Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	F01X01		
Policy Title	Haematopoietic Stem Cell Transplantation (HSCT)		
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Section K - Activity Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
K1 Current Patient Population & Demography / Growth	K 1.1 What is the prevalence of the disease/condition?	K1.1 This policy proposes to set out a **routine commissioning** position for haematopoietic stem cell transplantation (HSCT) for • **Adult patients with Lymphoplasmacytic Lymphoma (LL)** (of which Waldenström macroglobulinaemia (WM) is by far the most common type)[i] (LL/WM); and • **Teenage and young adult (TYA)[ii]** patients with immunodeficiencies, inborn errors, haemoglobinopathies and solid tumours. The epidemiology for the patient groups above is set out below.

		1) **LL/WM** is a form of non-Hodgkin Lymphoma (NHL).[iii] NHL has an estimated 20 year prevalence of c. 67,000 in 2014/15 in England.[iv] Only a small fraction (less than 2%) of patients diagnosed with NHL every year are registered as having LL/WM worldwide.[v] This results in an estimated prevalence of WM/LL in England in 2014/15 of c. 1,350 (or a prevalence rate of c. 2 per 100,000 of the total population living in England). [vi] 2) The prevalence for the four **TYA** indications is uncertain. Indicative figures can be obtained as follows: ▪ For **immunodeficiencies** the prevalence is unknown[vii]. A high level estimate for prevalence of primary immunodeficiencies (PID) in the overall population of England is in the region of c. 4,200.[viii] Specific estimates for TYAs could not be obtained as part of the review. If prevalence of PID is distributed homogeneously across age groups, this would imply a prevalence for TYA patients of c. 500 in 2014/15.[ix] ▪ Prevalence of **inborn errors** is difficult to quantify as there are over 200 different types of inborn errors of metabolism.[x] For reference, inherited metabolic disorders have a reported birth prevalence of 1in 784 live births.[xi] Ignoring mortality, this would translate to a prevalence of c. 8,700 among TYA patients in 2014/15. ▪ The prevalence of **haemoglobinopathies** in TYAs in England is estimated in the region of 1,200 in 2014/15.[xii] ▪ Finally, the 20 year prevalence of **solid tumours** in TYA patients is estimated at 13,100 in England in 2014/15.[xiii] This leads to an indicative, high level **prevalence for the TYA indications** considered in the region of c. 23,500 in 2014/15. As more detailed prevalence rates for the specific indications listed

		above could not be identified in most cases, these figures are illustrative only and likely over-estimate true prevalence.
	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 Of the population identified in K1.1, only a subset will be eligible for the treatment under the policy each year[xiv]: For the indications considered, a subset of adult patients with **LL/WM** is eligible for autologous stem cell transplants (autoSCT) and allogeneic haematopoietic stem cell transplants (alloSCT) respectively.[xv] It is estimated that c. 4 transplants for LL/WM were undertaken in 2014/15. [xvi] It is estimated that c. 6 – 7 patients would be eligible in 2014/15.[xvii] **TYA** with certain types of immunodeficiencies, inborn errors, haemoglobinopathies and solid tumours are also eligible to receive autoSCT and alloSCT according to paediatric guidance. [xviii] That is, paediatric recommendations for these four indications are extended to cover patients aged up to 24 years old. For this group, there are an estimated 25 patients[xix] eligible to receive HSCT in 2014/15, and this is likely to increase to c. 35 to 50 patients by 2020/21.[xx] Please refer to K1.7 for a split by indication.
	K1.3 What age group is the treatment indicated for?	K1.3 This treatment is indicated for adults for LL. Moreover, there are specific criteria for teenager and young adult (TYA) patients.[xxi]
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 LL can affect adults of any age but most people who develop LL are over the age of 65.[xxii] For the TYA indications, the population taking up treatment is per definition between the ages of 16-24.

