GIG CYMRU NHS WALES
Cyd-bwyllgor Comisiynu
Joint Commissioning Committee

Autologous haematopoietic stem cell transplantation for people aged 18 years and over with previously treated relapsing multiple sclerosis

Commissioning Policy: CP247

November 2024
Version: 1.0

Document information	
Document purpose	Commissioning Policy
Document name	Autologous haematopoietic stem cell transplantation for people aged 18 years and over with previously treated relapsing multiple sclerosis
Author	NHS Wales Joint Commissioning Committee
Publication date	November 2024
Commissioning Team	Cancer and Blood
Target audience	Chief Executives, Medical Directors, Directors of Finance,
Description	NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy
Document No	CP247
Review Date	November 2027

GIG CYMRU NHS WALES | Cyd-bwyllgor Comisiynu Joint Commissioning Committee

Contents

Policy Statement

NHS Wales Joint Commissioning Committee (NWJCC) will commission autologous haematopoietic stem cell transplantation for people aged 18 years and over, with previously treated relapsing multiple sclerosis in accordance with the criteria outlined in this document.

In creating this document NWJCC has reviewed this clinical condition and the options for its treatment. It has considered the place of autologous haematopoietic stem cell transplantation 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.

Welsh Language

NWJCC 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, NWJCC 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

NWJCC 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 NWJCC commitment.

Disclaimer

NWJCC 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.

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

1. Introduction

This policy has been developed as a Policy for the planning and delivery of autologous haematopoietic stem cell transplantation (auto-HSCT) for people aged 18 years and older with previously treated relapsing multiple sclerosis (RMS) resident in Wales. This service will only be commissioned by the NHS Wales Joint Commissioning Committee (NWJCC) and applies to residents of all seven Health Boards in Wales.

1.1 Plain Language Summary

Multiple sclerosis (MS) affects the nerves in the brain and spinal cord, also known as the central nervous system (CNS). The most common symptoms are fatigue, muscle weakness, difficulty walking, bladder problems, pins and needles, dizziness, muscle spasms, pain, visual disturbances and difficulties with memory. **Relapsing (or relapsing remitting) multiple sclerosis (RMS or RRMS)** is the most common form of MS which people are first diagnosed with. There is a pattern of relapses (symptoms getting worse)[1] with this type of MS.

Haematopoietic stem cells are found mainly in the bone marrow, although small numbers circulate in the blood. They develop into the different types of blood cells including some cells which are part of the immune system. They are produced in large numbers to continually replenish the blood and immune system as other cells die and are replaced.

The aim of **autologous haematopoietic stem cell transplantation (auto-HSCT)** is to replace or reboot the body's immune system so that it no longer attacks the myelin or causes inflammation in the brain and spinal cord. High doses of chemotherapy are used to wipe out the existing immune system, which is then rebuilt using stem cells collected from the blood beforehand.

1.2 Aims and Objectives

This policy aims to define the commissioning position of NWJCC on the use of auto-HSCT for people aged 18 years and over with RMS.

The objectives of this policy are to:

- ensure commissioning for the use of auto-HSCT is evidence based
- ensure equitable access to auto-HSCT
- define criteria for people with RMS to access treatment
- improve outcomes for people with RMS

[1] Multiple Sclerosis Trust

1.3 Epidemiology

There are roughly 1.3 million people worldwide who have relapsing MS out of 2.3 million with any type of MS[2]. In the UK, there are over 130,000 people living with MS and each year nearly 7,000 people are newly diagnosed. This means around 1 in every 500 people in the UK lives with MS and each week over 130 people are diagnosed with MS[3]. In Wales, it is estimated that 5,600 have MS[3]. When they were first told they had MS, 85% were diagnosed with the relapsing type.

In the UK people are most likely to find out they have MS in their 30s, 40s and 50s. The first signs of MS often start years earlier. MS affects nearly three times as many women as men for reasons not yet understood.

1.4 Current Treatment

Standard treatment for RMS are immune system targeted disease modifying therapies (DMTs) that are most likely to be effective for the relapsing phase of MS but are less effective as the disease progresses. Examples include alemtuzumab, cladribine, ocrelizumab and natalizumab[4]. Due to the lack of effective therapies for progressive MS, it is important to treat RMS early and aggressively so that disease progression can be delayed or halted.

1.5 Proposed Treatment

Autologous haematopoietic stem cell transplantation is a procedure where haematopoietic stem cells are harvested from the peripheral blood or bone marrow of the patient. The patient is then treated with chemotherapy and immunosuppressive therapy to destroy the self-reactive immune cells. The harvested stem cells are used to repopulate the patient's immune system.

Due to the many complex steps involved in delivering this treatment, the European Society for Blood and Marrow Transplantation (EBMT) Autoimmune Diseases Working Party and the Joint Accreditation Committee of the International Society for Cellular Therapy and EBMT (JACIE) recommends that only units with expertise both in the management of MS and AHSCT should offer AHSCT.

