Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	E04X01		
Policy Title	Use of Plerixafor for Stem Cell Mobilisation (Update to include paediatrics)		
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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 **routinely commission** the use of plerixafor for stem cell mobilisation in children, teenagers and young adults (≤24 years) with lymphomas and paediatric-type solid malignant tumours.[i] The prevalence of solid malignant tumours in children and young adults is difficult to estimate, however amongst those aged 0-24 it is estimated that approximately 1,740 new patients are affected by these cancers in England each year.[ii]	

	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 NHS England routinely commissions plerixafor for stem cell mobilisation in adults and children with Hodgkin's Disease, Non-Hodgkin's lymphoma or multiple myeloma.[iii] The policy would widen this to also include all children and young adults with solid malignant tumours. Plerixafor would only be used in patients: 1) As a pre-emptive measure to prevent a stem cell mobilisation failure; or 2) Who have already failed a stem cell mobilisation attempt. This population is estimated to be in the region of 30-40[iv] patients per year in 2014/15,[v] or around 2-3% of the incident population.
	K1.3 What age group is the treatment indicated for?	K1.3 For paediatric patients and young adults (up to the age of 24).[vi]
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 Those taking up the treatment tend to be towards the younger end of the age bracket identified in K1.3.[vii]
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 Of the eligible cohort of 30-40 patients, as identified in K1.2, it is estimated that: • 15-20 children or young adults with solid malignant tumours **currently receive plerixafor** for stem cell mobilisation,[viii] approximately 2 as a **pre-emptive** measure and around 13-18 for patients who have already **failed** a stem cell mobilisation attempt.[ix]

- The remaining 15-20 eligible **currently only receive G-CSF with or without chemotherapy** in the period prior to the attempt at mobilising sufficient CD34+ cells[x]. Based on current practice, it is estimated that around 2 patients in this group are eligible to receive plerixafor as a **pre-emptive** measure, whilst the remainder may be eligible to receive plerixafor after having **failed** a first attempt at mobilisation.[xi]

The use of plerixafor in stem cell mobilisation is estimated to be successful for[xii]:

1) c.90% of patients where is it used **as a pre-emptive measure to prevent a stem cell mobilisation failure**, compared to c. 80% for G-CSF or chemotherapy and G-CSF.
2) c.60 to 77% of patients **who have already failed a stem cell mobilisation attempt**, compared to the success rate of G-CSF or chemotherapy and G-CSF of c. 18 to 23% respectively.

Where **sufficient CD34+ stem cells are mobilised**, patients move on to having an autologous stem cell transplant. There would therefore be an estimated:

- c. 11-14 autologous stem cell transplants for the 15 – 20 patients currently receiving plerixafor, and
- c. 4-5 for those currently only receiving chemotherapy and G-CSF.

This implies an estimated 15 – 19 autologous stem cell transplants in the current state for this patient group.

Patients who are **unsuccessful at mobilising enough CD34+** will not be able to receive an autologous stem cell transplant and would instead receive:

		• A further mobilisation attempt (with plerixafor if it has not been used previously, otherwise without) • An allogeneic stem cell transplant • A bone marrow harvest then a transplant[xiii] • Other therapeutic options[xiv] The use of plerixafor is therefore expected to reduce the number of patients failing stem cell mobilisation who would need to undergo one of the treatment options listed above.[xv] The options listed above, however, have poorer clinical outcomes than an autologous stem cell transplant. For example, there is greater toxicity associated with allogeneic when compared to autologous transplants and a greater risk of mortality as a result.[xvi] There is also a clinical concern that a bone marrow harvest followed by an autologous transplant could impact on survival rates.[xvii]
	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 The incidence of these conditions may be expected to remain stable at current levels.[xviii] As such, population growth would drive the projected growth of the condition: the number of new persons affected by solid malignant tumours could be:[xix] • c. 1,750 in 2016/17 (year 1) • c. 1,755 in 2017/18 (year 2) • c. 1,775 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 Prior to applying the new policy, it assumed that activity would grow in line with demographic growth and therefore remain broadly equal to the 30 – 40 patients per year identified in K1.5. [xx]

