NHS
Commissioning Board

Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation

April 2013

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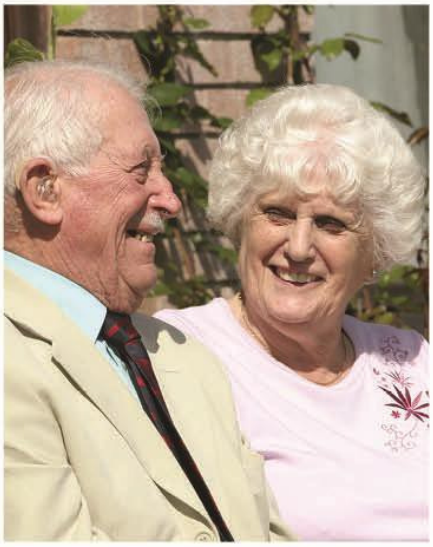

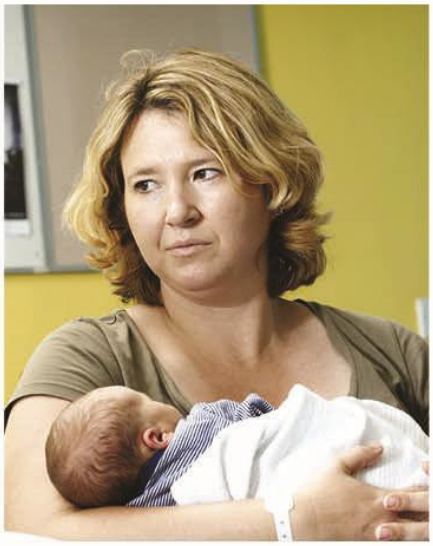

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NHS Commissioning Board

Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation

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Prepared by the NHS Commissioning Board Clinical Reference Group for

Blood and Marrow Transplant (BMT)

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Contents

Policy Statement

The NHS Commissioning Board (NHS CB) will commission haematopoietic stem cell transplantation for the clinical conditions and their sub-groups indicated in accordance with the criteria outlined in this document.

In creating this policy the NHS CB has reviewed this clinical condition and the options for its treatment. It has considered the place of this 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.

This policy document outlines the arrangements for funding of this treatment for the population in England.

Equality Statement

The NHS CB has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012.The NHS CB is committed to ensuring equality of access and non-discrimination, irrespective of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex (gender) or sexual orientation. In carrying out its functions, the NHS CB will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which they are responsible, including policy development, review and implementation.

Plain Language Summary

Haematopoietic stem cell transplantation is also known as blood and marrow transplantation (BMT). It is used to treat a wide spectrum of disorders. It is broadly divided into two main groups: autologous and allogeneic transplantation.

Allogeneic haemopoietic stem cell transplantation (HSCT) is used to treat carefully selected patients with a range of malignant and non-malignant blood-related disorders and other specific disorders of the immune system. It involves replacing the bone marrow stem cells of a patient following high-dose therapy, with stem cells from a tissue-type matched or mismatched donor.

Autologous transplantation uses the patient's own stem cells, which are harvested prior to high-dose therapy. It enables the patient to be treated with doses of chemotherapy which are higher than would be possible without subsequent replacement of the harvested cells, because the therapy destroys the patient’s remaining stem cell tissue.

The scientific evidence for these treatments is not clear cut, relying on clinical expertise and consensus. This policy will promote equity of access to treatment in England. It confirms the indications for which the NHS CB has agreed routine funding and the route for obtaining funding for conditions outside this policy.

1. Introduction

Haematopoietic stem cell transplantation (HSCT), also known as blood and marrow transplantation (BMT) is used to treat wide spectrum of haematological, and increasingly, non-haematological disorders. It is broadly divided into two main groups: autologous and allogeneic transplantation. These are explained in more detail in the next section.

Stem cell transplantation, particularly allogeneic transplantation, is a high cost and highly specialised procedure, performed by skilled and experienced transplant teams working in specialist centres. Allogeneic transplantation carries a relatively high mortality and morbidity, and these must be weighed against the potential longer-term survival benefits when considering a patient for transplantation. Rigorous patient selection is of paramount importance.

