GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Commissioning Policy: CP224

Allogeneic Haematopoietic Stem Cell Transplant (HSCT) for people of all ages with Sickle Cell Disease (SCD)

November 2021

Version 1.0

PARCH - RESPECT

PARTNERIAETH - PARTNERSHIP

GWELLA AC ARLOESI - IMPROVEMENT & INNOVATION

Document information	
Document purpose	Commissioning Policy
Document name	Allogeneic Haematopoietic Stem Cell Transplant for People with Sickle Cell Disease (all ages)
Author	Welsh Health Specialised Services Committee
Publication date	November 2021
Commissioning Team	Cancer & Blood
Target audience	Chief Executives, Medical Directors, Directors of Finance
Description	NHS Wales routinely commission this specialised service in accordance with the criteria described in this policy
Document No	CP224
Review Date	2024

Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) commission Allogeneic Haematopoietic Stem Cell Transplant (HSCT) for people of all ages with Sickle Cell Disease (SCD) in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed this clinical condition and the options for its treatment. It has considered the place of Allogeneic Haematopoietic Stem Cell Transplant 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 Allogeneic Haematopoietic Stem Cell Transplant (HSCT) for people of all ages with Sickle Cell Disease (SCD) who are resident in Wales. This proposed 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

Sickle cell disease (SCD)

This is an inherited disease which causes lifelong anaemia, episodes of severe pain and other problems including an increased risk of stroke, renal failure, heart and lung problems and leg ulcers. It is associated with a reduced life expectancy, severe chronic health problems and reduction in quality of life.

Allogeneic Haematopoietic Stem Cell Transplantation (Allo-HSCT)

This involves treating the recipient with chemotherapy to destroy their own bone marrow stem cells. The recipient will then receive donor stem cells which replace their blood cells with donor blood cells. The clinical effects of SCD are variable but those with severe sickle cell disease will require ongoing treatments and frequent hospital admissions. Allo-HSCT is the only currently available therapy that can cure sickle cell disease.

1.2 Aims and Objectives

This policy aims to define the commissioning position of WHSSC on the use of Allo-HSCT for people with SCD.

The objectives of this policy are to:

- ensure commissioning for Allo-HSCT is evidence based
- ensure equitable access to Allo-HSCT
- define criteria for people with SCD to access treatment
- improve outcomes for people with SCD.

1.3 Epidemiology

SCD is a hereditary disease affecting around 12,500-14,000 individuals in the UK. SCD can affect anyone although it predominantly affects people of African and Caribbean backgrounds. There are approximately 50 adults and 38 children with SCD in Wales. Around 3-4 babies could be born in Wales each year with SCD[1]. Nearly all SCD affected children born in Wales will be identified by neonatal testing or newborn bloodspot screening

[1] These figures were provided to WHSSC by the UHW haematology service in September 2021

programmes[2]. Other new patients may present through immigration or late diagnosis.

1.4 Current Treatment

Allo-HSCT is already commissioned for children with severe SCD having sibling and haploidentical donors[3]. This policy document covers all ages and formalises the existing commissioning position for the use of allo-HSCT in children with SCD.

Current treatments are supportive rather than curative. They include simple treatments such as long-term antibiotics to prevent infection, preventative vaccines and pain relief for the acute pain episodes. Apart from supportive measures there are two common therapies available for sickle cell disease – hydroxycarbamide and long-term blood transfusions.

Other therapies are crizanlizumab[4] (FDA and EMA approved for >16 years), voxelotor (FDA approved for people over 12 years old, EMA approval assessment underway) and L-glutamine (FDA people over 5 years old, EMA rejected). Hydroxycarbamide is by far the cheapest and reduces the incidence of pain episodes and the incidence of some of the other complications (e.g. acute chest syndrome). Hydroxycarbamide has several side effects including reduction of blood counts and some patients are not able to tolerate it or do not respond to it. Some patients are treated with long term blood transfusion therapy; this is the best treatment to prevent strokes but has many side effects. Some patients do not tolerate blood transfusion.