	K1.8 How is the population currently distributed geographically?	K1.8 There does not tend to be significant geographical differences in the prevalence of paediatric cancers.[xxi]
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 The new policy updates a current routine commissioning arrangement to widen the population eligible for plerixafor for stem cell mobilisations.
	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 No factors have been identified.[xxii]
	K 2.3 Are there likely to be changes in geography/demography of the patient population and would this impact on activity/outcomes? If yes, provide details.	K2.3 No changes have been identified.
	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 Whilst it is currently estimated that 15-20 patients receive plerixafor, under the policy the target population of 30-40 patients per year, as identified in K1.2, would now receive it. This is a **net increase of 15-20 patients.** Given the success rates in K1.5, an estimated 22–28 patients would now receive an autologous stem cell transplant when compared to the 15 – 19 in the current state, as estimated in K1.5. This represents a

		net increase of c. 6-9[xxiii] autologous stem cell transplants. These 6 - 9 patients would now receive this rather than one of the following treatment options: • A further mobilisation attempt (with plerixafor if it has not been used previously, otherwise without) • An allogeneic stem cell transplant • A bone marrow harvest then a transplant; or • Other therapeutic options. The policy therefore does not add a further line of treatment, but replaces alternative options.
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. K3.2 What will be the new activity should the new / revised policy be implemented in the target population? Please provide details in accompanying excel sheet. K3.3 What will be the comparative activity for the 'Next Best Alternative' or 'Do Nothing' comparator if policy is not adopted? Please details in	K3.1 The current activity for the target population is set out in question K1.5. K3.2 Under the policy, the number of patients treated each year with plerixafor is expected to be the full 30-40 identified in K1.5 each year[xxiv]. Based on current practice, four patients are estimated to receive this pre-emptively, and 26-36 following a failed mobilisation attempt. Given the success rates identified in K1.5, this would result in an estimated 22-28 patients receiving an autologous stem cell transplant. K3.3 If this policy is not adopted, then current activity, assumed to be the 'steady state' would be expected to roll forward in future years. The future activity levels are therefore estimated to be equal to those set out in K1.5.

	accompanying excel sheet.	
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 Plerixafor is routinely commissioned in patients with Hodgkin's Disease, Non-Hodgkin's lymphoma or multiple myeloma who fail to collect an adequate number of stem cells to proceed to stem cell transplant at the first attempt. These patients are eligible for either rescue or pre-emptive treatment with plerixafor. The former entails a second attempt at stem cell mobilisation; the latter involves administering plerixafor during the first attempt at stem cell mobilisation where the patient is deemed at risk of failing to collect an adequate number of stem cells. Patients for stem cell harvesting will normally be referred to the stem cell collection unit by the transplant team with a written prescription detailing the target stem cell dose required as per JACIE and Human Tissue Authority (HTA) recommendations. Either the transplant team or the collection team (depending on local factors) will be responsible for the authorisation and administration of plerixafor for patients requiring this intervention.
	K4.2. What are the current treatment access criteria?	K4.2 **1) Patients who have previously failed a mobilisation attempt (rescue)** should receive G-CSF (10 µg/kg, or in accordance with protocol) subcutaneously each day for 4 consecutive days:: • On the fourth day patients assessed as requiring plerixafor (usually if the peripheral blood CD34+ cell number are < 15 per microlitre) receive a dose of 240 µg/kg in the early evening as a subcutaneous injection into the abdomen. • On the morning of the fifth day, a full blood count and peripheral CD34 count should be performed prior to harvest. It is the responsibility of the Transplant Consultant, to decide whether the harvest should proceed on the basis of the blood CD34+ estimation (usually if above 10 CD34+ cells per microlitre). • If the count is insufficient to harvest cells that day, or if insufficient

