Plerixafor use for Peripheral Blood Stem Cell Mobilisation

1. Purpose
The purpose of this protocol is to ensure standardised practice for the use of Plerixafor (Mozobil®) in peripheral blood stem cell (PBSC) mobilisation. Plerixafor mobilises haematopoietic SCs from the bone marrow increasing their number in peripheral blood. Unlike the standard treatment of G-CSF, Plerixafor is not a growth factor but works alongside G-CSF to release cells more efficiently.

• NB - Patients should not be informed they are having plerixafor until the capacity to accommodate this is confirmed.

2. Eligible Patients
- Diagnosis of myeloma, non-Hodgkin lymphoma or Hodgkin lymphoma.
- Eligible and planned for an autologous stem cell transplant.
- Failed a previous attempt at PBSC mobilisation – so-called “rescue” or “planned” usage (see Protocol A) or
- Patients who appear to be failing standard chemotherapy mobilisation on the proposed day of PBSCH (D1 attendance at Therapeutic Apheresis Services TAS) – so-called “pre-emptive” or “just-in-time” use (see protocol B)

A failed attempt at PBSC mobilisation can be defined as collection of < 2 x 10^6 CD34/ kg.

The need for patients to receive “pre-emptive” or “just-in-time” Plerixafor is not predictable, such that resources cannot be allocated in advance. The ability to proceed with plerixafor is not guaranteed and will be assessed on an individual case basis depending on availability of apheresis slots, stem cell processing and ward care on the day. At least 2 consecutive further days of apheresis/processing slots should be available before the patient receives Plerixafor. Where possible, patients with risk factors known to adversely affect PBSC mobilisation (see appendix 1) will be identified in advance and resource issues discussed at the weekly stem cell planning teleconference. If there are no available slots, planned plerixafor can be considered for that patient for next mobilisation/harvest.

3. Pre-Assessment
See PBSCH protocols B.2.24 Consider whether patient needs accommodation in Oxford. Options include Churchill flat for planned Plerixafor usage and bed and breakfast accommodation when use not predicted.

4. Administration Protocols

4.1 Protocol A – Planned or “Rescue” Use

BLUETEQ form must be completed for each patient.
### Treatment Schedule:

<table>
<thead>
<tr>
<th>Day/Time</th>
<th>Treatment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 07:00</td>
<td>Start G-CSF at 1 MU/kg OD/SC injection</td>
</tr>
<tr>
<td>Day 2 07:00</td>
<td>G-CSF at 1 MU/kg/OD SC injection</td>
</tr>
<tr>
<td>Day 3 07:00</td>
<td>G-CSF at 1 MU/kg/OD SC injection</td>
</tr>
<tr>
<td>Day 4 07:00</td>
<td>G-CSF at 1 MU/kg OD/SC injection</td>
</tr>
<tr>
<td>Day 5 07:00</td>
<td>G-CSF at 1 MU/kg OD/SC injection</td>
</tr>
<tr>
<td>Day 5 08:30</td>
<td>Patient attends NHSBT apheresis unit:</td>
</tr>
<tr>
<td>17:00 or later</td>
<td>Plerixafor 240 mcg/kg OD/SC injection*</td>
</tr>
</tbody>
</table>

TAS = therapeutic apheresis service

*If harvest yield is less than target (usually minimum of 2 x 10^6 CD34/kg) repeat Plerixafor + G-CSF doses after ensuring there is apheresis and stem cell lab availability and after discussion with TAS consultant.

**See appendix 2 for background.

Patients may continue to receive this schedule up to a **maximum of 3 plerixafor doses.** If only one or 2 doses are given, the patient may receive the remaining dose(s) as part of another mobilisation episode as long as an individual patient does not receive more than 3 doses of plerixafor in total.

4.1.1 Actions to be taken by transfusion SpR:
- If WCC > 60, discuss with TAS consultant prior to proceeding with Plerixafor or G-CSF administration.
- Transfusion SpR to inform patient’s CNS and DTU if patient having apheresis or not and whether evening dose of plerixafor is needed.

