Clinical Commissioning Policy: Allogeneic Haematopoietic Stem Cell Transplant for Primary Immunodeficiencies (all ages)

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Policy Statement

NHS England will commission Allogeneic Haematopoietic Stem Cell Transplant for Primary Immunodeficiencies (all ages) in accordance with the criteria outlined in this document.
In creating this policy NHS England 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

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

Plain Language Summary

About tumours in children, teenagers and young adults
Primary Immunodeficiencies (PID) are a group of rare inherited diseases affecting the immune system. The roles of the immune system are to recognise and attack infection, respond to tissue damage, perform tumour surveillance and prevent autoimmunity. Patients with severe PID may be unable to produce normal levels of

immunoglobulins (antibodies), have dysfunctional immune cells, and are at risk of frequent and life-threatening infections, irreversible organ damage, severe inflammation, autoimmunity and cancer. Without treatment, many patients would die before reaching adulthood.

About current treatments

The current treatment for the most severe immune deficiencies in children is allogeneic haematopoietic stem cell transplantation (allo-HSCT). Allo-HSCT replaces the patient's own bone marrow stem cells with healthy stem cells from a donor. If successful, this cures the immune deficiency. The decision to treat a patient with allo-HSCT is made on an individual basis, depending upon the type and severity of the immune deficiency.

NHS England presently commissions allo-HSCT for adults with PID who meet the criteria outlined in the urgent clinical commissioning policy: https://www.england.nhs.uk/publication/urgent-clinical-commissioning-policy-statement-allogeneic-stem-cell-transplantation-for-adults-with-primary-immune-deficiency-disorders/

The alternative treatments to allo-HSCT include: immunoglobulin (IVIg) replacement; a range of different drugs to suppress abnormal immune responses and inflammation; chemotherapy for patients with cancers; antibiotics, anti-viral drugs, and anti-fungal drugs. In the absence of curative allo-HSCT, these are palliative treatments only.

About the new treatment

Allo-HSCT is not a new treatment in children with PID, but it has only recently been commissioned routinely for use in adults with PID. This policy document covers all ages. It supersedes the interim policy currently in place for adults with PID and formalises the existing commissioning position for the use of allo-HSCT in children with PID.

What we have decided

NHS England has carefully reviewed the evidence to treat primary immunodeficiencies with allogeneic haematopoietic stem cell transplantation. We have concluded that there is enough evidence to consider making the treatment available.

1 Introduction

Primary immunodeficiencies (PID) are a group of rare inherited diseases. These diseases are characterised by severe dysfunction of adaptive and / or innate immunity. Patients with severe PID may present with serious or life-threatening infections, auto-inflammatory disease, inflammation, organ damage as a result of treatment and repeated infections, and complications from a dysfunctional immune system such as malignancy.

Over 320 distinct immunodeficiencies have been described, including categories of 'unspecified' and 'other', with 20 specific diseases accounting for 90% of cases. All are rare, with many variations in clinical manifestations.

PID includes the following subgroups of conditions:

- Severe combined immune deficiency (SCID);
- Combined immune deficiency (CID);
- CID with associated features;
- Antibody deficiencies;
- Immune dysregulation, including haemophagocytic disorders, lymphoproliferative disorders, autoimmune disease, and early onset inflammatory bowel disease;
- Phagocytic cell disorders;
- Innate defects.

- PIDs can lead to ongoing recurrent, progressive, or life-threatening infection, autoimmunity and malignant disease. Even with optimal clinical management these complications sooner or later result in irreversible progression and premature death. Outcome data for some of the most common PIDs show that without transplantation there is a high disease burden and poor survival. For example, in X-linked lymphoproliferative disease, less than 25% of patients survive beyond 30 years, and the median survival of un-transplanted patients with Wiskott Aldrich Syndrome (WAS) is 4-20 years with very little data on survival beyond 30 years, indicating poor survival rates into adulthood (Pachlopnik Schmid et al 2011, Sullivan et al 1994).