		stem cells have been harvested, then patients should receive a further dose of GCSF and a repeat dose of plerixafor (240 µg/kg) that evening in an identical fashion to the day before. A second attempt at harvest should be made the following day. **2) Patients who appear to be failing a mobilisation attempt (pre-emptive)** – these are patients in whom the CD34+ cell count in the blood is < 15 per microlitre on the day of predicted day of stem cell harvest. • These patients are given a dose of subcutaneous plerixafor with GCSF 10 µg/kg and an attempt at harvesting is made the following day if the repeat CD34+ is sufficient. • If the CD34 level in the blood remains < 15 per microlitre then the harvest should be delayed and a further dose of G-CSF and plerixafor may be given that evening.
	K4.3 What are the current treatment stopping points?	K4.3 • A maximum of three doses of plerixafor in total may be used. • In general a collection totalling >2 X (106) CD34+ cells per kilogram body weight will be sufficient to adequately support a single high-dose therapy procedure.
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 For patients with other solid malignant paediatric tumours covered by this policy update, see question K1.5 for the next best commissioned pathway: Another option is bone marrow harvest, but there is clinical concern to the use of bone marrow (which may be cancerous) compared with stem cells. Moreover, the process is painful, requires a theatre session and is costly. The final comparator is palliation if not able to deliver high dose

		chemotherapy.
	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 10-20% of patients fail the 1st round of stem cell mobilisation (source: lead clinician). 2nd round of stem cell mobilisation is only effective in up to 20% of these patients. Bone marrow harvest has a low success rate. If the above fail, this is likely to have an adverse impact on patient survival.
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 New patient pathway will be as in K4.1, with the additional inclusion of other paediatric solid malignant tumours. Based on current practice, it is estimated that 4 of the 30-40 patients require pre-emptive plerixafor prior to PBSCT and c. 20% fail 1st round of mobilisation.
	K6.2 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.	K6.2 Stopping points are as in K4.2, although it is noted that, in terms of the collection of >2 X (10^6) CD34+ cells per kilogram body weight being sufficient for the procedure in adults, paediatric requirements may differ (refer to individual treatment protocols).

K7 Treatment Setting	K7.1 How is this treatment delivered to the patient? ○ Acute Trust: Inpatient/Daycase/ Outpatient ○ Mental Health Provider: Inpatient/Outpatient ○ Community setting ○ Homecare delivery	K7.1 Plerixafor is administered in an inpatient setting, during the days leading up to the collection of stem cells (apheresis).
	K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what? *e.g. service capacity*	K7.2 None identified.
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded?	K8.1 Plerixafor is a high cost drug excluded from tariff, so it should be captured in the high cost drug dataset for routine commissioning.[xxv]
	K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.2 Activity should be identified through the high cost drug dataset, by drug name and indication. A standard naming convention is recommended.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 None expected.
	K9.2 If this treatment is a drug, what	K9.2 N/A – monitoring is undertaken at the stem cell collection centre.

	pharmacy monitoring is required?	See K9.3 for information collected. Please see K9.7 for monitoring through Blueteq.
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Regular audit should be carried out on the use of plerixafor. Audit criteria will encompass the following: • % of total patients undergoing mobilisation who require plerixafor • Number of pre-emptive vs. rescue mobilisations • Criteria determining preferred intervention: pre-emptive or rescue usage • Number of doses of plerixafor used per patient • Total CD34+ cells mobilised or sufficient CFU (colony forming units) following plerixafor • Number of collection days required to obtain sufficient cells for indicated PBSCT • Time to neutrophil and platelet engraftment following PBSCT to assess the quality of the stem cell harvested. Serious unexpected side effects
	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 Plerixafor usage should be monitored via Blueteq to ensure starting criteria are met.
	K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 No change required.

	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 NICE: Improving outcomes in haemato-oncology cancer (2003)
	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 Blueteq or similar should be used to capture the starting and stopping points (and rationale) for all patients who receive plerixafor.
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 Treatment is administered at oncology centres by apheresis specialist team.
	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 No change anticipated
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Patients for stem cell harvesting will normally be referred to the stem cell collection unit by the transplant team with a written prescription detailing the target stem cell dose required as per JACIE and Human Tissue Authority (HTA) recommendations.
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 No change anticipated.