Because of the large number of possible indications for stem cell transplantation, the degree of variation in clinically important patient and disease parameters, and the diversity of conditioning and transplant regimes, it is extremely difficult to evaluate the clinical and cost-effectiveness of transplantation for every potential clinical condition. Moreover, age is an important factor in determining outcomes; thus the management of children and young people is very different to that in older adults. For all these reasons, current clinical practice in stem cell transplantation is largely based on clinical consensus and published case series.

For the above reasons, the development of a national commissioning policy requires a degree of pragmatism. Previous attempts to develop evidence-based policies have highlighted the paucity of good quality evidence from randomised controlled trials, and the small size and poor quality of the studies upon which current clinical guidelines are based.

There is a broad degree of clinical consensus concerning the BSBMT (British Society of Blood and Marrow Transplantation) recommendations on the clinical indications for BMT in adults, and these have until now formed the basis for most SCG commissioning policies for adult BMT. However, these have frequently been updated over the past 3 years, with the result that there are significant differences between the various Specialised Commissioning Group (SCG) policies.

Clinical practice in paediatric transplantation is mainly in line with the UK Paediatric BMT Group HSCT recommendations (November 2011), and in practice individual funding request for paediatric BMT are rarely declined by commissioners.

This policy document sets out the clinical indications for which autologous and allogeneic transplants will be commissioned routinely by the NHS Commissioning Board (NHS CB) for adults and children respectively. For a more detailed description of the transplantation services which will be commissioned and the service standards which should be met by transplant centres please refer to the BMT Service Specification.

The policy does not address the use of extra-corporeal photophoresis (ECP) for the treatment of chronic graft versus host disease (cGvHD), as this therapy is used for conditions other than GvHD, and is included within the scope of Rare Cancers. However, it is emphasised that the development of a commissioning policy for the use of ECP in treating cGvHD is a high priority.

2. Definitions

Allogeneic haemopoietic stem cell transplantation (HSCT) is used to treat carefully selected patients with a range of malignant and non-malignant haematological disorders and other specific disorders of the immune system. It involves replacing the bone marrow stem cells of a patient following high-dose therapy, with stem cells from a tissue-type matched or mismatched donor.

Patients require detailed pre-transplant assessment and investigations to assess their clinical status and fitness to proceed to transplant. The transplant procedure begins with 'conditioning' therapy (chemotherapy ± total body irradiation [TBI]) at a range of doses depending on the type and severity of disease being treated. The aim of conditioning is to:

- Kill leukaemia/tumour cells (in malignant diseases)
- Eradicate existing bone marrow tissue (in order to provide space for engraftment of transplanted donor stem cells)
- Suppress the patient's immune system, so as to minimise the risk of graft rejection

Bone marrow, peripheral blood or umbilical cord blood stem cells may be used as donor stem cell sources.

Autologous transplantation uses the patient's own stem cells, which are harvested prior to high-dose therapy. It is performed as part of dose escalation therapy, mainly in patients with lymphoma and myeloma, although it is also used in certain autoimmune and oncology cases. It enables the patient to be treated with doses of chemotherapy which are higher than would be possible without subsequent replacement of the harvested cells, because the therapy destroys the patient's remaining stem cell tissue.

3. Aim and Objectives

Aim

The policy document aims to specify the clinical indications and their subgroups for which autologous and allogeneic haematopoietic stem cell transplants will be commissioned routinely by the NHS Commissioning Board.

Objectives

- To optimise patient outcome after autologous and allogeneic stem cell transplantation
- To reduce variation in access to BMT
- To ensure that BMT is commissioned for those conditions for which there is acceptable evidence of clinical benefit and cost-effectiveness
- To promote the cost-effective use of resources
- To reduce unacceptable variation in clinical practice
- To ensure that experimental treatments are offered only in the context of properly conducted research.

4. Criteria for Commissioning

Adults

The BSBMT (February 2012) recommendations divide indications for BMT into four categories:

S = standard of care

CO = clinical option, can be considered after assessment of risks and benefits

D = developmental, further trials are needed

GNR = generally not recommended

- For the purposes of this commissioning policy ***first*** transplants for indications within categories S and CO (standard of care, and clinical option respectively) are accepted as established clinical practice, and will be commissioned routinely, without need for prior approval or Individual Funding Request (IFR). Repeat transplants for failure to engraft will also be commissioned routinely. However, ***repeat*** autologous or allogeneic transplants for relapsed disease will not be commissioned routinely unless explicitly recommended by the BSBMT guidelines (eg second autologous transplant for myeloma and POEMS).