1.5 Proposed Treatment

1.5.1 Adults

Previously it has been thought that allogeneic transplantation would not be suitable for adults who may have more co-morbidities and therefore not tolerate the procedure. Recent improvements in transplant protocols that make them suitable for adults now mean this option can be considered. The rationale for proposing allogeneic stem cell transplantation for adults is to provide a potentially curative option for those people with severe disease in whom other treatments have failed or have not been tolerated.

Access to allo-HSCT for adults can be divided by donor type and these will be considered separately as the outcomes from each type vary.

[2] http://www.newbornbloodspotscreening.wales.nhs.uk/home
[3] British Society of Blood and Marrow Transplantation and Cellular Therapy: UK Paediatric BMT HSCT Indications Table
[4] WHSSC Policy Position PP234 Crizanlizumab for preventing sickle cell crises in sickle cell disease in people aged 16 or over

Human leucocyte antigen (HLA) matched sibling HSCT

This is associated with the best survival figures and the lowest rates of adverse outcomes such as rejection and graft versus host disease (GvHD). The outcomes following this type of HSCT are better than outcomes with standard care for those with severe SCD. Only about 20% of patients will have a HLA matched sibling donor and will be able to have this type of HSCT.

Haploidentical HSCT

This usually uses stem cells from a parent or a non- HLA matched sibling HSCT. Most people will therefore have a donor. It is potentially associated with higher rates of rejection and GVHD than HLA matched sibling HSCT. If the transplant is rejected the patient continues to have sickle cell disease. There is currently insufficient evidence to support this type of transplant as standard care for those adults with severe SCD.

Matched unrelated donor HSCT

This type of transplant is associated with worse outcomes and more adverse outcomes in terms of GVHD than HLA matched sibling HSCT. There is currently insufficient evidence to support this type of transplant as standard care for those adults with severe SCD.

1.5.2 Children

Allo-HSCT is commissioned for children according to the British Society of Blood and Marrow Transplantation and Cellular Therapy: UK Paediatric BMT HSCT Indications Table,

1.6 What NHS Wales has decided

WHSSC has carefully reviewed the evidence of Allo-HSCT for SCD. We have concluded that there is enough evidence to fund Allo-HSCT, within the criteria set out in section 2.1.

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).

- **WHSSC policies and service specifications**
  - CP79 Haematopoietic Stem Cell Transplantation Service Specification
  - PP145 Haematopoietic Stem Cell Transplantation Policy Position

  - CP179 Sickle Cell Disorders, Thalassaemia Disorders and other Rare Hereditary Anaemias: all ages Service Specification
  - CP91 Extracorporeal Photopheresis (ECP) for the Treatment of Chronic Graft versus Host Disease in Adults
  - PP234 Crizanlizumab for preventing sickle cell crises in sickle cell disease in people aged 16 or over, Policy Position Statement

- **Relevant NHS England policies**
  - 190138P Clinical Commissioning Policy: Allogeneic Haematopoietic Stem Cell Transplant for adults with sickle cell disease

- **British Society for Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT)**
  - BSBMT Indications for Adult BMT
  - BSBMT Indications for Children BMT

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of Allogeneic Haematopoietic Stem Cell Transplant (HSCT) for people of all ages with Sickle Cell Disease (SCD), in line with the criteria identified in this policy.

2.1 Inclusion Criteria

2.1.1 Adults

Patients who meet **any one** of the following criteria could be considered for HSCT:

- Clinically significant neurologic vascular event or deficit lasting >24 hrs and confirmed radiologically.
- History of ≥2 acute chest syndrome despite optimum treatment with hydroxycarbamide (HC) or transfusion therapy.
- History of ≥3 severe pain crises or other acute complications per year despite the institution of supportive care measures (optimum treatment with HC or transfusion therapy). Other acute complications would include acute hepatopathy or splenic sequestration or acute priapism.
- Administration of regular transfusion therapy, either by simple transfusion or exchange transfusion with the aim to prevent severe sickle complications by maintaining a low Sickle Haemoglobin (HbS)%.
- Patients assessed as requiring transfusion but with red cell allo-antibodies/very rare blood type, rendering it difficult to continue/commence chronic transfusion.
- Patients requiring HC/transfusion for treatment of SCD complications who cannot tolerate either therapy due to significant adverse reactions.
- Established and related end organ damage relating to sickle cell disease, including but not limited to progressive sickle neurovasculopathy and hepatopathy.

