Clinical Commissioning Policy
Plerixafor for stem cell mobilisation in adults and children (Publication reference no: 200601P)

Commissioning position

Summary

The policy is for plerixafor to be available as a treatment option through routine commissioning for autologous haematopoietic stem cell transplant in adults and children within the criteria set out in this document.

Executive summary

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 stem cell mobilisation in autologous stem cell transplant

Haematopoietic stem cells (HSC) are special cells produced by bone marrow that can turn into different types of blood cells. A HSC transplant (HSCT), also known as blood and marrow transplantation, replaces damaged blood cells with healthy ones. HSCT is used to treat selected blood cell tumours and solid organ tumours. Autologous HSCT means that healthy stem cells are removed from a person, and later given back to that same person, rather than using stem cells from a donor (NHS, 2018).

Before HSCT, a process called stem cell 'mobilisation' dislodges the stem cells from the bone marrow. This process currently uses a growth factor (G-CSF) with or without chemotherapy to stimulate the bone marrow to produce more stem cells. Stem cells move from the bone marrow to the veins, which can then be collected (harvested) and prepared for the HSCT.

About current treatment

In about 10–20% of cases, mobilisation with G-CSF with or without chemotherapy does not dislodge enough stem cells from the bone marrow. A second attempt may use stronger chemotherapy or a medication called plerixafor.

About the new treatment

Plerixafor is a medication that can be used to dislodge stem cells more effectively. Plerixafor can be used either after G-CSF in people with a low level of circulating stem cells on the day of harvesting, known as pre-emptive treatment, or after an unsuccessful harvest attempt, known as rescue treatment.

NHS England currently commissions plerixafor as either a pre-emptive or a rescue treatment for HSC mobilisation for specific blood cancers (multiple myeloma and lymphoma) in people of any age, and specific solid tumours in people aged 24 years or under. Under current policies, two groups of patients are not eligible for plerixafor, even though they may be eligible for HSCT. These groups are:

1) People of any age with blood cancers other than multiple myeloma and lymphoma (e.g. acute promyelocytic leukaemia (aPML)), chronic lymphocytic leukaemia (CLL)); or a haematological paraneoplastic complication (e.g. AL amyloidosis) in line with NHS England commissioned indications for autologous HSCT.

2) People aged over 24 years with specific solid tumours (e.g. Germ cell tumour, Ewing's and soft tissue sarcoma and medullablastoma) in line with NHS England commissioned indications for autologous HSCT.

This policy considers the effectiveness and safety of plerixafor as a pre-emptive or rescue treatment in HSC mobilisation in the above groups.

In addition, this policy incorporates the existing Clinical Commissioning Policy: Use of Plerixafor for Stem Cell Mobilisation (Update) NHS England B04/P/b into a single policy which supports the use of plerixafor for HSC mobilisation for autologous HSCT in adults and children commissioned routinely by NHS England.

What we have decided

NHS England has carefully reviewed the evidence for the use of plerixafor for HSC mobilisation in selected cohorts of patients which are not covered by existing policies. We have concluded that there is enough evidence to make the treatment available at this time for people of any age with any type of blood cancer; and for people of any age with specific solid tumours, who are scheduled for autologous HSCT in accordance with national commissioned indications.

Links and updates to other policies

This document updates Clinical Commissioning Policy: Use of plerixafor for stem cell mobilisation (updated to include paediatrics). 2016. Reference: NHS England 16064/P; and Clinical Commissioning Policy: Use of plerixafor for stem cell mobilisation (update). 2015. Reference: NHS England B04/P/b.

Committee discussion

Clinical Panel considered whether the evidence base supported an extension to the existing published policies and determined supporting evidence reviews do not provide a basis for extending plerixafor to the eligible population but provide a small amount of data to justify treatment. Panel considered that the addition of plerixafor was unlikely to cause additional harm as a bone marrow transplant could potentially cause significant harm. Panel therefore agreed to take a pragmatic approach to support a routine commissioning position. The Clinical

Priorities Advisory Group considered the policy proposition and supporting documentation. See the committee papers (link) for full details of the evidence.