- Transplants for indications within categories D and GNR will ***not*** be commissioned routinely, and commissioner agreement will need to be sought for transplantation of all cases falling within these categories
- BMT is not commissioned for any indication which is not listed below Commissioner agreement will therefore need to be sought for transplantation for all indications not specifically listed in this policy document

Disease category	Commissioning policy
CML	As per BSBMT indications for transplantation (February 2012)
Myeloma	As per BSBMT indications for transplantation (February 2012). Second autografts will be commissioned for myeloma, but third or subsequent autografts will not routinely be commissioned.
Other plasma cell dyscrasias	As per BSBMT indications for transplantation (February 2012). Second autografts will be commissioned for POEMS, but third or subsequent autografts will not routinely be commissioned.
AML	As per BSBMT indications for transplantation (February 2012)
ALL	As per BSBMT indications for transplantation (February 2012)
Hodgkin's Disease	As per BSBMT indications for transplantation (February 2012)
Mantle Cell Lymphoma	As per BSBMT indications for transplantation (February 2012)
Follicular lymphoma/ lymphoplasmacytoid lymphomas	As per BSBMT indications for transplantation (February 2012)
DLBCL	As per BSBMT indications for transplantation (February 2012)
Peripheral T Cell Lymphoma	As per BSBMT indications for transplantation (February 2012)
CLL	As per BSBMT indications for transplantation (February 2012)
Aplastic Anaemia	As per BSBMT indications for transplantation (February 2012)
Myelodysplastic Syndrome	As per BSBMT indications for transplantation (February 2012)
Ewing's Sarcoma	As per BSBMT indications for transplantation (February 2012)
Neuroblastoma	As per BSBMT indications for transplantation (February 2012)
Germ Cell Tumour	As per BSBMT indications for transplantation (February 2012)
Soft tissue sarcoma	As per BSBMT indications for transplantation (February 2012)
Breast, ovary, lung, renal carcinoma	Not commissioned routinely. Commissioner agreement must be sought.
Sickle cell disease	Not commissioned routinely. Commissioner agreement must be sought.
Myelofibrosis	As per BSBMT indications for transplantation (February 2012)
Multiple sclerosis	As per BSBMT indications for transplantation (February 2012)
Systemic sclerosis	As per BSBMT indications for transplantation (February 2012)
Crohn's disease	As per BSBMT indications for transplantation (February 2012)
Systemic lupus erthematosis	As per BSBMT indications for transplantation (February 2012)
Rheumatoid arthritis	As per BSBMT indications for transplantation (February 2012)
Immune cytopenias (ITP, AIHA Evan's syndrome)	Not commissioned routinely. Commissioner agreement must be sought.
Chronic inflammatory demyelinating polyneuropathy (CIDP)	Not commissioned routinely. Commissioner agreement must be sought.

Children

The UK Paediatric BMT Group HSCT recommendations (December 2011) divide indications for BMT into four categories:

S = standard of care

CO = clinical option, can be considered after assessment of risks and benefits

D = developmental, further trials are needed

GNR = generally not recommended

- For the purposes of this commissioning policy ***first*** transplants for indications within categories S and CO (standard of care, and clinical option respectively) are accepted as established clinical practice, and will be commissioned routinely, without need for prior approval or Individual Funding Request (IFR). Repeat transplants for failure to engraft will also be commissioned routinely. However, ***repeat*** autologous or allogeneic transplants for relapsed disease will not be commissioned routinely, and commissioner agreement must be sought for such procedures
- Transplants for indications within categories D and GNR will ***not*** be commissioned routinely, and commissioner agreement will need to be sought for transplantation of all cases falling within these categories
- BMT is not commissioned for any indication which is not listed below. Commissioner agreement will therefore need to be sought for transplantation for all indications not specifically listed within this policy document.