To determine fitness to proceed to HSCT, patients should have **all** of the following:

- Karnofsky score ≥60
- Cardiac function: LVEF ≥45% or shortening fraction ≥25%
  Note: For subjects who have history of iron overload or serum ferritin levels >1000 ng/mL, a cardiac MRI is required. Cardiac T2* <10 ms results in exclusion.
- Lung Function: FEV1, FVC and DLCO ≥50%
- Renal function: EDTA GFR ≥40 ml/m^2/1.73m^2
- At least one first degree relative willing to act as a donor and confirmed as fully matched sibling donor.

Bone marrow or peripheral blood stem cells may be used as donor stem cell sources. Use of umbilical cord cells is not recommended as a donor stem cell source.

2.1.2 Children

Allo-HSCT will be routinely commissioned for children with SCD according to the UK Paed BMT HSCT Indications Table.

2.2 Exclusion Criteria

Allo-HSCT will not be commissioned for any patients not meeting the criteria in 2.1.1 above.

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.

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 policy 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 Patient Pathway (Annex i)

- Patient is assessed as meeting criteria by a physician with expertise in SCD.
- Patient is referred to a transplant physician for evaluation and discussion of eligibility for transplant.
- Patient is discussed at the National Haemoglobinopathy Panel and a decision made as to whether the patient can proceed or not proceed to transplant. The MDT should consist of physicians experienced in the treatment of SCD and transplantation.
- Patient admitted to an agreed JACIE accredited transplant centre. Transplant centre must have access to an experienced sickle team who are able to attend on site for joint review of patients.
- Patient discharged to transplant and sickle service for ongoing follow-up.

2.6 Designated Centres

- Imperial College Healthcare NHS Trust
  St Mary's Hospital
  Praed Street
  London
  W2 1NY

2.7 Exceptions

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 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

2.8 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to the lead commissioner.

The centre must 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.

Complete data must be submitted to the BSBMT registry for all transplants carried out by centres in England. This will enable better evaluation of clinical outcomes broken down by patient and disease-related variables. All centres must undergo regular JACIE inspection. All centres must provide the data required for the BMT Quality Dashboard. Audit requirements are described in more detail in the BMT service specification.

Outcome data for allogeneic transplants for sickle cell disease must be separately identifiable within the BSBMT database, and included within the annual BSBMT report to commissioners, which is fed back to participating centres.

It is a requirement that a complete data set is submitted to the European Society for Blood and Marrow Transplantation's Registry (EBMT)

To ensure shared practice and expertise, all providers will participate in an 'all ages annual confidential audit meeting' where the outcomes of all transplanted patients are discussed.

2.9 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.

In all other circumstances an IPFR must be submitted.

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.

Please refer to the NHS England Commissioning Policy for Allogeneic Haematopoietic Stem Cell Transplantation for Adults with Sickle Cell Disease for information on the evidence base.

3.1 References

190138P NHS England Commissioning Policy for Allogeneic Haematopoietic Stem Cell Transplantation for Adults with Sickle Cell Disease

3.2 Date of Review

This document is scheduled for review before 2024 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).

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.

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 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.