The condition

HSCT is used to treat various haematological and non-haematological disorders. It is broadly divided into 2 main types: allogeneic and autologous transplantation.

Allogeneic HSCT involves replacing a person's bone marrow stem cells with stem cells from a donor. Autologous transplantation uses the person's own peripheral blood stem cells (PBSCs).

Before an autologous transplant is undertaken, 'mobilisation' is needed to dislodge the haematopoietic stem cells from the bone marrow and increase the number of PBSCs in the circulating blood flow. The circulating PBSC can then be collected using a cell separator in a procedure called apheresis.

Current treatments

For mobilisation, intravenous chemotherapy and a growth factor called granulocyte-colony stimulating factor (G-CSF) are usually given. This results in successful mobilisation and collection of PBSCs in about 80% of people. However, insufficient cells are collected for autologous transplant in about 10–20% of cases. These people are usually offered a second round of stem cell mobilisation and collection using a more intensive chemotherapy regimen. This needs another inpatient admission with more chemotherapy and G-CSF and has associated adverse effects and costs. Additional attempts at mobilisation are effective only in a small proportion of people (up to 20%). Mobilisation in children can be particularly challenging because of the intensity of chemoradiotherapy regimes given earlier in the treatment pathway and the increasing use of sequential high-dose therapy.

Proposed treatments

Plerixafor is used to help dislodge or 'mobilise' the stem cells from the bone marrow so they can be released into the blood. It works by blocking the activity of a protein called the CXCR4 chemokine receptor. This protein normally helps to keep stem cells within the bone marrow. By blocking its activity, plerixafor allows the stem cells to be released into the blood, so that they can be collected.

Plerixafor can be used with G-CSF to increase the amount of PBSCs collected. Using plerixafor after unsuccessful PBSC collection is known as rescue treatment.

Plerixafor has also been used after chemotherapy and G-CSF in people with a low level of circulating PBSCs in the blood on the day of collection. This is known as pre-emptive treatment. Pre-emptive treatment with plerixafor can improve the number of stem cells mobilising into the blood, avoid a failure of stem cell harvesting, and prevent a second attempt at mobilisation.

NHS England currently commissions plerixafor for specific haematological cancers (multiple myeloma and lymphoma) in people of any age, and non-haematological solid tumours in people aged 24 years or under.

Plerixafor is licensed for use in combination with G-CSF to enhance mobilisation of HSCs to the peripheral blood for collection in adults with lymphoma and multiple myeloma whose cells mobilise poorly. As of May 2019, plerixafor is licensed to enhance mobilisation in children over 1

year with lymphoma or solid malignant tumours, either pre-emptively, or in those who have previously failed to collect sufficient haematopoietic stem cells.

Using plerixafor for stem cell mobilisation in people with haematological tumours (apart from multiple myeloma and lymphoma), people with haematological paraneoplastic complications, or adults with non-haematological solid tumours who are receiving autologous HSCT is off label.

This policy considers the effectiveness and safety of plerixafor as a pre-emptive or rescue treatment in stem cell mobilisation for people of any age with haematological tumours (apart from multiple myeloma and lymphoma) or haematological paraneoplastic complications (such as amyloidosis), and people of any age with non-haematological solid tumours, who are scheduled for autologous HSCT in accordance with national guidance (British Society of Blood and Marrow Transplantation Adult BSBMT Indications Table 2012, Paediatric BSBMT Indications Table 2011).

Epidemiology and needs assessment

NHS England currently commissions plerixafor for specific haematologic cancers: multiple myeloma, lymphoma and non-haematologic solid tumours in patients aged $\leq$ 24 years. This means that patients aged >24 years with non-haematologic solid tumours; or patients of any age with haematological tumours other than multiple myeloma and lymphoma (e.g. aPML, CLL) who are eligible for HSCT, are not eligible for plerixafor.

Currently, commissioned usage of plerixafor within England is 509 patients per year (data from NHS England, 2018). Based on British Society of Blood and Marrow Transplantation (BSBMT) registry data, there are approximately 50-70 patients per year who are eligible for HSCT but ineligible for plerixafor. Assuming 10-20% of this population will fail HSC mobilisation and require plerixafor, there will be an additional 5-14 patients per year requiring plerixafor.

