commissioned LSD drug treatments**

Lysosomal Storage Disorder	Drug Treatment
Gaucher type I	**Miglustat** (Zavesca®) **Imiglucerase** (Cerezyme®)
MPS II (Hunters syndrome)	**Idursulfase** (Elaprase®)
MPS VI (Maroteaux-Lamy syndrome)	**Galsulfase** (Naglazyme®)
MPS VII (Sly syndrome)	**Vestronidase alfa** (Mepsevii®)
Niemann-Pick type C	**Miglustat** (Zavesca®)

WHSSC will continue to fund drug treatments listed in Table 2, for people with a lysosomal storage disorder approved for treatment (via the WHSSC prior approval process) prior to the publication of this revised policy (2022). Retrospective Blueteq forms will not be required for this group of patients.

2.5. 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.

2.6. Blueteq and reimbursement

The drug treatments listed within this policy as being commissioned, will only be funded for patients registered via the Blueteq system. Where the patient meets the criteria listed within section 2.1.2 and the referral is received by an agreed centre, a Blueteq form should be completed for approval.

If the drug treatment is stopped, it is the responsibility of the prescribing team to discontinue the Blueteq form.

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 listed within this commissioning policy, they should contact WHSSC (e-mail: WHSSC.IPC@wales.nhs.uk). They will be asked to demonstrate they have an appropriate MDT in place.

2.7. Patient Pathway

See annex i

2.8. Service Providers

- **Childrens service**

  Department of Inherited Metabolic Disease
  Children's Hospital for Wales
  Heath Park
  Cardiff
  CF144XN

- **Adult service**

  Department of Metabolic Medicine
  University Hospital of Wales
  Heath Park
  Cardiff
  CF144XN

- **Adult service**

  Department of Metabolic Medicine
  Wrexham Maelor Hospital
  Croesnewydd Rd,
  Wrexham
  LL13 7TD

Onward referral of patients may be considered by the lead clinicians, for each of these services in Cardiff. Shared care arrangements will be made for patients from North Wales with the National Commissioning Group (NCG) designated centres, in Manchester and Salford, if clinically required.

The Childrens service at the Department of Inherited Metabolic Disease, Children's Hospital for Wales, is supported by the IMD team at Birmingham Children's Hospital.

2.9. Clinical Outcome and Quality Measures

The Commissioned provider should work to written quality standards and provide monitoring information to the lead commissioner.

The centre should enable the patient's, carer's and advocate's informed participation and to be able to demonstrate this. Provision should be made for patients with communication difficulties and for children, teenagers and young adults.

2.10. 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.

Clinicians considering treatment should:

- discuss all alternative treatments with the patient
- advise the patient of any side effects 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.

3. Evidence

WHSSC is committed to regularly reviewing and updating all of its commissioning policies based upon the best available evidence of both clinical and cost effectiveness.

- **NICE Guidance**
  www.nice.org.uk/guidance/

- **AWMSG Guidance**
  www.awmsg.nhs.wales/medicines-appraisals-and-guidance/

3.1. Date of Review

This document is scheduled for review in 2026 where we will check if any new evidence is available. If no new evidence or intervention is available the review date will be progressed.

If an update is carried out, the policy will remain extant until the revised policy is published.

4. 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).

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 for each commissioned medicines included in this commissioning policy by NICE/AWMSG during their medicines appraisal process. For further details, please refer to the NICE/AWMSG website.

5. Putting things Right

5.1. 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 fo. 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.

5.2. Individual Patient Funding Request (IPFR)

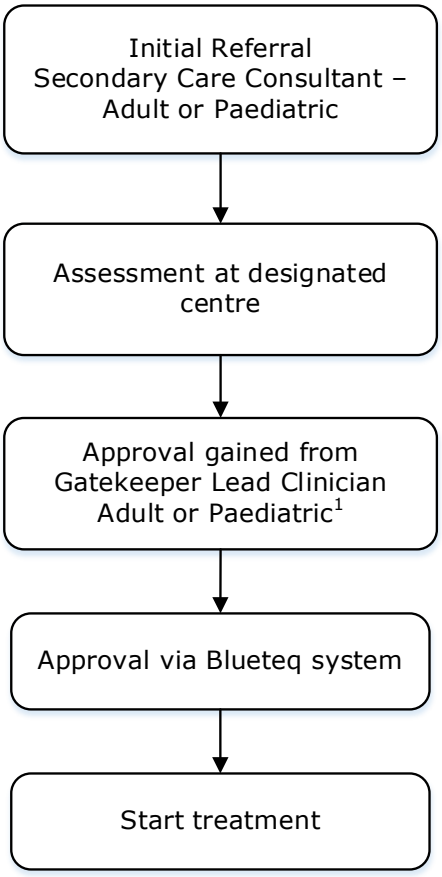
If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All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

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, and 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 Patient Pathway



[1] Onward referral of patients may be considered by the gatekeeper/lead clinicians, for each of these services in Cardiff. Shared care arrangements will be made for patients from North Wales with the NCG designated centres, in Manchester and Salford, if clinically required.

Annex ii Codes

Code Category	Disease Area	Code	Description
ICD-10	Metabolic disorders	E70-E88	Metabolic disorders
		E76	Disorders of glycosaminoglycan metabolism
		E75	Disorders of sphingolipid metabolism and other lipid storage disorders
	Pompe Disease	E74.02	Pompe Disease
		E76.01	Hurler Syndrome
		E76.02	Hurler-Scheie Syndrome
		E76.03	Scheie Syndrome
	Mucopolysaccharidosis type II	E76.1	Hunter Syndrome
	Morquio A Mucopolysaccharidoses	E76.210	Morquio Syndrome
	Other mucopolysaccharidoses	E76.29	Maroteaux- Lamy Syndrome
	Other mucopolysaccharidoses	E76.2	Sly Syndrome
	Gaucher Disease	E75.22	Gaucher Disease
	Fabry(-Anderson) Disease	E75.21	Fabry disease
	Niemann-Pick disease type C	E75.242	Niemann-Pick Type C

Annex iii Abbreviations and Glossary

Abbreviations

WHSSC Welsh Health Specialised Services

AWMSG All Wales Medicines Strategy Group

NICE National Institute for Health and Care Excellence

IPFR Individual Patient Funding Request

SMC Scottish Medicines Consortium

LSD Lysosomal storage disorders

ERT Enzyme replacement therapy

SRT Substrate reduction therapy

Glossary

Individual Patient Funding Request (IPFR)
An IPFR is a request to Welsh Health Specialised Services Committee (WHSSC) to fund an intervention, device or treatment for patients that fall outside the range of services and treatments routinely provided across Wales.

Welsh Health Specialised Services Committee (WHSSC)
WHSSC is a joint committee of the seven local health boards in Wales. The purpose of WHSSC is to ensure that the population of Wales has fair and equitable access to the full range of Specialised Services and Tertiary Services. WHSSC ensures that specialised services are commissioned from providers that have the appropriate experience and expertise. They ensure that these providers are able to provide a robust, high quality and sustainable services, which are safe for patients and are cost effective for NHS Wales.