	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Current activity for this population group is as follows: 1) For the **WM/LL** population, there are estimated to be around 4 transplants undertaken per year[xxiii], of which c. 25% would be allogeneic and 75% autologous.[xxiv] 2) For the **TYA** population, current activity for the indications is in the region of 26 currently, with a detailed break-up between indications of:[xxv] ▪ Immunodeficiencies: c. 4 transplants (all allogeneic) ▪ Inborn errors: no transplants ▪ Haemoglobinopathies: 4 transplants (all allogeneic) ▪ Solid tumours: 17 transplants (all autologous)
	K1.6 What is the projected growth of the disease/condition prevalence (prior to applying the new policy) in 2, 5, and 10 years?	K1.6 Were the prevalence rates in K1.1 to remain constant, then the future population group would be expected to grow in line with demographic growth. This could be in the region of: 1)For **LL/WM**: • ~ 1,365 in 2016/17 (year 1) • ~ 1,375 in 2017/18 (year 2) • ~ 1,405 in 2020/21 (year 5) 2)For **TYA**: • ~ 22,915 in 2016/17 (year 1) • ~ 22,690 in 2017/18 (year 2) • ~ 22,375 in 2020/21 (year 5)

	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2,5 and 10 years?	K1.7 It is estimated that the current activity in K1.5 would grow in line with the trend in activity growth from the BSBMT registry.[xxvi] Please note that this excludes the potential impact from newer drugs entering the market and therefore reducing the requirement for transplants.[xxvii] Future activity could be in the region of: 1) LL: • ~ 5 in 2016/17 (year 1) • ~ 5 in 2017/18 (year 2) • ~ 7 in 2020/21 (year 5) 2) For the TYA indications, it is expected that:[xxviii] For immunodeficiencies, activity is expected to reach c. 10 – 15 by 2020/21 (year 5). Assuming a linear increase, this could be c.: • ~ 6 – 8 in 2016/17 (year 1) • ~ 7 – 10 in 2017/18 (year 2) • ~ 10 – 15 in 2020/21 (year 5) For inborn errors, activity would be expected to remain equal to current levels of c. 0 – 2 each year. For haemoglobinopathies, activity would be expected to increase to c. 10 – 15 by 2020/21 (year 5). Assuming a linear increase, this could be c.: • ~ 6 – 7 in 2016/17 (year 1) • ~ 7 – 9 in 2017/18 (year 2) • ~ 10 – 15 in 2020/21 (year 5)

		For solid tumours, activity would be expected to remain equal to current levels of c. 17 each year.
	K1.8 How is the population currently distributed geographically?	K1.8 Haemoglobinopathies affect minority groups disproportionally.[xxix] Otherwise, across England, no geographic differences were identified in the literature.[xxx]
K2 Future Patient Population & Demography	K2.1 Does the new policy: move to a non-routine commissioning position / substitute a currently routinely commissioned treatment / expand or restrict an existing treatment threshold / add an additional line / stage of treatment / other?	K2.1 This policy moves to a routine commissioning position for a certain number of HSCT indications.[xxxi]
	K2.2 Please describe any factors likely to affect growth in the patient population for this intervention (e.g. increased disease prevalence, increased survival).	K2.2 The full causes of **LL** are not yet known. In some cases they are related to genetic factors. [xxxii] However, it is difficult to quantify these factors. **Immunodeficiencies** can occur more frequently if there is a family history[xxxiii], **inborn errors and haemoglobinopathies** are inherited conditions[xxxiv] and **solid tumours** can have a multitude of causes (such as infections, genes and family history, smoking or UV radiation).[xxxv]
	K 2.3 Are there likely to be changes in geography/demography of the patient population and would this impact on	K2.3 No changes in geography/demography were identified.