Data from a compassionate use programme for patients with non-haematological diseases reported 33 patients received plerixafor on a rescue or pre-emptive basis in the European Union (Jaimovich et al, 2016).

Evidence summary

NHS England has concluded that there is sufficient evidence to support a policy for the extension of routine commissioning of this treatment to include people of all ages with any type of blood cancer; and to include people of any age with specific solid tumours, who are scheduled for autologous HSCT in accordance with national guidance (British Society of Blood and Marrow Transplantation Adult BSBMT Indications Table 2012, Paediatric BSBMT Indications Table 2011, NHS England Clinical Commissioning Policy B04/P/b).

From a biological perspective, the Policy Working Group was not aware of any published evidence demonstrating that the efficacy of plerixafor is significantly influenced by the underlying cancer diagnosis. Therefore, while acknowledging the limitations of existing evidence for the use of plerixafor in patients with these less common diagnoses, there is strong rationale for commissioning this treatment across the spectrum of transplant-eligible conditions.

This section summarises the evidence for extending the current commissioning arrangements to include people of all ages with any type of blood cancer and to include people of any age with

specific solid tumours. Evidence summaries supporting the existing use of plerixafor (NHS England B04/P/b; NHS England 16064/P) are included in Appendix 1 of this document.

A. Use of plerixafor for stem cell mobilisation in people with haematological tumours (apart from multiple myeloma and lymphoma) or haematological paraneoplastic complications who are receiving autologous haematopoietic stem cell transplantation

One case series identified from the evidence search (Lee et al. 2014) was included in this evidence summary.

An overview of the results for clinical effectiveness and safety and tolerability can be found in the evidence summary table (NICE evidence review, 2019). The research questions for the evidence review and the key outcomes identified in the scope are discussed in this section.

> **In people of any age with haematological tumours (apart from multiple myeloma and lymphoma) or haematological paraneoplastic complications that can be treated with HSCT and who are scheduled for autologous HSCT, what is the clinical effectiveness of plerixafor in stem cell mobilisation compared to standard care?**

Stem cell mobilisation

In the 3 participants who did not achieve a PBSC yield of ≥1.5 million CD34+ cells/kg with G-CSF alone, rescue plerixafor was added until the target CD34+ cell count of 2.5 to 5.0 million cells/kg was achieved. The total PBSC yield in these 3 participants was 2.9, 5.7 and 5.9 million cells/kg over 3, 2, and 2 days respectively.

Autologous haematopoietic stem cell transplantation (HSCT)

All 3 participants who received rescue plerixafor and achieved a target CD34+ cell count yield of 2.5 to 5.0 million cells/kg proceeded to autologous HSCT.

Neutrophil and platelet engraftment

Neutrophil engraftment occurred at a median of 11 days (range 9 to 12 days) and platelet engraftment occurred at a median of 13 days (range 12 to 16 days). Neutrophil and platelet engraftment occurred in all 3 participants who received plerixafor as rescue treatment (within 12 days for neutrophils and 16 days for platelets).

> **In people of any age with haematological tumours (apart from multiple myeloma and lymphoma) or haematological paraneoplastic complications that can be treated with HSCT and who are scheduled for autologous HSCT, what is the safety of plerixafor in stem cell mobilisation compared to standard care?**

One participant had sepsis, renal toxicity and hyperglycaemia and another participant had hepatic toxicity. The authors reported that these adverse events were suspected to be due to underlying amyloidosis and complications of high-dose chemotherapy, neutropenia and immunosuppression. Adverse events and deaths were categorised according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v3.0.

One participant who had rescue plerixafor died 224 days after transplant from large bowel obstruction and septic shock.

Summary of product characteristics

According to the plerixafor summary of product characteristics, very common adverse effects seen in at least 1 in 10 people in studies of lymphoma and multiple myeloma are diarrhoea, nausea and injection site reactions. Common adverse effects (in between 1 in 100 and 1 in 10 people) are insomnia, dizziness, headache, vomiting, abdominal pain, stomach discomfort, dyspepsia, abdominal distention, constipation, flatulence, oral hypoaesthesia (reduced sense of touch or sensation), dry mouth, hyperhidrosis, erythema, arthralgia, musculoskeletal pain, fatigue and malaise.