	L2.3 Is the new policy likely to improve equity of access?	L2.3 Yes, by ensuring that individual patients are given the appropriate treatment suited to their needs.
	L2.4 Is the new policy likely to improve equality of access / outcomes?	L2.4 Yes, by ensuring that all patients have access to a consistent level of care across England.
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 N/A.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 No extra equipment required.
	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 change required.
	L3.5 Are there changes in the support services that need to be in place?	L3.5 No change required.

	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements / prime contractor)	L3.6 Use of plerixafor will be subject to internal governance arrangements.
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 No change required.
	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 Publication of new policy.
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, see M1.2.
	M1.2 Is this treatment excluded from	M1.2 Plerixafor is a high cost drug excluded from tariff.

	national prices?	
	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 As an excluded drug, the price is subject to local negotiations. The list price is £4,883 for 1 vial of 24mg/1.2ml.[xxvi] Including 20% VAT the cost is £5,859. Note that in the 5-year horizon considered, no change to the price of plerixafor is expected.[xxvii]
	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[xxviii]. It is assumed here that VAT would not be recoverable and is therefore included in the calculations in sections M2 and M3.
	M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new policy?	M1.6 No.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 The cost per patient comprises: i. the costs of the stem cell mobilisation attempts themselves; and ii. the subsequent costs depending on whether sufficient stem

		cells can be mobilised. When attempting to mobilise stem cells, the cost for plerixafor itself is estimated to be between c. **£5,860 and £17,580** in year 1. The mid cost estimate of **£11,720** uses an average number of two doses per patient. This is based on a unit cost of plerixafor of £5,860, as identified in M1.3, and based on an estimated 1 to 3 doses per patient.[xxix] This would be given alongside chemotherapy and G-CSF but these costs would not increase with the policy as they are incurred currently. As noted in K1.5, the use of plerixafor increases the likelihood that the sufficient stem cells will be mobilised. In case of a successful mobilisation, the patient will be able to: • undergo an apheresis[xxx], which has an estimated cost of c. **£665**;[xxxi] and thereafter • proceed to an autologous stem cell transplant, at an estimated cost for those aged 18 years and younger of c. **£42,330** for the transplant only.[xxxii] Patients in whom plerixafor is unsuccessful may alternatively undergo: • A further stem cell mobilisation attempt (without plerixafor). This would incur additional cycles of chemotherapy, G-CSF and hospital bed days; • An allogeneic transplant (at an estimated cost of c. **£79,000**[xxxiii]); • A bone marrow harvest then transplant (at an estimated cost of c. **£18,300**[xxxiv]) ; or • Other therapeutic options. The number of patients incurring each of these costs is uncertain. It is expected, however, that the bone marrow harvest then autologous transplant would be the most likely option.[xxxv]

		Please note that the transplant costs above are sourced from national reference costs. Local tariffs were extracted and analysed, however given the variation in the currency and components of care included, no meaningful insights can be drawn. As such, reference costs have been used for the analysis.[xxxvi]
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 Patients where plerixafor is successful and who underwent the autologous transplant may then be treated successfully. As described in M2.1, patients where plerixafor is not successful may go to one of the other treatment options.[xxxvii] The associated follow-up costs are likely to vary by patient, but not be additional to those in the current state.
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 There would be an estimated cost pressure to NHS England of broadly **£0.27m to £0.32m** in each of years 1, 2 and 5. This comprises: • the use of plerixafor for the additional 15-20 patients, c. **£0.18m to £0.24m**; • the increase in the number of apheresis and autologous transplants as a result of plerixafor likely to have higher success rates of mobilising sufficient CF34+ stem cells, c. **£0.27m to £0.37m**; and • the **costs avoided** for patients who now receive an autologous stem cell transplant who previously would have received an alternative treatment. Of the 6 – 9 patients, it is estimated that 1 – 2 would have received an allogeneic stem cell transplant and the remainder would have received a bone marrow harvest then transplant. This would **offset** the cost pressure by c. **£0.18 - £0.28m**. Please note that there is no cost impact for the current 15-20 patients receiving plerixafor currently, as this expenditure is thought to be in