	activity/outcomes? If yes, provide details.	
	K2.4 What is the resulting expected net increase or decrease in the number of patients who will access the treatment per year in year 2, 5 and 10?	K2.4 Under the policy, it is estimated that where the procedure is routinely commissioned (for LL and the TYA indications), the entire target population in K1.5 would receive a transplant. 1) For LL, this would represent a **net increase** in activity in the region of: • ~ 1 – 3 in 2016/17 (year 1) • ~ 1 – 3 in 2017/18 (year 2) • ~ 2 – 3 in 2020/21 (year 5) As discussed in K1.5, it is estimated that 75% of LL transplants would be autologous. For these patients the transplant is expected to be additional as it is likely to defer other therapies.[xxxvi] It is expected that the additional patients receiving an allogeneic transplant under the policy would previously have been treated with rituximab and bendamusitine, which they may no longer require.[xxxvii] 2) For the TYA indications, it is expected that there would be **no net increase** as a result of the policy.[xxxviii] It is expected that activity would increase in both the 'do-nothing' and under the policy to the levels identified in K1.7 and K1.5.
K3 Activity	K3.1 What is the current annual activity for the target population covered under the new policy? Please provide details in accompanying excel sheet.	K3.1 Current activity is as described in K1.5.

	K3.2 What will be the new activity should the new / revised policy be implemented in the target population? Please provide details in accompanying excel sheet.	K3.2 Based on the 'do-nothing' activity in K1.7 and the net change in activity from the policy in K2.4, future activity is expected to be in the region of: 1) For **LL**: • ~ 6 – 8 in 2016/17 (year 1) • ~ 7 – 8 in 2017/18 (year 2) • ~ 8 – 10 in 2020/21 (year 5 *Please note that this does not account for the development of a number of new drugs which may or may not be commissioned for LL in the future which could impact on the future numbers of transplants for this indication*[xxxix]*.* 2) For **TYA**: • ~ 30 – 35 in 2016/17 (year 1) • ~ 30 – 35 in 2017/18 (year 2) • ~ 35 – 50 in 2020/21 (year 5)
	K3.3 What will be the comparative activity for the 'Next Best Alternative' or 'Do Nothing' comparator if policy is not adopted? Please details in accompanying excel sheet.	K3.3 'Do nothing'; activity is assumed to be the same as described in K1.7.
K4 Existing Patient Pathway	K4.1 If there is a relevant currently routinely commissioned treatment, what is the current patient pathway? Describe or include a figure to outline associated activity.	K4.1 HSCT is routinely commissioned based on BSBMT guidelines for adults (2013), and paediatrics (2012). A multi-disciplinary team consisting of a haematology specialist, specialist nurse and transplant physicians assess what clinical

		options are available. The transplant procedure begins with 'conditioning' therapy (which may include chemotherapy) at a range of doses depending on the type and severity of disease being treated. The aim of conditioning is to: 1. To cytoreduce disease through chemotherapy related cytotoxicity 2. Suppress host immunity to allow for donor cell engraftment 3. To establish a platform for the development of a graft vs malignancy effect. The patient pathway is described in detail in the BMT service specifications for adults and UK Paediatric BMT Group HSCT recommendations.
	K4.2. What are the current treatment access criteria?	K4.2 Haematopoietic 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. Patients require detailed pre-transplant assessment and investigations to assess their clinical status and fitness to proceed to transplant.
	K4.3 What are the current treatment stopping points?	K4.3 Patients may choose not to undergo the procedure due to its severity. Repeat autologous or allogeneic transplants for relapsed disease are not commissioned routinely unless explicitly recommended by the BMT service specifications for adults and UK Paediatric BMT Group HSCT recommendations. Planned tandem transplants are not commissioned routinely unless explicitly recommended by the BSBMT guidelines.

K5 Comparator (next best alternative treatment) Patient Pathway	K5.1 If there is a 'next best' alternative routinely commissioned treatment what is the current patient pathway? Describe or include a figure to outline associated activity.	K5.1 There are no direct alternatives treatments to HSCT, the next best treatments are chemotherapy and radiotherapy, with WBRT.
	K5.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	K5.2 No different stopping points.
K6 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy.	K6.1 The patient pathway for lymphoplasmacytic lymphoma will remain the same. The new patient pathway will commission HSCT for patients with immunodeficiencies, inborn errors, haemoglobinopathies and solid tumours in the teenage and young adult (TYA) age range (16-24 years) by extending the paediatric guidelines for these diseases upwards. Please refer to K1.5 for current activity for the patient groups.
	K6.2 Where there are different stopping points on the pathway please indicate how many patients out of the number	K6.2 LL & TYA: Stopping points same as current policy.

	starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	
K7 Treatment Setting	K7.1 How is this treatment delivered to the patient? o Acute Trust: Inpatient/Daycase/ Outpatient o Mental Health Provider: Inpatient/Outpatient o Community setting o Homecare delivery K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what? *e.g. service capacity*	K7.1 HSCT involves two to three different stages depending on the type of transplant. Harvesting, (for autoSCTs), 'conditioning' therapy and the main transplant procedure. The conditioning and transplant procedure are typically performed in an inpatient setting.[xl] K7.2 No change expected.
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded? K8.2 How will this activity related to the	K8.1 This in an inpatient procedure and would be recorded in SUS. In addition, activity related to stem cell transplants is recorded in the British Society of Blood and Marrow Transplantation (BSBMT) registry.[xli] K8.2 Although this would be recorded in SUS, this would not be at a

	new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	sufficient level of granularity to isolate the specific sub-indications by using OPCS and ICD-10 codes.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 No
	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	K9.2 N/A
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Complete data must be submitted to the BSBMT registry for all transplants carried out by UK centres. All centres must provide the data required for the BMT Quality Dashboard.
	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 No additional monitoring required.
	K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 See K9.3

	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 Improving Outcomes Guidance for Children and Young People with Cancer, NICE 2005
	K9.7 Do you anticipate using Blueteq or other equivalent system to guide access to treatment? If so, please outline. *See also linked question in M1 below*	K9.7 No
Section L - Service Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
L1 Service Organisation	L1.1 How is this service currently organised? (i.e. tertiary centres, networked provision)	L1.1 HSCT is a highly specialised procedure, performed by experienced transplant teams in specialist transplant centres. Post-transplant follow-up in local haemato-oncology providers as agreed between providers.
	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 No change.
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Patients are under care of specialised MDT.
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 No

	L2.3 Is the new policy likely to improve equity of access?	L2.3 No
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 No change
L3 Implementation	L3.1 Is there a lead in time required prior to implementation and if so when could implementation be achieved if the policy is agreed?	L3.1 No lead in time required.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 No
	L3.3 Is there a change in provider staffing required?	L3.3 No change required.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 No
	L3.5 Are there changes in the support services that need to be in place?	L3.5 No

	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 LL: No change. TYA: There is commissioning action required to agree provider selection criteria.
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 No
	L3.8 How will the revised provision be secured by NHS England as the responsible commissioner? (e.g. publication and notification of new policy, competitive selection process to secure revised provider configuration)	L3.8 N/A
L4 Collaborative Commissioning	L4.1 Is this service currently subject to or planned for collaborative commissioning arrangements? (e.g. future CCG lead, devolved commissioning arrangements)	L4.1 No
Section M - Finance Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
M1 Tariff	M1.1 Is this treatment paid under a national prices*, and if so which?	M1.1 No

	M1.2 Is this treatment excluded from national prices?	M1.2 Yes
	M1.3 Is this covered under a local price arrangements (if so state range), and if so are you confident that the costs are not also attributable to other clinical services?	M1.3 Yes; the cost of a transplant varies substantially across regions and this is likely to reflect the local differences in packages (i.e. whether or not the price includes just the transplant or the whole package of care).[xlii] It is estimated that for autologous transplants, this is in the region of £20,000 and £30,000 per procedure. For allogeneic transplants, the estimated costs range between £50,000 and £120,000.[xliii]
	M1.4 If a new price has been proposed how has this been derived / tested? How will we ensure that associated activity is not additionally / double charged through existing routes?	M1.4 Not applicable.
	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 VAT would be recoverable under certain specific conditions[xliv]. It is assumed here that VAT would not be recoverable.
	M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new policy?	M1.6 Not applicable.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 As described in M1.3, the costs of a transplant are estimated to range between £20,000 and £30,000 for autologous and £50,000 and