> **In people of any age with haematological tumours (apart from multiple myeloma and lymphoma) or haematological paraneoplastic complications that can be treated with HSCT and who are scheduled for autologous HSCT, what is the cost-effectiveness of plerixafor in stem cell mobilisation compared to standard care?**

No evidence was found to determine whether plerixafor is cost-effective for treating people with haematologic tumours or haematological paraneoplastic complications who are receiving autologous HSCT.

B. Use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation

Two studies identified from the search are included in this evidence summary. One is a retrospective case series (Horwitz et al. 2012) in men with germ cell tumours and the other is a retrospective case series in people with various non-haematological tumours (including germ cell tumours, Ewing sarcomas, Wiscott-Aldrich disease and neuroblastomas; Worel et al. 2012).

An overview of the results for clinical effectiveness and safety and tolerability can be found in the evidence summary table (NICE, 2019). The research questions for the evidence review and the key outcomes identified in the scope are discussed in this section.

> **In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT, what is the clinical effectiveness of plerixafor in stem cell mobilisation compared to standard care?**

Mobilisation of cells from the bone marrow

Successful mobilisation of cells from the bone marrow was defined as collection of at least 2 million CD34+ cells/kg during treatment with plerixafor plus granulocyte-colony stimulating factor (G-CSF, with or without chemotherapy). CD34+ is the protein expressed on the PBSC that can be detected and measured, allowing the number of stem cells in the blood or the harvest to be counted.

In the study by Horwitz et al. (2012), a median of 3.2 million CD34+ cells/kg (range 0.76 to 15.80 million cells/kg) were collected in 21 men with germ cell tumours. At least 2 million CD34+ cells/kg were collected in 17/21 people (81%) in a median of 2 days (range 1 to 3 days). At least 4 million CD34+ cells/kg were collected in 9/21 people (43%) in a median of 3 days (range 1 to 4 days).

In the study by Worel et al. (2012), a median of 4.1 million CD34+ cells/kg (range 0.9 to 29.5 million cells/kg) were collected in 33 people (73% adults) with various non-haematological tumours. At least 2 million CD34+ cells/kg were collected in 28/33 people (85%) in a median of

2 days (range, 1 to 4 days). This study also reported the peak CD34+ cell count, which was 32 million/litre (range 9 to 250 million/litre) after plerixafor treatment, a 5.3-fold increase compared with baseline (4 million/litre).

It is not reported how big the improvements in the numbers of cells mobilised were compared with baseline or previous mobilisation attempts without plerixafor. Nevertheless, these results suggest that using plerixafor to help mobilise stem cells results in enough cells for transplant in about 80% of adults with solid tumours (mainly men with germ cell tumours).

Autologous HSCT

In the study by Horwitz et al. (2012), of the 17 people from whom at least 2 million CD34+ cells/kg were collected, 14 (82%) subsequently had HSCT (67% of the total study population [14/21]). Three of the men from whom at least 2 million CD34+ cells/kg were collected did not proceed to transplant because of death (n=1) or unknown reasons (n=2), and 2 additional men who did not collect 2 million CD34+ cells/kg had HSCT using pooled stem cells from an earlier harvest. The first stem cell graft failed in 8/16 men (50%) who then had a second transplant. The second graft did not fail in any of these men.

In the study by Worel et al. (2012), of the 28 people from whom at least 2 million CD34+ cells/kg were collected, 19 (68%) received a transplant (58% of the total study population [19/33]). Of these people, 7 had germ cell tumours (all adults), 4 had Wiscott-Aldrich disease (all children), 3 had Ewing sarcomas (age unclear), 1 had neuroblastoma (age unclear) and 4 had other non-haematological diseases (all adults). It is not reported why 9 people did not proceed to transplant. There were no reports of the first graft failing during this study.