		the baseline spend due to current local commissioning agreements in certain areas of England.[xxxviii]
	M3.2 Where this has not been identified, set out the reasons why this cannot be measured.	M3.2 N/A
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 This is expected to be cost neutral for other parts of the NHS.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole.	M4.2 There would therefore be an estimated **net cost pressure of £0.27m to £0.32m** to the NHS as a whole, as identified in M3.1.
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured.	M4.3 N/A
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 N/A
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 To be discussed at CPAG

M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1 The extent to which this would represent a cost pressure, be broadly cost neutral, or cost saving would depend on how the 6 – 9 patients who now receive an autologous stem cell transplant, would have been distributed across each of the following treatments when sufficient stems cells could not be mobilised without plerixafor: • A further mobilisation attempt • An allogeneic stem cell transplant • A bone marrow harvest then a transplant; or • Other therapeutic options. An estimate based on best clinical judgement has been presented in M3.1. A further potential risk is around the level of confidence in the activity assumptions. These are based on assumptions from current clinical practice and therefore may either under, or overstate future activity. A final potential risk concerns the amount of plerixafor currently funded by NHS England. The cost pressure to NHS England could be overstated if some of the current use of plerixafor is funded by Trusts themselves. This would, however, not impact the cost pressure to the NHS as a whole in M4.2.
	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 Two scenarios have been developed. One provides the low cost estimate range, the other the high cost estimate range in M3.1. The low cost impact scenario assumes: • 26 patients would receive plerixafor for their 2nd attempt at mobilisation, and 4 who would receive it as a pre-emptive measure. 30 patients therefore receive plerixafor each year.

		• An additional 6 to receive an apheresis and autologous stem cell transplant, instead of:
		  ○ 1 allogeneic stem cell transplant; and
		  ○ 5 bone marrow harvests and autologous transplants.
		
		The high cost impact scenario assumes:
		• 36 patients who would receive plerixafor for their 2nd attempt at mobilisation, and 4 who would receive it as a pre-emptive measure. 40 patients therefore receive plerixafor each year.
		• An additional 9 to receive an apheresis and autologous stem cell transplant, instead of:
		  ○ 2 allogeneic stem cell transplant; and
		  ○ 7 bone marrow harvests and autologous transplants.
		
		Both scenarios assume
		• NHS England currently does not pay for any units of plerixafor administered to the target population
		• A success rate in the first attempt of 90% with plerixafor and 80% without[xxxix]
		• A success rate in the 2nd attempt of 69% (range: 60-77%) with plerixafor; and 21% without (range: 18-23%).[xl]

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* M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.1 A review of the evidence on cost-effectiveness of plerixafor in children was undertaken as part of the previous policy B04/P/b – see Section 6 of the policy. The updated evidence review for this policy update found no studies on cost-effectiveness of plerixafor in children undergoing PBSCT[xli] for solid tumours. M7.2 There are no studies on cost-effectiveness of plerixafor in children for the specific indications considered in this policy update.

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] Solid tumours are named for the type of cells that form them. Examples of solid tumours are sarcomas, carcinomas, and lymphomas.

NCI Dictionary of Cancer Terms, http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45301,

[ii] For patients of age 0-14, see http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/incidence#heading-One for patients of age 15-24, see http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-One, last accessed: 08/12/2015. To calculate this figure, based on discussions with the policy working group, patients with the following categories of cancers were counted: Brain Other CNS and Intracranial Tumours, Lymphomas, Soft Tissue Sarcoma, Renal Tumours, Bone Sarcoma, Germ Cell and Gonadal Tumours, Germ Cell Tumours, Bone Tumours. The total was then multiplied by the ratio of the population in England to the population in the UK (84% in 2014) based on ONS data.