[2] Understanding Relapsing Remitting MS, MS Society
[3] MS in the UK 2020, MS Society
[4] NICE: Multiple Sclerosis

1.6 What NHS Wales has decided

NWJCC has carefully reviewed the evidence of Auto-HSCT for RMS. We have concluded that there is enough evidence to fund the use of Auto-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).

- **NHS Wales Joint Commissioning Committee policies and service specifications**
  - CP79 Haematopoietic Stem Cell Transplantation Service Specification
  - PPS142 Haematopoietic Stem Cell Transplantation Policy Position

- **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 NHS Wales Joint Commissioning Committee will approve funding of autologous hematopoietic stem cell transplant (Auto-HSCT) for people aged 18 years and over with relapsing multiple sclerosis (RMS) in line with the criteria identified in this policy.

2.1 Inclusion Criteria

Patient selection for Auto-HSCT for RMS should be made by a neurology MDT and confirmed by a second consultant neurologist experienced in managing MS.

Auto-HSCT will be commissioned for people with a confirmed diagnosis of RMS, **and**:

- are aged 18 years and over[5*]
- be independently mobile with an Expanded Disability Severity Status (EDSS) score ≤ 6.0 **and**
- have clinical or radiological evidence of inflammatory activity (a relapse as confirmed by a clinician) **or** have at least one new T2 lesion or gadolinium enhancing lesion in MRI within the last 12 months, compared to a reference scan not older than 36 months and preferably within the last 24 months from the date of the eligibility review while adequately treated by a high efficacy disease modifying therapy of similar efficacy to alemtuzumab, natalizumab and ocrelizumab.

2.2 Exclusion Criteria

HSCT is not suitable for patients with primary or secondary progressive disease.

2.3 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.

2.4 Patient Pathway (Annex i)

The patient pathway can be divided into a number of stages: prior to treatment, treatment and post treatment.

[5] People aged 16 and over and those who are transitioning from Paediatric services and meet the inclusion criteria may be referred.

2.4.1 Prior to treatment

Prior to treatment a two-stage decision process should be followed:

- ***Is the patient eligible for treatment?***

  This question will be considered at the local neurology MDT and confirmed by a second consultant neurologist with expertise in MS.

  Patients who meet the inclusion criteria set out in 2.1 above who are agreed by the local neurology MDT and confirmed by a second consultant neurologist with expertise in MS as being eligible for treatment are then referred to the designated treatment centre.

  Is the patient likely to tolerate treatment?

- This question will be considered by consultant transplant haematologists at the designated treatment centre. The patient will be assessed by the transplant team and a decision is made based on the individual.

2.4.2 Treatment

Auto-HSCT will take place at a designated JACIE accredited centre where there is also access to neurologists with experience in MS (see 2.5 below).

2.4.3 Post-treatment

Due to the intensive nature of Auto-HSCT, patients require several months to recover. During this time patients also undergo monitoring. This follow up will be organised by the treating centre in conjunction with the referrer and local services. Initially this is focused on prevention and treatment of infections as well as early post-transplant complications. Over time regular monitoring focuses on the disease course as well as late post-transplant complications[6].

2.5 Designated Centres

Sheffield Teaching Hospitals NHS Foundation Trust:
Royal Hallamshire Hospital
Broomhill
Glossop Road
Sheffield
S10 2JF

[6] Health Technology Wales Evidence Appraisal Report: Autologous haematopoietic stem cell transplantation to treat people with previously treated relapsing-remitting multiple sclerosis, August 2020

The Clatterbridge Cancer Centre NHS Foundation Trust
65 Pembroke Place
Liverpool
L7 8YA

2.6 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: Individual Patient Funding Requests

2.7 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.

2.8 Responsibilities

Referrers should:

- inform the patient that this treatment is not routinely funded outside the criteria in this policy
- complete the notification form in Annex iii
- 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 NWJCC for the treatment.

In all other circumstances an IPFR must be submitted.

3. Evidence

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

The evidence of clinical and cost effectiveness to support the decision by NWJCC to commission autologous haematopoietic stem cell transplantation for people with previously treated relapsing multiple sclerosis was based on guidance published by Health Technology Wales (HTW) in July 2020[7].

The evidence review was presented to the WHSSC (now NWJCC) Prioritisation Panel in July 2020 who recommended autologous haematopoietic stem cell transplantation for people with previously treated relapsing multiple sclerosis as a high priority. Funding was approved in the 2021-2024 WHSSC (now NWJCC) Integrated Commissioning Plan.

HTW guidance evidence summary

One randomised control trial (RCT), the Multiple Sclerosis International Stem Cell Transplant Trial (MIST), was included in the evidence review. Four systematic reviews were also identified. Ten additional primary studies were identified that had not been included in the systematic reviews.