Overall, the studies suggest that using plerixafor to help mobilise stem cells results in HSCT in about two-thirds of adults with solid tumours (mainly men with germ cell tumours), and about three-quarters of those who mobilised at least 2 million CD34+ cells/kg.

Neutrophil and platelet engraftment

In Horwitz et al. (2012), the median time to neutrophil engraftment was 11 days (range 9 to 18 days) in men who had a first stem cell transplant, and the median time to platelet engraftment was 20 days (range 12 to 48 days). The median time to neutrophil engraftment was 10.5 days (range 9 to 12 days) in men who had a second transplant, and the median time to platelet engraftment was 24 days (range 12 to 44 days).

In Worel et al. (2012), the median time to neutrophil engraftment was 11 days (range 9 to 12 days) and the median time to platelet engraftment was 15 days (range 10 to 25 days).

In summary, neutrophil and platelet engraftment occurred in all participants who received plerixafor and HSCT in the studies (in about 11 days for neutrophils and 3 weeks for platelets).

> **From the evidence selected, are there any subgroups of patients who would gain greater benefit or harm from treatment with plerixafor, in particular pre-emptive treatment or rescue treatment in stem cell mobilisation?**

Across the studies, about 70% of people had rescue treatment (when insufficient cells are collected) and 30% had pre-emptive treatment (when not enough PBSC are circulating in the blood on the day of collection). However, results were not reported separately for these

subgroups and it is not possible to determine whether people receiving rescue or pre-emptive treatment are likely to gain greater benefit or harm from stem cell mobilisation with plerixafor.

> **In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT what is the cost effectiveness of plerixafor in stem cell mobilisation compared to standard care?**

No evidence was found to determine whether plerixafor is cost-effective for treating people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT.

Safety and tolerability

> **In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT, what is the safety of plerixafor in stem cell mobilisation compared to standard care?**

Adverse events

In the study by Worel et al. (2012), no treatment-related adverse effects were reported in 33 people with various non-haematological tumours.

In the study by Horwitz et al. (2012), 8/21 men with germ cell tumours (38%) reported 17 adverse events felt to be possibly, probably or definitely related to plerixafor. None of the events were classified as serious. One man experienced chills, which were moderate in severity. All other adverse events were considered mild. They included diarrhoea (n=3), nausea (n=2), injection site reactions (n=3), bone pain (n=2), chills (n=1), neck pain (n=1), lip swelling (n=1), abnormal dreams (n=1), blurred vision (n=1) and fatigue (n=1). These are consistent with adverse effects listed in the plerixafor summary of product characteristics.

According to the plerixafor summary of product characteristics, very common adverse effects seen in at least 1 in 10 people in studies of lymphoma and multiple myeloma are diarrhoea, nausea and injection site reactions. Common adverse effects (in between 1 in 100 and 1 in 10 people) are insomnia, dizziness, headache, vomiting, abdominal pain, stomach discomfort, dyspepsia, abdominal distention, constipation, flatulence, oral hypoaesthesia (reduced sense of touch or sensation), dry mouth, hyperhidrosis, erythema, arthralgia, musculoskeletal pain, fatigue and malaise.

Implementation

Criteria

Eligibility criteria:

Patients of any age with any type of blood cancer; and for people any age with specific solid tumours, who are scheduled for autologous HSCT in accordance with national guidance (British Society of Blood and Marrow Transplantation Adult BSBMT Indications Table 2012, Paediatric BSBMT Indications Table 2011, NHS England Clinical Commissioning Policy B04/P/b) but:

> 1) have failed one previous attempt at mobilisation using a standard mobilisation regimen combining chemotherapy + G-CSF or G-CSF alone (rescue treatment). These patients will be offered a second mobilisation attempt with planned use of combination high dose G-CSF and plerixafor.

or

2) while undergoing mobilisation with a standard chemotherapy + G-CSF or G-CSF based regimen, have a low peripheral blood CD34+ cell count on the day of expected harvest and are not considered by the transplant consultant to have a reasonable chance of collecting enough cells (pre-emptive treatment). These patients will be given plerixafor as an unplanned addition to their mobilisation regimen.