4.2. **Protocol B - Pre-Emptive or “Just-In-Time” Use**

BLUETEQ form must be completed for each patient.
Note: GCSF timings are different than for the planned protocol. GCSF is given in the evenings.

<table>
<thead>
<tr>
<th>Day/Time</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Day 0             | Expected day 1 of apheresis after G-CSF, with or without chemotherapy, and WCC greater than/equal to 2 x 10^9/l.** Patient attends NHSBT apheresis unit:  
  - If PB CD34 >/= 15 per ul (or HPC >0.045), proceed to harvest as standard.  
  - If PB CD 8-14 per ul proceed to harvest but consider plerixafor if yield suboptimal.  
  - If CD34 count is insufficient to harvest cells (< 8 per ul) or yield is insufficient patient should receive or be considered to receive a dose of plerixafor in evening*  
  (Check patient is receiving correct dose of G-CSF)  
  Plerixafor 240 mcg/kg OD/SC injection  
  G-CSF to continue (to be administered at same time as before Plerixafor was started). Check dose patient is receiving.  
  If patient only on 0.5 MU/kg for PBSC mobilisation (e.g. myeloma patient) dose should be increased to 1 MU/kg for use with Plerixafor.  

Day 1 08:30 Patient attends NHSBT apheresis unit:  
  - If PB CD34 >/= 8 per ul, proceed to harvest.  
  - If PB CD 8-14 per ul proceed to harvest but consider plerixafor if yield suboptimal*.  
  - If PB CD34 < 8 per ul, discuss with consultant.  

*If harvest yield is less than target (usually minimum of 2 x 10^6 CD34/kg) repeat Plerixafor + G-CSF doses after ensuring there is apheresis and stem cell lab availability (for at least 2 consecutive days after the first plerixafor dose) and after discussion with TAS consultant.  
** See Contraindications section below.  

Patients may continue to receive this schedule up to a maximum of 3 plerixafor doses. If only one or 2 doses are given, the patient may receive the remaining dose(s) as part of a planned plerixafor mobilisation as long as an individual patient does not receive more than 3 doses of plerixafor in total.  

4.2.1 Actions to be taken by Transfusion SpR:  
  - If WCC > 60, discuss with TAS consultant prior to proceeding with Plerixafor or G-CSF administration.  
  - Patients should not be informed they are having plerixafor until the capacity to accommodate this is confirmed with the referring team.  
  - If patient being considered for plerixafor (CD 34 count < 8 per ul or CD 34, 8-14 per ul, or low harvest yield) liaise early with referring consultant or CNS to establish local capacity for administration at 1700.
For OUH patients inform patient’s CNS, Churchill Cancer Satellite Pharmacy (Ext 35615) and DTU co-ordinating nurse (bleep 5126)

- Complete BLUETEQ online registration form.
- For OUH patients prescribe 3 doses of Plerixafor and GCSF on ARIA. If it is not clear whether patient has consented to Plerixafor, re-take consent and give patient a copy to take to DTU to be filed in hospital notes
- Ask CNS to review whether patient needs help with accommodation or transport.

5. Dose

<table>
<thead>
<tr>
<th>Creatinine clearance (ml/min)</th>
<th>Plerixafor dose (based on body weight)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50</td>
<td>240 mcg/kg once daily given as subcutaneous injection (total dose not to exceed 40 mg/day)</td>
</tr>
<tr>
<td>20-50</td>
<td>160 mcg/kg once daily given as subcutaneous injection (total dose not to exceed 27 mg/day)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>Insufficient clinical evidence to recommend dose alterations *</td>
</tr>
</tbody>
</table>

**The patient’s weight should be obtained within 1 week of the first dose. The dose of Plerixafor is calculated based on actual body weight in patients up to 175% of ideal body weight (IBW). Plerixafor dose and treatment of patients weighing more than 175% of IBW have not been investigated, the Plerixafor dose should be capped at the dose for 175% IBW. Based on increasing exposure with increasing body weight, the Plerixafor dose should not exceed 40 mg/day.