		£120,000 for allogeneic transplants.[xlv] The costs of comparator treatments are difficult to quantify as these are highly variable and depend on the specific indication and patient circumstances.[xlvi]
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 The number of follow-ups would depend on patient survival rates. These could cost c. £100 per attendance.[xlvii]
M3 Overall Cost Impact of this Policy to NHS England	M3.1 Indicate whether this is cost saving, neutral, or cost pressure to NHS England.	M3.1 Based on the **net change in activity** identified in K2.4, there are estimated to be the following cost impacts: The **total cost pressure** to NHS England from the increased number of transplants for LL is estimated to be in the region of: [xlviii] • ~ £35k - £130k in 2016/17 (year 1) • ~ £35k - £140k in 2017/18 (year 2) • ~ £45k - £175k in 2020/21 (year 5) As noted in K2.4, the additional patients receiving an allogeneic transplant under the policy may have reduced use of other drugs, however, this impact has not been quantified, given the uncertainty around the treatment pathway and outcomes.[xlix]
	M3.2 Where this has not been identified, set out the reasons why this cannot be measured.	M3.2 Not applicable.

M4 Overall cost impact of this policy to the NHS as a whole	M4.1 Indicate whether this is cost saving, neutral, or cost pressure for other parts of the NHS (e.g. providers, CCGs).	M4.1 For the routinely commissioned indications, this policy is expected to be **broadly cost neutral** to other parts of the NHS, as this is all NHS England funded activity.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 Please refer to M3.1.
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 Not applicable.
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 Not applicable.
M5 Funding	M5.1 Where a cost pressure is indicated, state known source of funds for investment, where identified. *e.g. decommissioning less clinically or cost-effective services*	M5.1 Not applicable.
M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 The significant variability in the cost of the transplant and the difficulty in estimating the costs of comparator treatments result in a high degree of uncertainty around the financial impacts of the policy.

	M6.2 Can these be mitigated, if so how?	M6.2 No mitigations have been identified.
	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	M6.3 The low cost scenario in M3.1 assumes the lower cost estimates per patient in M2.1, and the lower net change in activity in K2.4. The high cost scenario in M3.1 assumes the high cost estimates per patient in M2.1 and the higher net change in activity in K2.4.
M7 Value for Money	M7.1 What evidence is available that the treatment is cost effective? *e.g. NICE appraisal, clinical trials or peer reviewed literature*	M7.1 The literature search did not identify any studies addressing the comparative cost effectiveness of stem cell transplant compared to other management strategies.
	M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.2 The literature search used only published peer reviewed evidence.
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs associated with this policy? *e.g. Transitional costs, periodical costs*	M8.1 None expected.
	M8.2 If so, confirm the source of funds to meet these costs.	M8.2 Not applicable.

[i] Based on Lymphoma Association (2013). *Lymphoplasmacytic lymphoma and Waldenström's macroglobulinaemia*. [Online] Available from Lymphoplasmacytic lymphoma and Waldenström's macroglobulinaemia [Accessed: 11/01/2016].

[ii] TYA patients are defined as patients aged 16-24 years.

[iii] Waldenström macroglobulinaemia (WM) is a rare type of slow growing non-Hodgkin lymphoma [Source: Macmillan (2014). *Waldenstrom's macroglobulinaemia.* [Online] Available from http://www.macmillan.org.uk/information-and-support/lymphoma/lymphoma-non-hodgkin/understanding-cancer/types-of-non-Hodgkin-lymphoma/waldenstroms-macroglobulinaemia.html [Accessed: 01/12/2015].

[iv] Based on an estimated prevalence of 64,389 in 2010 [Source: Macmillan-NCIN Cancer Prevalence Project (2015). 20-year cancer prevalence in the UK. [Online] Available from http://www.ncin.org.uk/about_ncin/understanding_the_cancer_population [Accessed: 19/01/2016]. This number is grown with demographic growth rates in England to arrive at a 2014/15 figure [Source: Office for National Statistics (ONS) (2012). Population projections].