In addition:

- Patients must be managed at a recognised centre commissioned to provide specialised blood and marrow transplantation services
- For “rescue treatment” (for patients who have failed one previous attempt at mobilisation using a standard mobilisation regimen combining chemotherapy + G-CSF or G-CSF alone) the decision to prescribe plerixafor needs to be agreed by the relevant specialist Multi-Disciplinary Team (MDT)
- For “pre-emptive treatment” (for patients given plerixafor as an unplanned addition to their mobilisation regimen while undergoing mobilisation with a standard chemotherapy + G-CSF or G-CSF based regimen who have a low peripheral blood CD34+ cell count on the day of expected harvest and are not considered by the transplant consultant to have a reasonable chance of collecting enough cells) the decision to prescribe plerixafor can be made by the transplant consultant but must be retrospectively reviewed by the relevant specialist MDT
- The MDT meeting must include consultants with active and credible expertise in the relevant field and a consultant paediatrician for paediatric cases
- A request for drug funding should be completed through the prior approval system
- Consent, patient evaluation and investigations prior to the commencement of the mobilisation procedure must be carried out at the stem cell collection centre in accordance with relevant transplant centre policy.

Starting criteria

1) **Patients who have previously failed a mobilisation attempt (rescue)** should receive G-CSF (10 micrograms/kg, or in accordance with protocol) subcutaneously each day for 4 consecutive days. (It is usually prescribed to the nearest ampoule size multiple, in accordance with transplant centre policy):

- 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 0.24mg/kg in the early evening as a subcutaneous injection into the abdomen. Note – for adult patients weighing ≤83kg, a flat dose of 20mg can be used instead
- 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 G-CSF and a repeat dose of plerixafor (as above) 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 G-CSF 10 micrograms/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.

Stopping criteria

- A maximum of three doses of plerixafor in total may be used
- In general, a collection totalling >2 X 10^6 CD34+ cells per kilogram body weight will be sufficient to adequately support a single high-dose therapy procedure in adults. Paediatric requirements may differ – clinicians should refer to individual treatment protocols.

Exclusions

- Plerixafor should not be used in pregnant patients. Male and female patients should be recommended to use suitable birth control for three months during and after its use.
- Plerixafor is not funded for patients undergoing a first attempt at stem cell mobilisation unless they meet the criteria for pre-emptive therapy
- Plerixafor should not be used for patients who have already received it pre-emptively during a previous attempt at mobilisation
- Plerixafor should not be used for haematopoietic stem cell mobilisation and harvest in patients with leukaemia.

In a compassionate use programme, plerixafor and G-CSF had been administered to patients with acute myelogenous leukaemia and plasma cell leukaemia. In some instances, patients experienced an increase in the number of circulating leukaemia cells. For the purpose of haematopoietic stem cell mobilisation, plerixafor may cause mobilisation of leukaemic cells and subsequent contamination of the apheresis product. Therefore, plerixafor should not be used for haematopoietic stem cell mobilisation and harvest in patients with leukaemia.

Patient pathway

Patients for stem cell harvesting will 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. There will be no change to existing arrangements following approval of this policy.

Governance arrangements

Consent, patient evaluation and investigations prior to the commencement of the mobilisation procedure must be carried out at the stem cell collection centre in accordance with relevant transplant centre policy.

No additional investigations are required for the provision of plerixafor. All processes involved in the provision of plerixafor and the subsequent harvesting of peripheral blood stem cells must fulfil HTA requirements and must meet JACIE accreditation standards.

Any provider organisation treating patients with this intervention will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics Committee (or similar) and NHS England may ask for assurance of this process.

Each provider organisation treating children with a medicine approved under this policy will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics Committee (or similar) and NHS England can ask for documented evidence that these processes are in place.

Provider organisations must register all patients on plerixafor, using a prior approval process and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Mechanism for funding

Plerixafor for HSC mobilisation for autologous stem cell transplantation in adults and children under this policy will be commissioned and funded by NHS England Specialised Commissioning under existing arrangements for the provision of Blood and Marrow Transplantation Services.