Disease Category	Commissioning Policy
AML	As per UK Paediatric BMT Group recommendations (November 2011)
CML	As per UK Paediatric BMT Group recommendations (November 2011)
CLL	As per UK Paediatric BMT Group recommendations (November 2011)
T Cell NHL	As per UK Paediatric BMT Group recommendations (November 2011)
Lymphoblastic B cell NHL	As per UK Paediatric BMT Group recommendations (November 2011)
Anaplastic Large Cell Lymphoma	As per UK Paediatric BMT Group recommendations (November 2011)
Burkitt NHL	As per UK Paediatric BMT Group recommendations (November 2011)
Hodgkin's disease	As per UK Paediatric BMT Group recommendations (November 2011)
Myelodysplasia	As per UK Paediatric BMT Group recommendations (November 2011)
Immuno-deficiencies	Selected indications; as per UK Paediatric BMT Group recommendations (November 2011)
Inborn errors of metabolism	Selected indications; as per UK Paediatric BMT Group recommendations (November 2011)
Haemo-globinopathies	As per UK Paediatric BMT Group recommendations (November 2011)
Bone marrow failure Acquired aplastic anaemia Constitutional monocytopenia Fanconi anaemia Dyskeratosis congenita Diamond-Blackfan syndrome	As per UK Paediatric BMT Group recommendations (November 2011)
Solid tumours: Neuroblastoma Primitive neuroectodermal tumour (medulloblastoma) Atypical Teratoid Rhabdoid Tumour (CNS) Germ cell tumour Ewings sarcoma Wilms tumour Multisystem Langerhans cell histiocytosis	As per UK Paediatric BMT Group recommendations (November 2011)
Autoimmune disease	Selected indications; as per UK Paediatric BMT Group recommendations (November 2011)

Policy development

Clinical practice continues to evolve, and it is important that the commissioning policy is reviewed regularly and updated to reflect current evidence. The following topics have been submitted for review as a priority:

- Planned tandem transplants
- Repeat transplants following relapse of disease
- Transplants for solid tumours
- Transplants for autoimmune diseases
- ECP for cGvHD
- Paediatric BMT
- Double cord transplants (added at the request of the Clinical Assurance Group)

In the interim, and for other indications, requests for transplantation of in cases which do not meet the policy criteria will be considered on an individual basis by commissioners.

Individual funding requests

It is recognised that HSCT is a highly complex clinical area, and that consideration of requests for transplantation in cases which fall outside the commissioning policy requires specialised knowledge and experience. All such requests should be supported by detailed clinical information in order that they may be reviewed by an expert clinical panel including transplant physicians and commissioners.

The Specialised Services Clinical Reference Group (CRG) proposes that IFR panels should seek advice from an expert clinical panel when considering requests for HSCT falling outside the commissioning policy.

Research

It is recognised that involvement in clinical trials is an integral part of high quality service provision in stem cell transplantation. Treatment provided as part of NCRI-approved trials will be commissioned routinely for patients who meet the commissioning policy criteria, provided that there are no excess treatment costs to commissioners. (For example, trials comparing different conditioning regimens will be supported, provided there is no significant cost differential between the treatment arms.)

However, pure research will not be funded with resources diverted from the provision of routine transplant services. Transplantation undertaken as part of research into the treatment of conditions not covered by the commissioning policy will not be commissioned routinely, irrespective of whether or not the trial has NCRI approval. Similarly, any excess treatment costs relating to trial participation will not be met by the NHS CB unless prior approval has been given.

5. Patient pathway

The patient pathway is described in detail in the BMT service specifications for adults and children respectively.

The BMT commissioning pathway commences with the decision to transplant, and ends 100 days following the transplantation procedure. This pathway does not preclude shared-care arrangements for post-transplant follow-up between the transplant centre and local haemato-oncology providers, where this has been agreed between providers. Beyond 100 days, commissioning responsibility will automatically return to the patient's Clinical Commissioning Group.

6. Governance arrangements

The governance arrangements are described in detail in the BMT service specifications for adults and children respectively. All providers of HSCT must have JACIE accreditation.

7. Epidemiology and needs assessment

The data below are taken from the BSBMT Registry for transplants undertaken by UK centres. There are considerable year to year fluctuations in numbers, but an underlying increasing trend. In the ten year period 2001-2010 inclusive there has been an apparent 45% increase in the overall number of transplants performed annually. (NB This does not take account of probable improvements in reporting and data capture.)