- The current standard treatment for severe combined immune deficiencies (SCID) in children (18 years and under) is allo-HSCT. Allo-HSCT is a curative treatment for SCID, and without it no patients would survive to adolescence. For other types of PID in children the decision to treat with allo-HSCT is made on an individual basis. NHS England has routinely commissioned allo-HSCT in children in accordance with the 2011 BSBMT paediatric indications table, since 1993 it has been commissioned routinely as part of the Highly Specialised Service (HSS) for Severe Combined Immunodeficiency and Related Disorders (children).
- The standard alternative treatments for PID patients include: immunoglobulin (IVIg) replacement therapy for patients with B cell deficits; systemic immunosuppressive therapy for patients with auto-inflammatory/immune dysregulation complications; chemotherapy for patients with PID-associated malignancies and broad-spectrum antimicrobials (including anti-virals and anti-fungals) for all patients with susceptibility to infections.
- Currently, other than allo-HSCT, the only alternative curative therapy for patients with PID is gene therapy. However, gene therapy, which utilises autologous HSCT with gene-corrected stem cells, is currently only available for four selected monogenic immunodeficiencies, and mainly in the context of clinical trials at present.

Allo-HSCT replaces the patient's own bone marrow stem cells with healthy stem cells isolated from an appropriately tissue-type matched or mis-matched donor. Asthe inherited genetic mutation in PID affects immune cells derived from bone marrow stem cells, replacing the mutation carrying stem cells with healthy stem cells has the potential to cure the immune deficiency.

Allo-HSCT is a high-cost and specialised procedure performed by skilled and experienced transplant teams working in specialist centres. The procedure itself carries risks of mortality and morbidity, and these must be weighed against the potential longer-term survival benefits and opportunity for cure, when considering a patient for transplantation. Patients therefore undergo careful selection by multi-disciplinary transplant teams and only a proportion of patients will be suitable for transplant. This proportion will be much smaller in adults than in children. The

decision to proceed to allo–HSCT is based on clinical features, immune cell numbers and function, infectious and non-infectious complications and anticipated clinical course without transplantation. The risks of transplant are increased considerably in patients who have already sustained significant damage to their vital organs (for example to kidneys or lungs) and in patients with uncontrolled infection or inflammation.

Advances in allo-HSCT design have significantly improved safety of the procedure, facilitating its more recent application to adult PID. Compared with the paediatric experience, much smaller numbers of allo-HSCT for adult PID have been reported. Overall, reported survival rates, event free survival, transplant-related deaths, chimerism and immune reconstitution are comparable between adults and children undergoing allo-HSCT for PID.

- This policy covers all ages. It is intended to supersede the urgent policy statement currently in place for adults with PID, and to provide a formal policy position to support the existing routinely commissioned highly specialised service for children.

2 Definitions

Allogeneic Haematopoietic stem cell transplantation (**HSCT** – also known as BMT): A procedure which replaces the patient's own blood stem cells and immune system with those from a healthy donor, enabling the establishment of normal immune system functions.

Autoimmunity: A misdirected immune response that occurs when the immune system goes awry and attacks the body itself.

Chronic Active Epstein-Barr virus (CAEBV): a life-threatening multi-system inflammatory disorder driven by aberrant response to EBV infection.

Gene Therapy: The introduction of normal genes into cells in place of missing or defective ones in order to correct genetic disorders.

Haemophagocytic Lymphohistocytosis (HLH): a life-threatening multi-system inflammatory disorder that requires intensive treatment.

Primary immunodeficiency: A group of rare inherited disorders of the immune system which cause serious, debilitating and often life-threatening diseases. Although many patients with Primary Immunodeficiency will have a clearly defined genetic aetiology, others will remain genetically undefined.