IBW can be determined using the following equations:
Male (kg): 50 + 2.3 x ((height (cm) x 0.394) – 60)
Female (kg): 45.5 + 2.3 x ((height (cm) x 0.394) – 60)

*See section 7 for use of Plerixafor in dialysis-dependent patients.

6. Administration

Plerixafor is supplied in ready-to-use vials. Each vial contains 1.2ml of 20 mg/ml solution containing 24 mg of plerixafor. The volume of Plerixafor 240 mcg/kg to be administered can be calculated as follows: 0.012 x patient’s actual body weight (in kg) = dose to be administered (in ml).

- Plerixafor should be administered as a subcutaneous injection over the abdominal area. If the volume to be given exceeds 1.2ml the dose may be split and given in 2 injections.
- Patients should be monitored for one hour after drug administration (see Nursing care plan N.113)

*Timings are crucial to the success of Plerixafor treatment; any variations to the administration must be reported to the NHSBT apheresis unit.

Contraindications:
- Hypersensitivity to active substance or any of the excipients.
• **Patients whose total WCC suggests they are out with the PBSC “mobilisation window” on the basis of a WCC below 2 x 10^9/l or, after chemotherapy, above 20 x 10^9/l. Exceptions to this may be made at the discretion of the TAS consultant.

• Plerixafor may mobilise tumour cells and should not be used in any acute or chronic leukaemia.

7. Use of Plerixafor in Renal Impairment – Planned Protocol

<table>
<thead>
<tr>
<th>Day</th>
<th>Day -4 (Plan for Friday start)</th>
<th>Day -3</th>
<th>Day -2</th>
<th>Day -1</th>
<th>Day 0</th>
<th>Day +1</th>
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<tr>
<td>Morning 07:00</td>
<td>G-CSF 1MU/Kg</td>
<td>G-CSF 1MU/Kg</td>
<td>G-CSF 1MU/Kg</td>
<td>G-CSF 1 MU /Kg</td>
<td>G-CSF 1 MU /Kg</td>
<td>G-CSF 1 MU /Kg</td>
</tr>
<tr>
<td>Morning after G-CSF</td>
<td></td>
<td></td>
<td>Apheresis*</td>
<td>Apheresis*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>HD anytime</td>
<td>HD anytime</td>
<td></td>
<td>HD afternoon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evening 17:00 or later</td>
<td></td>
<td>Plerixafor</td>
<td>?Plerixafor*</td>
<td>?Plerixafor*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HD – Haemodialysis; * dependent on CD34 count or yield

8. Adverse Effects

• Commonly occurring side effects:
• Vasovagal reactions (can occur up to 1 hour after admin. hence monitoring need)
• Gastrointestinal effects including diarrhoea (more than 1 in 10 patients), nausea, vomiting, flatulence, dyspepsia, constipation.
• Reaction at injection site and allergic reactions
• Headache
• Arthralgia
• Dizziness
• Fatigue and insomnia
• Nightmares

Potentially serious side effects:
• Hyperleucocytosis
• Thrombocytopenia,
• Splenic enlargement with potential for rupture (Rare)
• Allergic reactions including anaphylaxis
• Myocardial infarction.

9. Audit
Regular audit is required with data on the following:
• No. of patients treated
• % of all mobilised patients attending for PBSCH who receive plerixafor
- No. of doses of Plerixafor used per patient
- Stem cell yield following Plerixafor
- Number of apheresis collection days for sufficient cells
- Time to engraftment

Quality reports will be compiled by the TAS and BMT Quality Managers and reviewed at appropriate TAS and BMT Quality meetings.