Audit requirements

All providers involved in the provision of plerixafor and the subsequent harvesting of peripheral blood stem cells must fulfil HTA requirements and must meet JACIE accreditation standards. In addition, 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 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.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Definitions

Apheresis	The name given to the flow of the person'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.
Haematopoietic stem cells, CD34+ cell	Cells in the bone marrow that can develop into different types of blood cells. CD34 is the protein expressed on the surface of the stem cells (HSCs) that can be detected and measured, allowing the number of stem cells in the blood or the harvest to be counted.
Haematological paraneoplastic complications	This policy refers to amyloidosis. Amyloidosis is when an abnormal protein builds up in organs and may be treated with HSCT in some cases.
Lymphoma	A cancer that affects cells of the immune system called 'lymphocytes'.
Myeloma	A cancer that affects the bone marrow.
Peripheral blood stem cells (PBSC)	Stem cells in the circulating blood flow, rather than in the bone marrow.
Pre-emptive treatment	Use of plerixafor when there is a low level of circulating PBSC on the day of planned collection.
Rescue treatment	Use of plerixafor with high-dose G-CSF when a previous attempt at mobilisation has failed to collect enough PBSC.
Solid tumours	Different types of solid tumours are named for the type of cells that form them (e.g. germ cell tumour, Ewing's and soft tissue sarcoma and medullablastoma) Leukaemias (cancers of the bone marrow and blood) generally do not form solid tumours.
Stem cell harvest	Collection of the stem cells (PBSC) from the blood using a cell separator machine.
Stem cell mobilisation	A process to dislodge the stem cells from the bone marrow and increase the amount circulating in the blood from where they can be collected.
Target dose	Optimal number of peripheral blood stem cells (CD34+ cells) required to safely proceed to a transplant.

Documents that have informed this policy

This document updates and replaces:

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

NHS England Clinical Commissioning Policy Use of Plerixafor for Stem Cell Mobilisation (updated to include paediatrics) August 2016. Reference: NHS England 16064/P

Documents that have informed this policy:

British Society of Blood and Marrow Transplantation, 2012. Adult BSBMT Indications Table 2012. http://bsbmt.org/wp-content/uploads/2013/12/Indications-Table-Updated-Feb2012-PDF-Version.pdf accessed on 18/06/19

British Society of Blood and Marrow Transplantation, 2011. Paediatric BSBMT Indications Table 2011.http://bsbmt.org/wpcontent/uploads/2013/12/UK_Paed_BMT_Gp_HSCT_Indications_23Dec111. pdf accessed on 18/06/19

European Medicines Agency. 2019. Mozobil, Summary of Product Characteristics. accessed on 18/06/19

European Medicines Agency. 2018. Mozobil European public assessment report.

NHS. 2018. Stem cell and bone marrow transplants. https://www.nhs.uk/conditions/stem-cell-transplant/ accessed 21/05/19

NHS England. 2019, Evidence review for policy 1902.

Douglas KW, Gilleece M, Hayden P et al. (2017) UK consensus statement on the use of plerixafor to facilitate autologous peripheral blood stem cell collection to support high-dose chemoradiotherapy for patients with malignancy. Journal of Clinical Apheresis 33(1):46-59

References

Horwitz ME, Long G, Holman P et al. (2012) Efficacy and safety of hematopoietic stem cell remobilization with plerixafor+G-CSF in adult patients with germ cell tumors. *Bone marrow transplantation* 47(10): 1283-6

Lee SY, Sanchorawala V, Seldin DC et al. (2014) Plerixafor-augmented peripheral blood stem cell mobilization in AL amyloidosis with cardiac involvement: a case series. *Amyloid* (3): 149–53

Jaimovich G, Castro M, Ostriz B, Fernandez M, Silveyra D, Campestri R. (2016). Plerixafor, cyclophosphamide and G-CSF and blood cell mobilization in a patient with acute promyelocytic leukaemia. Journal of Clinical Apheresis, 32, pp 592-593.

Worel N, Apperley JF, Basak GW et al. (2012) European data on stem cell mobilization with plerixafor in patients with nonhematologic diseases: an analysis of the European consortium of stem cell mobilization. *Transfusion* 52(11): 2395-400.