3 Aims and Objectives

This policy considered: NHS England's position on commissioning Allogeneic Haematopoietic Stem Cell Transplant for Primary Immunodeficiencies for all ages. This policy aims to:

- Specify the clinical indications for which allo-HSCT will be commissioned routinely by NHS England for patients with Primary Immunodeficiency.

The objectives were to:

- Review the evidence base via evidence reviews to identify the clinical effectiveness and safety of allo-HSCT for patients of all ages with PID.
- Develop a documented clinical commissioning policy for the existing routinely commissioned allo-HSCT service for PID in children.

Define the subgroups of patients with PID for whom allo-HSCT will be commissioned routinely.

4 Epidemiology and Needs Assessment

Over 320 different genetic forms of PID are described, all of which are rare. The estimated prevalence of PID in the UK is around 4500 patients. Most patients with severe combined immune deficiency (SCID) present shortly after birth and require immediate intervention, but other forms of immune deficiency may present in later childhood or adulthood.

From British Society of Bone and Marrow Transplant (BSBMT) data between 2013 and 2016, 60-68 people per year received allo-HSCT for PID in the UK. These transplants were mainly in children, but a small number in adults have been funded through this period based on the assessment of individual cases. The Urgent Clinical Commissioning Policy Statement: Allogeneic stem cell transplantation for adults with

Primary Immune Deficiency disorders published in March 2018 has resulted in around 10-15 transplants per year in adults. It is estimated that the implementation of an ‘all ages’ clinical commissioning policy for PID will result in a total of 75-85 transplants per year for PID.

5 Evidence Base

NHS England has concluded that there is sufficient evidence to support the routine commissioning of this treatment for the indication.

NHS England has undertaken two evidence reviews in PID. The first was a review of the evidence for allo-HCST for PID covering all ages and a second review considered the evidence for allo-HSCT specifically in adult PID patients.
The summaries from both reviews are combined below to allow direct comparison between published data in all ages (predominantly paediatric) and adults.

Evidence

- **All Ages Evidence:** The evidence review found 16 uncontrolled studies with 100 or more patients. Six of these included patients with any PID and ten focused on one type of PID e.g. SCID or Wiskott-Aldrich syndrome (WAS). Five of the 16 studies included patients who were more than 18 years old at HSCT. No studies compared allo-HSCT with alternative treatment strategies.
- **Adult Specific Evidence:** Twelve uncontrolled studies were included in this evidence review (Albert et al 2018; Fox et al 2018; Jin et al 2018; Leiding et al 2018; Parta et al 2017; Shah et al 2017; Fu et al 2016; Oshima et al 2015; Wehr et al 2015; Grossman et al 2014; Güngör et al 2014; Spinner et al 2014). Four studies reported outcomes for adults or adults/adolescents (Fox et al 2018; Jin et al 2018; Fu et al 2016; Grossman et al 2014) and the remaining eight studies had mixed populations of adults and children from which data on outcomes for adult patients were extracted. Study sample sizes ranged from four to 29 and median follow-up (when reported) ranged from 14 months to five years. No studies compared allo-HSCT with alternative treatment strategies.

Clinical Effectiveness

Overall Survival

- **All Ages Evidence:** (15 uncontrolled studies; n=5,043): Survival after allo-HSCT, reported as overall survival or for a fixed term (e.g. five years), ranged from 62% to 90% but was mostly over 70%. Some studies reported survival for sub-groups of patients with rates generally higher for patients who received allo-HSCT in more recent years (e.g. after 2000) or who received genotypically matched donor cells. One study reported nine-year survival for a sub-group of patients who had survived more than two years after allo-HSCT as 92% (confidence intervals not reported). In multivariate analysis common risk factors significantly associated with survival included age at allo-HSCT (favouring younger ages), donor type (favouring matched sibling donors) and infection prior to allo-HSCT (favouring no infection).