[v] Based on: Leukemia & Lymphoma Society (2013). *Non-Hodgkin Lymphoma*. [Online] Available from https://www.lls.org/sites/default/files/file_assets/nhl.pdf [Accessed: 13/01/2016].

[vi] Please refer to the policy proposition.

[vii] PID UK (2015). *The basics*. [Online] Available from http://www.piduk.org/whatarepids/basics [Accessed: 19/01/2016].

[viii] Based on a clinical estimate of c. 5,000 patients with PID in the UK [Source: PID UK (2015). The basics. [Online] Available from http://www.piduk.org/whatarepids/basics [Accessed: 19/01/2016], which is corrected to cover only the population of England [Source: ONS (2015). Population Estimates for UK, England and Wales, Scotland and Northern Ireland, Mid-2014].

[ix] Based on ONS (2015). Population Estimates for UK, England and Wales, Scotland and Northern Ireland, Mid-2014.

[x] Gray R G F et al. (2000). "Inborn errors of metabolism as a cause of neurological disease in adults: an approach to investigation." *Neurol Neurosurg Psychiatry*;**69**:5-12 doi:10.1136/jnnp.69.1.5

[xi] *The frequency of inherited metabolic disorders in the West Midlands, United Kingdom*. [Online] Available form http://www.phgfoundation.org/file/2515 [Accessed: 19/01/2016].

[xii] Based on the prevalence of sickle cell and thalasemia in patients aged 15-24 in the UK [Source: National Haemoglobinopathy Registry Report 2013/14] corrected to cover only the population of England [Source: ONS (2015). Population Estimates for UK, England and Wales, Scotland and Northern Ireland, Mid-2014].

[xiii] Based on a reported 20 year prevalence of TYA cancers in England of 13,886 in 2010[Source: NCIN (2013) Macmillan – NCIN work plan – Segmenting the cancer population: All cancers combined, 20-year prevalence at the end of 2010, UK], which is grown by demographic growth to arrive at 2014/15 figures. Moreover, an estimated 10% of these patients are diagnosed with leukaemia and are hence not considered [Source: Macmillan (2013). The rich picture on teenagers and young adults with cancer. [Online] Available from http://www.macmillan.org.uk/Documents/AboutUs/Research/Richpictures/TeenagersandYoungAdultsRichPicture.pdf [Accessed: 19/01/2016]].

[xiv] Based on the policy proposition document and the British Society of Blood and Marrow Transplantation (BSBMT) indications table for adults, and children.

[xv] Please refer to the indications table in the policy proposition document for more detail.

[xvi] Based on 22 transplants registered between 2010 and 2014 inclusive [Source: Clinician from the policy working group in reference to the BSBMT registry].

[xvii] This is based on the assumption that an additional 25-50% would be eligible to receive a transplant under the policy (source: policy working group). Please note that figures are rounded.

[xviii] Please refer to the indications table in the policy proposition document for more detail.

[xix] C. 10 – 15 with immunodeficiencies, 0 – 2 with inborn errors, c. 10 – 15 with haemoglobinopathies and c. 17 for solid tumours. Source: based on discussions with the policy working group.

[xx] Based on discussions with the policy working group.

[xxi] Based on the policy proposition. Please refer to the policy proposition for more detail.

[xxii] Based on Lymphoma Association (2013). *Lymphoplasmacytic lymphoma and Waldenström's macroglobulinaemia*. [Online] Available from http://www.nhs.uk/ipgmedia/national/Lymphoma%20Association/Assets/Waldenstr%C3%B6msmacroglobulinaemiaWMLA8pages.pdf [Accessed: 11/01/2016].

[xxiii] Based on 22 transplants registered between 2010 and 2014 inclusive [Source: Clinician from the policy working group in reference to the BSBMT registry].

[xxiv] Based on discussions with the policy working group

[xxv] Based on discussions with the policy working group

[xxvi] Between 2008 and 2013, a CARG of c. 7% was identified. This is based on "Totals ALL SCTS". [Available online} http://bsbmt.org/about-the-registry/

[xxvii] Based on discussions with the policy working group

[xxviii] Based on discussions with the policy working group

[xxix] NHS England 2013/14 Standard Contract for Specialised Services for Haemoglobinopathy Care (All Ages) [B08/S/a].