10. Stock Control

**Plerixafor stock management on Haematology Ward/DTU**
- Churchill Cancer Satellite Pharmacy (opening hours 9am-5pm) will hold a minimum of 6 vials of Plerixafor.
- One dose of Plerixafor will be dispensed for each patient every day on receipt of an ARIA prescription.
- Dispensed Plerixafor will be kept in the controlled drug cupboard in DTU until administration.

Appendix 1

**Factors that may predict poor PBSC mobilisation include:**
1. Heavy pre-treatment with any chemotherapy agents;
2. Previous treatment with any of fludarabine, alkylating agents, lenalidomide and possibly thalidomide,
3. Previous radiotherapy to large bone marrow-containing areas;
4. History of low grade lymphoma;
5. Bone marrow involvement.

Appendix 2

**Audit of Correlation between Pre-CD34 Counts and Stem Cell Yield**
47 patients received plerixafor May 2012-Nov 2015, 45 in planned fashion. In 64 of their apheresis episodes, pre-CD34 counts were available. In 19 cases the pre-count was less than 8/ul. Only 3 of these episodes resulted in a yield that may have been useful (0.85, 1.0 and 1.12 x 10^6 CD34/kg). In all 3 of these cases the pre-CD34 count was 7. A pre-CD34 count of 6 or below was never associated with a useful yield (defined as >= 0.7 x 10^6 CD34/kg). R Pawson, unpublished data Feb 2016

11. References
1. Mozobil®: Summary of Product Characteristics: [Link](https://www.medicines.org.uk/emc/product/790#PHARMACOKINETIC_PROPS) last updated on the eMC: 13.05.2019
3. Personal communication from Claire Foreman, chair of BMT CRG, via Rachel Pawson.

6. Douglas K W et al Plerixafor for PBSC mobilisation in myeloma patients with advanced renal failure: safety and efficacy data in a series of 21 patients from Europe and the USA. Bone Marrow Transplantation advance online publication 28 February 2011; doi: 10.1038/bmt.2011.9


**Author:** Dr Rachel Pawson, Consultant Haematologist

**Audit:** These processes are subject to OxBMT audit programme

**Circulation:** NSSG Haematology Website

### Review

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
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<tbody>
<tr>
<td>Dr Rachel Pawson</td>
<td>Change to include rescue and pre-emptive use; G-CSF dosing in MIU/kg; change in layout.</td>
<td>April 2012</td>
<td>1.1</td>
<td>May 2014</td>
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<tr>
<td>Julia Wong, Pharmacist</td>
<td>Changed GCSF units from MIU to MU Changed Pre-Emptive Day 0 GCSF doses. Stock management.</td>
<td>15/08/14</td>
<td>1.2</td>
<td>August 2016</td>
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<tr>
<td>Sandy Hayes, Quality manager</td>
<td>Removal of pre-assessment information. Formatting. Change of location to DTU.</td>
<td>October 2014</td>
<td>2.0</td>
<td>October 2016</td>
</tr>
<tr>
<td>Dr Rachel Pawson</td>
<td>Change of earliest time for administration of plerixafor to 1700 in view of data on 147 patients in new references.</td>
<td>April 2015</td>
<td>2.1</td>
<td>October 2016</td>
</tr>
<tr>
<td>Dr Rachel Pawson</td>
<td>Re-formatting to simplify tables. Inclusion of HPC to assess mobilisation. Expansion of criteria for pre-emptive use to include patients with CD34 &lt;15 per ul as per NHSE policy, Change to waiting for PB CD34 counts before harvest. Option to split doses across 2 mobilisation episodes. Reformat of document, logo update</td>
<td>March 2016</td>
<td>3.0</td>
<td>March 2018</td>
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<tr>
<td>Cheuk-kie Cheung, Pharmacist</td>
<td>Update of pharmacy supply, Blueteq requirement</td>
<td>May 2017</td>
<td>3.1</td>
<td>March 2018</td>
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<tr>
<td>Asif Khan, Consultant BHT</td>
<td>Minor edits</td>
<td>June 2019</td>
<td>3.2</td>
<td>Jun 2021</td>
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