- **Adult Specific Evidence:** (11 studies, total n=158; range 4 to 29). Overall survival ranged from 54% to 100% and was at least 80% in eight of the 11 studies. For the seven studies reporting median follow-up for overall survival this ranged from 14 months to five years. One study described overall survival for eight patients who received allo-HSCT (88%) and 10 patients who did not receive allo-HSCT (20%) (p=0.006). No studies reported 95% confidence intervals (CI).

- Event-free survival (4 studies, total n=68; range 4 to 29). Event-free survival ranged from 71% to 100% and was at least 90% in three of the four studies (95%CI not reported). For the three studies reporting median follow-up this ranged from two to five years.

Engraftment

- **All Ages Evidence:** (eight uncontrolled studies; n=2,189): Engraftment rates ranged from 72% to 96% but were mostly over 80%. Some studies reported neutrophil and platelet engraftment separately with rates ranging from 76% to 89%.

- **Adult Specific Evidence:** (11 studies, total n=141; range 4 to 29). The reporting of this outcome varied. Nine studies reported graft failures/ rejections[1]. In five studies there were no graft failures or rejections. In four studies the proportion of graft failures ranged from 8% to 50%. More of these were secondary graft failures (six cases) than primary graft failures (three cases). Median time to neutrophil engraftment[2] was between 12 and 15 days in four studies. In three studies, median time to platelet engraftment (defined as >20 x 10^9/L for seven consecutive days) was between 13 and 21 days and was 14 days in a fourth study (defined as ≥50 x 10^9/L). A further study reported median time to white blood cell viability as 11.5 days and median time to platelet engraftment as 13 days (without further definition of these outcomes).

Chimerism (the presence of donor cells)

- **All Ages Evidence:** (three uncontrolled studies; n=683): In one study (n=194) the rate of mixed chimerism 12 months or more after allo-HSCT was 28% (confidence intervals not reported). Donor type affected chimerism with one study reporting that significantly fewer patients from mismatched related donors had full[3] or mixed chimerism (39%) compared to matched sibling donors (80%) or other donors (71%) (n=240; p<0.001). **Adult Specific Evidence:** (8 studies, total n=106; range 4 to 29). The reporting of this outcome varied with different cut-off values and timescales for assessing 'complete' or 'full' chimerism. For example, in one study 94% of patients achieved complete chimerism (donor DNA >90%[4]) and in another study 48% achieved multi-lineage[5] full donor chimerism (donor DNA ≥97%[6]). Most studies reported chimerism rates of 100% or around 97% to 99% for almost all patients.

Immune Reconstitution

- **All Ages Evidence:** (eight uncontrolled studies; n=1,365): Studies reported various T and B lymphocyte outcomes after allo-HSCT; generally reporting

normalisation of cell counts in at least 60% of patients. Factors significantly affecting immunologic reconstitution in multivariate analyses were donor type, conditioning regimen and degree of donor of chimerism. The proportion of patients that did not require intravenous immunoglobulin (IVIg) at follow-up varied between studies from 14% to 89%. In one multivariate analysis factors significantly increasing long-term requirement for IVIg included the ARTEMIS gene defect, poor T-cell reconstitution, requirement of an additional transplant procedure and allo-HSCT from a haploidentical donor ($p<0.05$). In another multivariate analysis independence from IVIG therapy at two years was significantly associated with donor type (favouring matched siblings), and conditioning regimen (favouring reduced-intensity or myeloablative conditioning) ($p<0.05$).

- **Adult Specific Evidence:** (3 studies, total n=60; range 13 to 29). The reporting of this outcome varied. In the three individual studies respectively: 94% of patients had ceased immunosuppression and intravenous immunoglobulin; 89% of 9 patients who were receiving replacement pre-transplantation had ceased monthly immunoglobulin and 76% were not receiving immunosuppression at last follow-up; and 100% were off immunosuppressive medications.