[xxx] Quality appraisal comparing data from the National Cancer Data Repository (NCDR) with the population-based Haematological Malignancy Research Network (HMRN) (2012). "Haematological malignancies & cancer registration in England (2004-2008)"

[xxxi] The indications are based on the BSBMT indications table for adults and children as well as the policy proposition for TYA patients. Please refer to the policy proposition for the detailed breakdown of indications and commissioning positions.

[xxxii] Based on Macmillan (2015). *Causes and risk factors for WM*. [Online] Available from https://www.macmillan.org.uk/information-and-support/lymphoma/lymphoma-non-hodgkin/understanding-cancer/types-of-non-Hodgkin-lymphoma/waldenstroms-macroglobulinaemia.html#tcm:9-153499 [Accessed: 11/01/2016].

[xxxiii] Based on indicative information for primary immunodeficiency: Mayo Clinic. *Primary immunodeficiency*. [Online] Available from http://www.mayoclinic.org/diseases-conditions/primary-immunodeficiency/basics/risk-factors/con-20031958 [Accessed: 19/01/2016].

[xxxiv] Based on: UCSF Children's Hospital. *Inborn Errors of Metabolism*. [Online] Available from https://www.ucsfbenioffchildrens.org/pdf/manuals/53_Metabolism.pdf [Accessed: 19/01/2016]; and: Newcastle upon Tyne Hospitals. *Haemoglobinopathies*. [Online] Available from http://www.newcastle-hospitals.org.uk/services/ng_npcg_ns_haemoglobinopathies.aspx [Accessed: 19/01/2016].

[xxxv] Macmillan (2013). The rich picture on teenagers and young adults with cancer. [Online] Available from http://www.macmillan.org.uk/Documents/AboutUs/Research/Richpictures/TeenagersandYoungAdultsRichPicture.pdf [Accessed: 19/01/2016].

[xxxvi] Based on discussions with the policy working group

[xxxvii] Based on discussions with the policy working group

[xxxviii] Based on discussions with the policy working group

[xxxix] Based on discussions with the policy working group

[xl] NHS Choices (2015). *Stem cell and bone marrow transplants - What happens*. [Online] Available from http://www.nhs.uk/Conditions/Bone-marrow-transplant/Pages/How-is-it-performed.aspx [Accessed: 11/01/2016].

[xli] Activity for stem cell transplants is already recorded within the BSBMT registry. High level figures are accessible under: http://bsbmt.org/about-the-registry/.

[xlii] Based on discussions with the NHS England Finance Lead.

[xliii] Based on. EBMT Autoimmune Diseases and Immunobiology Working Parties, 16-17, Nov 2012, Paris, France. This assumes that the costs for the indications considered are similar to costs for HSCT in autoimmune diseases. The figures also fall within the costs identified in a high level IFR data extract for 2014/15 and 2015/16 received from NHS England for all haematopoietic stem cell transplants.

[xliv] Please refer to Section 3.2 of VAT Notice 701/557 (https://www.gov.uk/government/publications/vat-notice-70157-health-professionals-and-pharmaceutical-products/vat-notice-70157-health-professionals-and-pharmaceutical-products)

[xlv] Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages) (2015) “Draft content for revision of Blood and Marrow Transplant policy to include second allogeneic transplants for relapsed disease.” These costs cover all the stages of the transplant (physical examination, harvesting, conditioning, transplanting the stem cells and recovery period) based on discussions with the policy working group.

[xlvi] Based on discussions with the policy working group.

[xlvii] 2014/15 National Tariff, Follow Up Attendance - Single Professional for oncology of £91. A 10% Market Forces Factor is applied as well as an efficiency factor of -3.9% and inflation of 1.9% to the tariff figures in the first year.

[xlviii] Based on the target population set out in K2.4 and K3.1 and the costs outlined in M1.3 and M2.2.

[xlix] Based on discussions with the policy working group