[iii] Policy Proposition.

[iv] Based on estimations from the policy working group.

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

[vi] Policy Proposition.

[vii] Based on discussions with the policy working group

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

[ix] Based on estimations from the policy working group

[x] This is the protein expressed on the stem cells (PBSC) that we can detect allowing us to count the number of stem cells in the blood or the harvest.

[xi] Based on estimations from the policy working group.

[xii] All success rates have been sourced from the policy proposition.

[xiii] It was stated by the policy working group that this is a sub optimal option as there is a risk of the cancer returning.

[xiv] It was stated by the policy working group that for some conditions, not having chemotherapy could decrease survival rates.

[xv] Policy Proposition.

[xvi] Based on discussions with the policy working group

[xvii] Based on discussions with the policy working group

[xviii] Based on discussions with policy working group

[xix] The future figures were calculated based on the prevalence figures set out in K1.1 and assuming that growth is in line with population estimates, based on ONS population projections (2012) for the years 2014/15 to 2020/21. The figures were calculated by using current 0-14 male cancer figures and using projected population levels to calculate future levels. Group-specific growth rates were also used for 15-24 year old males, 0-14 year old females and 15-24 year old females. Figures are rounded.

[xx] This lack of increase is due to the low population growth rate and the low base on which the growth applies.

[xxi] Based on discussions with the policy working group

[xxii] Based on discussions with the policy working group

[xxiii] Please note figures may not sum exactly due to rounding

[xxiv] Please note that these figures are likely to increase with demographic growth, however given the low number of patients and low growth rate, this is expected to stay broadly constant over a five year period.

[xxv] See section K9 for further information.

[xxvi] Dictionary of medicine, http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=16185411000001108&toc=nofloat, last accessed: 25/11/2015.

[xxvii] The Supplementary Protection Certificate for plerixafor is set to expire in August 2024. Based on data provided from UKMi. It is assumed that it would take time for generics to enter the market and as such would not impact on costs prior to 2025/26.

[xxviii] 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)

[xxix] Based on discussions with the policy working group, the cost used in the cost impact calculation uses an average of 2 doses per patient for a mobilisation attempt.

[xxx] This is the name given to the flow of the patient's blood through the cell separator during which the stem cells (PBSC) are separated and collected into a separate container in which they can then be frozen for later use.

[xxxi] This is based on the cost of £615 for an apheresis (2014/15 tariff, HRG code SA13B), the application of -1.6% for efficiency and inflation to arrive at 2015/16 figures, and 10% MFF.

[xxxii] This figure is based on the £39,702 national reference cost figure in 2013/14 for "Peripheral Blood Stem Cell Transplant, Autologous, 18 years and under", to which -1.5% and -1.6% are applied to account for efficiency and inflation over two years to arrive at 2015/16 cost figures. This includes a 10% MFF uplift. This is assumed to proxy for the price that would be paid by NHS England.

[xxxiii]This is based on 2013/14 national reference costs, HRG code SA28B (Peripheral Blood Stem Cell Transplant, Allogeneic, 18 years and under) and applying both efficiency and inflations assumptions of -1.6% for 14/15; -1.5% for 15/16. This is assumed to proxy for the price that would be paid by NHS England.

[xxxiv]Calculated using the 2013/14 National Reference Costs for "Bone Marrow Transplant, Autograft, 18 years and under" at a cost of £14,761, and for a "Bone Marrow Harvest" at £2,399. This is then adjusted by -1.5% to estimate the 2014/15 cost figure, and by -1.6% to estimate the 2015/16 figure. This includes a 10% MFF uplift.

[xxxv] Based on discussions with the policy working group

[xxxvi] This has been confirmed with the NHS England analytics lead and the policy working group.

[xxxvii] Based on correspondence with policy working group.

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

[xxxix] See Policy Proposition.

[xl] See Policy Proposition.

[xli] Peripheral blood stem cell transplantation