The evidence in the primary studies is limited by the variability in treatment protocols (conditioning regimens), patient inclusion criteria, outcome definitions, lack of comparator treatment and short follow up periods.

The evidence extracted from the RCT, the relevant studies in the systematic reviews and the ten additional primary studies related to numerous relevant clinical outcomes (over twenty). Two measures reported most widely (including by the RCT) are 'no evidence of disease activity' (NEDA) and expanded disability status scale (EDSS). NEDA-3 was attained by 76% and 70% of patients at 24 months and five years post-AHSCT respectively (two studies, RRMS population) with NEDA-4 reached by 50% at five years post-AHSCT. A third study described NEDA-3 attainment by 90%, 70% and 60% of RRMS patients at one-, two- and three-years post-AHSCT respectively.

A non-randomised study reported NEDA-3 to be higher for AHSCT compared with alemtuzumab for RRMS patients while the MIST RCT also found NEDA-3 to be significantly higher for AHSCT compared with DMTs. EDSS decreased from baseline with AHSCT in all studies, with the exception of one, that reported this endpoint (seventeen studies). EDSS

[7] Autologous haematopoietic stem cell transplantation to treat people with previously treated relapsing remitting multiple sclerosis. Health Technology Wales, July 2020.

also decreased where reported for RRMS specifically (six studies). The MIST RCT found the difference in EDSS between AHSCT and DMTs at one-year post-AHSCT to be statistically significantly in favour of AHSCT.

No studies evaluating the cost-effectiveness of AHSCT for previously treated relapsing remitting multiple sclerosis were identified. Therefore, HTW developed a cost-utility analysis to determine the cost effectiveness of AHSCT compared with DMTs for people with highly active RRMS.

A Markov model was used to estimate costs and quality-adjusted life years (QALYs) over a five-year time horizon, from the UK NHS and personal social services perspective. Costs and QALYs were discounted at 3.5% per year as recommended in the NICE reference case. AHSCT was found to be dominant (more effective and less costly than DMTs) in most modelled scenarios with some notable exceptions. In these scenarios, AHSCT was still found to be more effective but it was also found to be more costly. When compared against all DMTs, the ICER was found to be £38,359 per QALY gained indicating that AHSCT was not cost effective as the ICER was above the threshold of £20,000 per QALY gained. When compared against natalizumab only, the ICER was found to be £2,741 per QALY gained indicating that AHSCT was cost-effective as the ICER was below the threshold of £20,000 per QALY gained. Probabilistic sensitivity analysis (PSA) was conducted to assess the combined parameter uncertainty in the model. In this analysis, the mean values that were utilised in the base case are replaced with values drawn from distributions around the mean values. The model is run 10,000 times. At a threshold of £20,000 per QALY, AHSCT was found to have a 100% probability of being cost-effective while standard care with DMTs had a 0% probability of being cost-effective.

Pan-London MS-AHSCT Collaborative Group

The criteria for commissioning presented in section 2 of this policy were adapted from those developed by the pan-London MS-AHSCT Collaborative Group. Agreement to adapt these criteria is part of a formal collaboration between NWJCC and the pan-London MS-AHSCT Collaborative Group. NWJCC would like to thank the Group for sharing their documentation and acknowledge their input into this process.

3.1 References

- Autologous haematopoietic stem cell transplantation for previously treated, relapsing-remitting multiple sclerosis, HTW 2020

3.2 Date of Review

This document is scheduled for review before November 2027, 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 NHS Wales Joint Commissioning 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 NWJCC.