Table 1: Number of transplants by transplant type 2001-2010 inclusive

Year	Allografts	Autografts	Total	% Increase
2001	879	1354	2233	
2002	922	1336	2258	1.1
2003	898	1481	2379	5.4
2004	983	1551	2354	6.5
2005	1069	1664	2378	8.1
2006	1144	1563	2706	-1.2
2007	1196	1569	2765	2.2
2008	1263	1676	2939	6.3
2009	1200	1623	2823	-3.9
2010	1321	1919	3240	14.7

Source: BSBMT Register

Table 2 below shows a breakdown of transplants by disease category for 2009. Myelomas and lymphomas remain the most common indications for autologous transplantation. Most allogeneic transplants are for acute leukaemias, followed by the lymphomas. This suggests that the great majority of current clinical indications for BMT are covered by the commissioning policy.

Table 2: Number of transplants by disease category and transplant type 2009

Indication	Allograft	Autograft	Total
Plasma Cell Disease	36	919	955
Lymphoma	204	584	788
Acute Leukaemia	508	8	516
MDS/MPS	176	1	177
Solid Tumour	8	103	111
Chronic Leukaemia	108	2	110
Primary Immune Deficiency	58	0	58
Bone Marrow Failure	52	0	52
Haemoglobinopathy	20	0	20
Inherited Disorders of Metabolism	15	1	16
Auto Immune Diseases	5	5	10
Other	10	0	10
Total	1200	1623	2823

Source: BSBMT Register

8. Evidence Base

Because of the large number of possible indications for stem cell transplantation, the degree of variation in clinically important patient and disease parameters, and the diversity of conditioning and transplant regimes, it is extremely difficult to evaluate the clinical effectiveness of transplantation for every potential clinical condition.

The BSBMT and UK Paediatric BMT Group HSCT recommendations are well referenced, although the quality of the evidence is generally poor, being based largely on case series.

There is very little published evidence as to the cost-effectiveness of BMT. The NHS Commissioning Board will include a program of evidence review and policy development for BMT within its work program.

9. Rationale behind the policy statement

Stem cell transplantation, particularly allogeneic transplantation, is a highly specialised procedure with significant opportunity costs. The evidence base for treatment is not clear cut, as described above, relying on clinical expertise and consensus. This policy will promote equity of access to treatment in England. It confirms the indications for which the NHS CB has agreed routine funding and the route for obtaining funding for conditions outside this policy.

10. Mechanism for funding

Funding will be made through the responsible area team.

The funding arrangements are described in detail in the BMT service specifications for adults and children respectively.

The NHS commissioning board funds all transplanted-related care from the point of decision to transplant until 100 days following transplantation.

HSCT is a highly complex clinical area, and consideration of requests for transplantation in cases which fall outside the commissioning policy requires specialised knowledge and experience. All such requests should be supported by detailed clinical information in order that they may be reviewed by an expert clinical panel including transplant physicians and commissioners.

11. Audit Requirements

Complete data must be submitted to the BSBMT registry for all transplants carried out by UK centres. This will enable better evaluation of clinical outcomes broken down by patient and disease-related variables.

All centres must undergo regular JACIE inspection.

Audit requirements are described in more detail in the BMT service specification.

12. Documents which have informed this policy

Pan Thames CYP Prior Approval Policy Procedure Form: Haematopoietic progenitor cell transplantation
Pan Thames Adult Prior Approval Policy Procedure Form: Haematopoietic progenitor cell transplantation
SWSCG Prior Approval – criteria based access– Form CBA.10.01
SC SCG Adult Haematopoietic Stem Cell Transplant Policy - September 2009
WM SCG Commissioning policy; Adult Haematopoietic Stem Cell Transplant. Draft May 2010
Yorkshire and Humber SCG BMT commissioning policy
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13. Links to other policies

To be confirmed – the IFR process will be critical to the success of the BMT policy, because we should expect a significant volume of funding requests to fall outside the policy. The CRG has recommended an expert panel to review these, but we need to retain commissioner/public health involvement in order to manage financial risk and identify new areas for policy development

14. Date of Review

April 2014