Safety

Transplant Related Mortality (TRM)

- **All Ages Evidence:** (14 uncontrolled studies; n=5,716): Transplant related mortality (TRM) rates were 10 – 22% in all studies reported. One study (n=124) reported that 67% of deaths were transplant related. The most common cause of death following allo-HSCT was infection accounting for between 20% and 76% of deaths reported by studies. The most common causes of death in patients who did not receive HSCT (reported in one study; n=176) were malignancy and liver failure (both 27%) and infection (23%).
- **Adult Specific Evidence:** (2 studies, total n=47; range 18 to 29). Two studies reported a transplant-related mortality of 6% (one patient) and 14% (four patients) respectively. Causes of death were multi-organ failure secondary to sepsis (two patients), granulomatous meningoencephalitis (one patient), sepsis in the context of extensive chronic graft-versus-host disease (one patient) and adenovirus (one

patient). In a third study (n=4) mortality was 100%, however the study authors did not specify that these deaths were transplant-related.

Graft Versus Host Disease (GVHD)

- **All Ages Evidence:** The proportion of patients experiencing acute graft versus host disease (GVHD) (grades II to IV) at 100 days ranged from 19% to 25%. The proportion of patients experiencing acute GVHD (grades III to IV) at 100 days was 8%. The proportion of patients experiencing chronic GVHD at one or two years was 15 to 16%. In a multivariate analysis, decreased risk of GVHD was associated with use of a fully matched sibling donor and HSCT performed after 1998 (p=0.002).
- **Adult Specific Evidence:** (10 studies, total n=124; range 4 to 29). In nine studies the proportion of patients experiencing any acute GVHD ranged from 25% to 80%. Most patients experienced mild to moderate acute GVHD (grades I-II). In four studies with any cases of severe to life threatening acute GVHD (grade III-IV), the proportion of patients affected was between 3% and 21%. In one study there were no cases of moderate to life threatening GVHD but the proportion of patients experiencing mild acute GVHD, if any, was not reported. Seven studies reported the proportion of patients experiencing any chronic GVHD as ranging from 0% to 60%. In the two studies that specified the severity of the chronic GVHD, this was mild in most patients. One study did not report acute and chronic GVHD separately but reported that 21% of patients experienced severe or life threatening acute GVHD or extensive chronic GVHD.

Non-Infectious Transplant Related Complications

- **All Ages Evidence:** In one study (n=194) 46% of patients experienced complications in the year after allo-HSCT, with the most common being infection requiring hospitalisation (28%). In multivariate analysis, the only significant risk factor for complications was allo-HSCT from a mismatched family donor compared to a matched sibling donor (p=0.019). Another study (n=145) reported late clinical complications in 49% of patients who had survived more than two years after allo-HSCT with the most common being autoimmune manifestations

(24%), severe or recurrent infections (24%) and poor growth (29%). In multivariate analysis the factors significantly associated with late clinical complications included diagnosis of the ARTEMIS gene defect, viral infection prior to allo-HSCT, treatment with alkylating agents, requirement of an additional allo-HSCT procedure and requirement for IVIG ($p<0.01$).

- **Adult Specific Evidence:** (4 studies, total n=50; range 4 to 29). The proportion of patients experiencing transplant-related complications in three of the studies ranged from 46% to 75%, with a fourth study stating that there were four complications within their study population (n=4) but not specifying how many patients were affected. Only one of these studies reported median follow-up which was 31 months. Examples of complications included requirement for donor lymphocyte infusions, multi-organ failure, EBV post-transplant lymphoproliferative disease, renal impairment, prolonged cytopenias, severe transfusion-dependent thrombocytopenia, gastrointestinal haemorrhage and transient red-cell aphasia. No grading system was reported to indicate the seriousness of the complications reported.