5.2 Individual Patient Funding Request (IPFR)

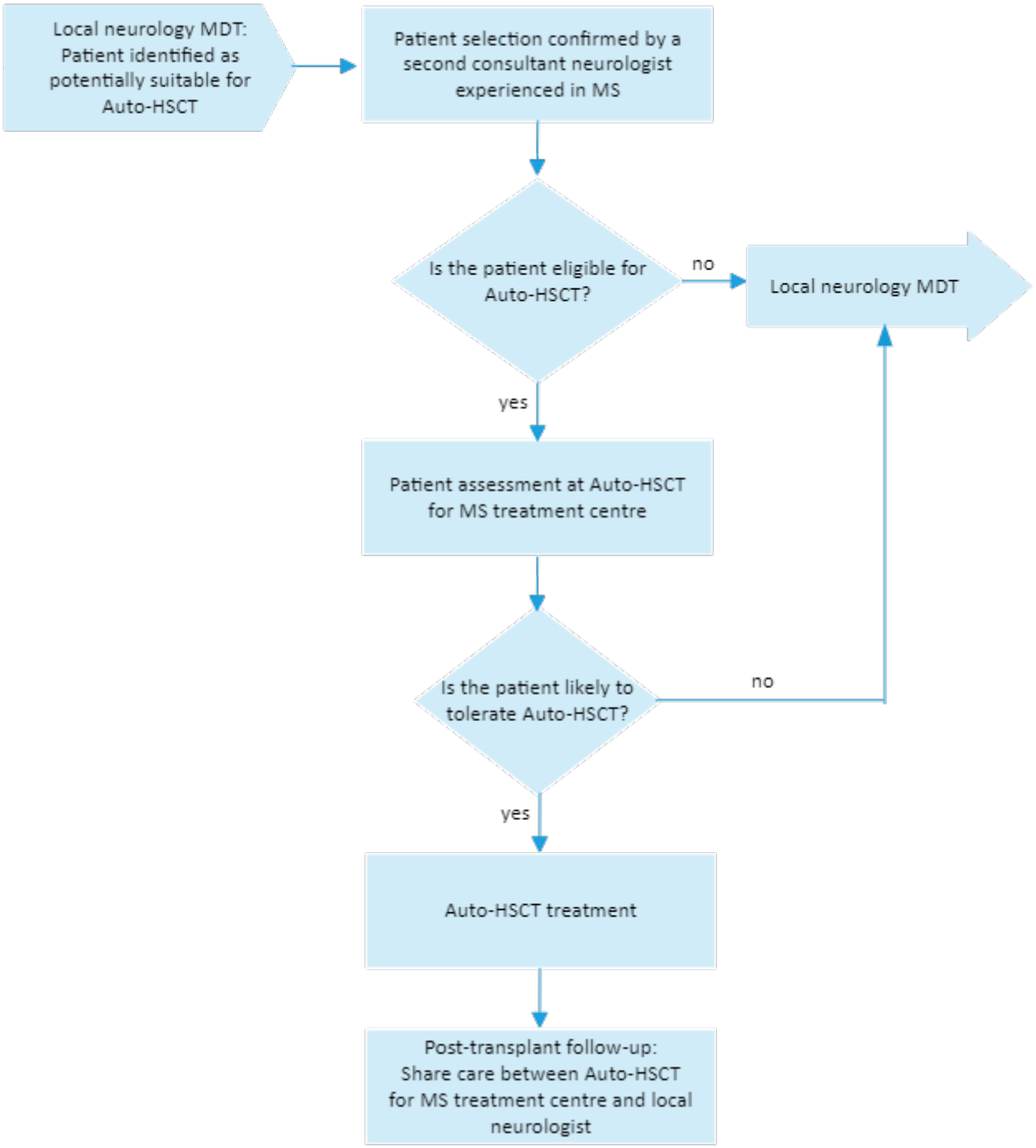
If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All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

Annex i Patient Pathway



Annex ii Codes

Code Category	Code	Description
ICD-10	G35	Multiple Sclerosis
OPCS	W341	Autograft of bone marrow

Annex iii Auto-HSCT for RMS Notification Form

Please use this form to notify NWJCC of patients referred to an Auto-HSCT for RMS centre for consideration for treatment.

Details of clinician making the referral:	**Details of clinician patient is being referred to:**
Name:	Name:
Designation:	Specialty:
Address:	Address:
Postcode:	Postcode:
Telephone number:	Telephone number:
Fax number:	Fax number:
Email:	Email:

Details of patient's GP:
Name:
Address:
Postcode:
Telephone number:
Fax number:
Email:

Patient Details	
Forename:	Surname:
Address:	Date of birth:
	Telephone number:
	NHS number:
Postcode:	Hospital number:

Clinical details
Details of diagnosis (alternatively, please attach a copy of the referral letter to the Auto-HSCT for RMS service provider):

Medical history and current clinical status (alternatively, please attach a copy of the referral letter to the Auto-HSCT for RMS service provider).
What plans are in place to ensure the patient is returned to local services following the treatment/intervention requested?
Has advice been sought from other colleagues?

Clinicians signature: **Date:**

Please return this form with a copy of the referral letter to: Patient Care Team NWJCC, Unit G1, Treforest Industrial Estate, Pontypridd, CF37 5YL Email: nwjccipc@wales.nhs.uk or Fax: 01443 843247 If you have any questions, please telephone 01443 443443 ext.78123

Annex iv Abbreviations and Glossary

Abbreviations

DMT	Disease Modifying Therapies
IPFR	Individual Patient Funding Request
MS	Multiple Sclerosis
NWJCC	NHS Wales Joint Commissioning Committee
RMS	Relapsing Multiple Sclerosis
WHSSC	Welsh Health Specialised Services Committee

Glossary

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

NHS Wales Joint Commissioning Committee (NWJCC)
NWJCC is a joint committee of the seven local health boards in Wales. The purpose of NWJCC is to ensure that the population of Wales has fair and equitable access to the full range of Tertiary Services. NWJCC ensures that services within our portfolio 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.