5.2 Individual Patient Funding Request (IPFR)

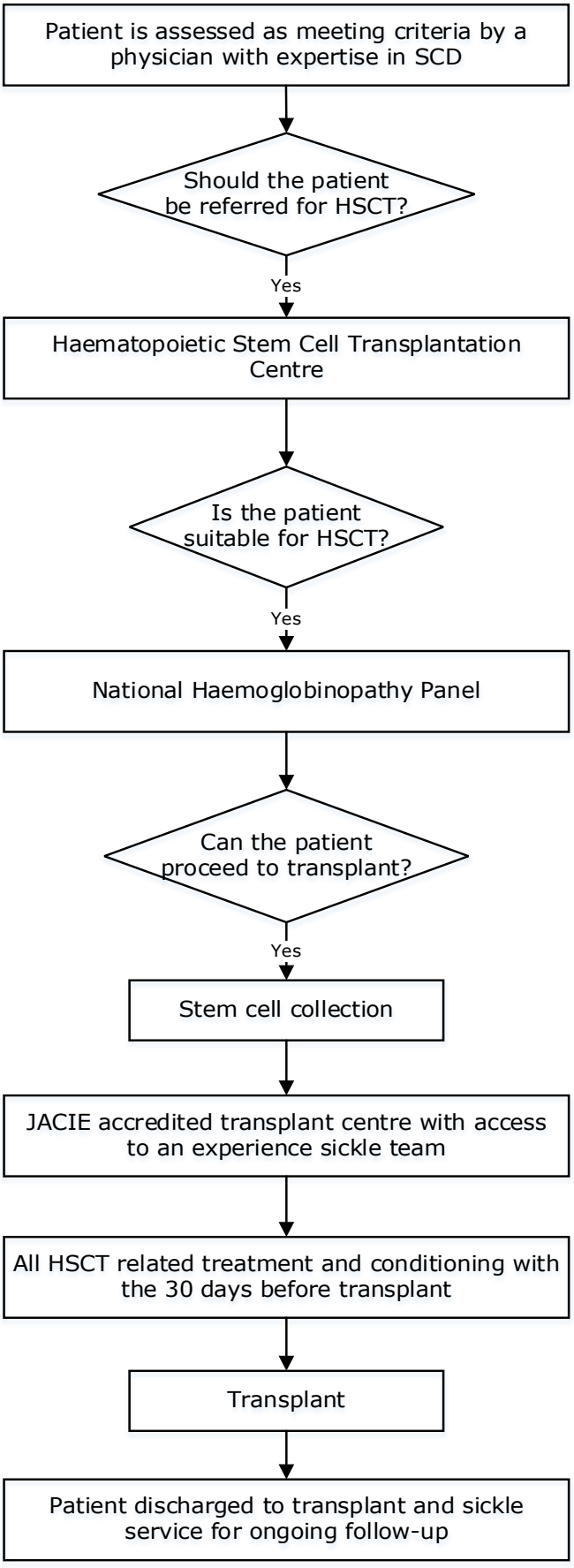
If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All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



Annex ii Codes

Code Category	Code	Description
OPCS	W342	Allograft of bone marrow NEC
	W343	Allograft of bone marrow from sibling donor
	W344	Allograft of bone marrow from matched unrelated donor
	W345	Allograft of bone marrow from haploidentical donor
	W346	Allograft of bone marrow from unmatched unrelated donor
	W348	Other specified graft of bone marrow
	W349	Unspecified graft of bone marrow
	W991	Allograft of cord blood stem cells to bone marrow
	W998	Other specified graft of cord blood stem cells to bone marrow
	W999	Unspecified graft of cord blood stem cells to bone marrow

Annex iii Abbreviations and Glossary

Abbreviations

Allo-HSCT	Allogeneic Haematopoietic Stem Cell Transplantation
BSBMTCT	British Society of Blood And Marrow Transplantation and Cellular Therapy
DLCO	Diffusing Capacity of the Lungs for Carbon Monoxide
EDTA	Ethylenediamine tetraacetic acid
FEV_1	Forced Expiratory Volume
FVC	Forced Vital Capacity
GFR	Glomerular Filtration Rate
HSCT	Haematopoietic Stem Cell Transplantation
IPFR	Individual Patient Funding Request
LVEF	Left Ventricular Ejection Fraction
SCD	Sickle Cell Disease or Sickle Cell Disorder
WHSSC	Welsh Health Specialised Services Committee

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.