Evidence Reported in All Ages Review

- Requirement for more than one allo-HSCT (eight uncontrolled studies; n=1,365): The proportion of patients who required more than one transplant ranged from 9% to 28%.
- Admission to intensive care (one uncontrolled study; n=111): 35% of patients required at least one ICU admission at a median of 31 days after allo-HSCT with the most common reason for admission being respiratory problems (59%). The median duration of admission was six days.
- Post-transplant malignancy (one uncontrolled study; n=2,266): 2.3% of patients developed a confirmed post-transplant malignancy. Of those, lymphoproliferative disorders were the most common malignancy (87%) with a median time to development of three months after allo-HSCT.
- Activities of daily living (two uncontrolled studies; n=346) assessed using Karnofsky/ Lansky scores: One study (n=176) reported that surviving patients treated with allo-HSCT had significantly higher median scores (100%) than patients who were not transplanted (90%), at last follow-up ($p<0.001$). Another

study (n=170) reported that for 84% of patients the score did not fall below 100% between two and 14 years after allo-HSCT. A further 13% had a lowest score of 90% at any time post allo-HSCT.

- Quality of Life (one uncontrolled study; n=111): One study reported that 86% of patients were considered to be healthy by their families with 36% reporting no health problems in the last two years. Where health problems were reported the most common (affecting ≥10%) were persistent rash (25%), sinusitis (20%), asthma (14%), diarrhoea (14%), attention deficit hyperactivity disorder (ADHD) (21%) and developmental delay (10%). 12% of patients were below the 3rd percentile for height and weight and 3% required special schooling.
- Centre assessment of post-HSCT outcome (one uncontrolled study; n=170): 53% of patients were considered ‘cured’, 18% were considered ‘improved’, 3% were considered ‘unchanged’ and 3% were considered ‘worse’. For 23% of patients the status was unknown. No definitions were provided for the categories used.

Evidence Reported in Adult Specific Review

- Post-transplant infection or viral reactivation (8 studies, total n=92; range 4 to 29). The proportion of patients experiencing any post-transplant infection or viral reactivation ranged from 20% to 100% with median follow-up (where reported) from 20.9 months to 3.5 years. More commonly reported infections included cytomegalovirus (CMV) reactivation (not infection), respiratory infections, sepsis, fungal infections and Epstein Barr virus (EBV) reactivation. No grading system was reported to indicate the seriousness of the infections.

Cost–effectiveness

- No studies assessing the cost-effectiveness of allo-HSCT for PID patients were identified.

Summary

- Descriptive results from uncontrolled studies provide evidence of generally positive outcomes for surviving patients after allo-HSCT with most studies reporting survival rates of over 70%. However, where reported, approximately half of surviving patients still experienced complications one and two years after allo-HSCT.

- Overall, the evidence base is limited to uncontrolled, mostly retrospective studies, which are at risk of selection bias. The limitations of the evidence base limit the strength of the conclusions that can be drawn.
  Although there are no formal studies assessing cost of palliative treatment, the majority of patients assessed as appropriate for allo-HSCT would have a minimal chance of survival without transplant.

6 Criteria for Commissioning

Inclusion Criteria

Allo-HSCT for PID will be commissioned routinely in the patients that meet any of following criteria:

1. All PID patients with a diagnosis of SCID. SCID is invariably fatal without allo-HSCT, and no patients would survive to adulthood.
2. Patients with a genetically defined PID which is known to be life-limiting, even with best supportive care.
3. Patients with genetically undefined combined immune deficiency (CID) with a history of opportunistic infections that predict a severe course and poor long-term outcome.
4. PID patients with bone marrow failure requiring long-term blood, platelet or cytokine support, who are at high risk of:

    a) uncontrolled infection or bleeding,
    b) transfusion-associated iron overload affecting liver or cardiac function OR
    c) alloimmunisation (a complication of transfusion that increases the risk of stem cell transplant rejection).

5. PID patients with, or at risk of, lymphoma or other cancers where delays in allo-HSCT will increase the risk of treatment resistance or relapse/cancer progression.
6. Patients with haemophagocytic lymphohistocytosis (HLH) or Chronic Active EBV (CAEBV), and who meet the criteria below. Allo-HSCT will be commissioned in cases where:

a. there is a documented genetic cause for PID and a high risk of HLH recurrence following treatment.
   OR
b. the genetic cause for the PID is not known, but where HLH or CAEBV is refractory to treatment or has relapsed following treatment.

7. Patients who have developed because of their PID vital organ complications or severe autoimmunity (e.g. to the kidney, lung or gut) and which have failed to respond to alternative treatments and where delay in treatment will lead to irreversible organ injury.

All patients must be assessed by the current regional paediatric MDTs or the adult national PID HSCT MDT in England and the recommendation recorded. This will standardise practice in England, permit sharing of experience in the clinical management of rare indications for transplant and provide patient specific advice regarding the risk of transplant and choice of conditioning regimens.

Exclusion Criteria

Allo-HSCT will not be commissioned for the following groups of patients:

1. Patients with non-severe PID, which is well managed with other modalities.
2. Patients who are not clinically fit for allo-HSCT.
3. Patients for whom the risks associated with the procedure out-weigh the potential benefits or outcome would be of marginal net benefit.
4. Patients for whom no suitable donor is available.

7 Patient Pathway

The patient pathway is described in detail in the BMT service specifications for adults (B04/S/a) and children (B04/S/b) respectively.
The BMT commissioning pathway commences with the decision to transplant, and ends 100 days following the transplant procedure. This pathway does not preclude shared-care arrangements for post-transplant follow-up between the transplant centre and local providers, where this has been agreed between providers.

Beyond 100 days, commissioning responsibility for immunology and/or haematology follow-up of adult patients will transfer to the patient's relevant Clinical Commissioning Group.

8 Governance Arrangements

The governance arrangements are described in detail in the BMT service specifications for adults (B04/S/a) and children (B04/S/b) respectively.

All providers of HSCT must be Joint Accreditation Committee-ISCT & EBMT (JACIE) accredited.

NHS England will commission from specialised HSCT centres, which must have the appropriate level of expertise, experience and infrastructure to deliver allo-HSCT in this patient population which must consist of Adult and Paediatric PID services. Decisions on patient treatment will be undertaken by the existing regional paediatric or national adult PID HSCT MDTs, with commissioner oversight of the governance arrangements.

A Combined All Ages National PID HSCT MDT will review the outcome of each case at bi-annual meetings, with commissioner involvement, and annually audit outcomes against this policy.

It may be considered more appropriate clinically for the procedure to be undertaken by an alternative HSCT centre, where this is advised by the Combined All Ages National PID HSCT MDT. Networking arrangements between providers must be in place, with the appropriate level of governance for shared care agreements.

Bone marrow, peripheral blood stem cells, or umbilical cord blood stem cells may be used as donor stem cell sources. Use of umbilical cord cells must be in line with the BSBMT UK Cord Blood Working Group Recommendations for donor selection. (Hough R et al, 2015).

9 Mechanism for Funding

Funding for stem cell transplantation is through the NHS England teams responsible for specialised commissioning. The funding arrangements are described in detail in the BMT service specifications for adults (B04/S/a) and children (B04/S/b) respectively.

10 Audit Requirements

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 PID 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 and to SCETIDE (Stem CEll Transplant for ImmunoDeficiencies in Europe); the comprehensive database for PID HSCT held in Paris and linked with the EBMT and ESID Registries.

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. This will be an extension of paediatric meeting where this presently occurs.

11 Documents which have informed this Policy

This document updates and replaces the interim urgent commissioning policy statement:

https://www.england.nhs.uk/publication/urgent-clinical-commissioning-policy-statement-allogeneic-stem-cell-transplantation-for-adults-with-primary-immune-deficiency-disorders/

Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised (January 2015). Reference: NHS England B04/P/a

BMT Service Specifications B04/S/a Haematopoietic Stem Cell Transplantation (adults) and B04/S/b Haematopoietic Stem Cell Transplantation (children) B04/S/b

12 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

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