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Plerixafor use in patients with sickle cell disease (SCD) who are eligible for treatment with exagamglogene autotemcel (Ages 12 years and above) [URN: 2348a]

NHS England commissioning statement

26 February 2025

Commissioning Position

1. This commissioning statement aims to standardise the criteria for plerixafor use for stem cell mobilisation in patients with sickle cell disease (SCD) who are eligible to receive treatment with exagamglogene autotemcel to optimise the use of limited resources and ensure equitable access for patients across England.
2. This commissioning statement supports the delivery of the NICE TA1044 for exagamglogene autotemcel use in patients with SCD and should be used in line with the existing Service Specification: Specialist-Haemoglobinopathy-Teams-Service-Specification.pdf (england.nhs.uk). which sets out standards for commissioned providers.

Information considered

3. SCD is an inherited disease that affects around 12,000-15,000 individuals in England (NICE, 2021). SCD often causes a lifelong anaemia, due to increased haemolysis and a lack of sufficient red blood cells to carry oxygen throughout the body. Sickle cell shaped red blood cells do not flow easily throughout the body and this can cause blockages (vaso-occlusion). Episodes of vaso-occlusion are known as vaso-occlusive crises. Chronic complications of SCD include a reduced life expectancy, severe chronic health problems and reduction in quality of life. Sickle cell crises may be extremely painful and often require emergency admission to hospital for oxygen therapy and pain control. Regular blood transfusions are often required in patients with SCD. Medical management with hydroxycarbamide can be used to improve anaemia and reduce vaso-occlusive crises.
4. Exagamglogene autotemcel is an autologous ex-vivo gene therapy medicinal product (GTMP). This is a type of cell therapy which is given to an individual as a one-off dose using haematopoietic stem cell transplantation (HSCT). Exagamglogene autotemcel is licensed for the treatment of SCD in patients 12 years of age and older with recurrent vaso-occlusive crises who have the β^S/β^S , β^S/β^+ or β^S/β^0 genotype, for whom HSCT is appropriate and a human leukocyte antigen (HLA) matched related haematopoietic stem cell donor is not available.
5. Exagamglogene autotemcel is made from the patient's own blood stem cells and is made specifically for the individual patient. Blood stem cells can turn into other blood cells, including

red cells, white cells and platelets. Cells are taken from the patient, which are then modified using exagamglogene autotemcel and given back to the patient as a cell-based transplant in hospital. As the patient's own blood stem cells are used in the transplant, this process is referred to as autologous HSCT. For autologous HSCT an HLA-matched, related donor is not required.

6. Prior to receiving treatment with exagamglogene autotemcel, patients with SCD are required to undergo mobilisation of their blood stem cells. This is to ensure that a sufficient quantity of their own blood stem cells can be harvested and treated with exagamglogene autotemcel. In most patients, mobilisation of stem cells can be achieved using a medicine called granulocyte colony stimulating factor (GCSF). However, in patients with SCD the use of GCSF is best avoided except in exceptional clinical circumstances due to the high risk of life-threatening complications resulting from hyperleukocytosis (excess white blood cell production) and neutrophil activation (activation of white blood cells).
7. Plerixafor can be used to mobilise stem cells in patients with SCD who are suitable to receive treatment with exagamglogene autotemcel. Plerixafor is given by injection under the skin (subcutaneous injection) and works by mobilising patients' own blood stem cells from the bone marrow into the blood stream. Patients undergo a procedure to have their blood stem cells harvested (apheresis). The patient's stem cells can then be treated with exagamglogene autotemcel. The use of plerixafor as outlined in this commissioning statement is off-label.
8. Once a patient's blood stem cells have been harvested, they are sent away for treatment with exagamglogene autotemcel. This treatment works by increasing the production of a special type of haemoglobin within the patient's red blood cells called foetal haemoglobin. Having larger amounts of foetal haemoglobin increases the oxygen-carrying capacity of the patient's red blood cells and improves their function. For patients with SCD this can reduce, or even stop, vaso-occlusive crises from occurring. It takes approximately 6 months from the time the patient's blood cells are collected, for the cells to be treated with exagamglogene autotemcel and returned to the site of patient administration.
9. Once the treated cells have been returned, patients receive a conditioning medicine in hospital, a few days before the planned stem cell transplant. Patients remain in hospital to receive the transplant of their treated stem cells, which are delivered via an infusion. The patient will then remain in hospital until after the infusion.
10. This NHS England Commissioning Statement commissions the use of plerixafor for stem cell mobilisation in patients with SCD who are eligible to receive treatment with exagamglogene autotemcel.

Commissioned use

11. In order for a patient with SCD to receive treatment with plerixafor, all requirements set out in Annex A must be met. Service providers need to ensure they can fully support this patient group as defined by NICE, including pre- and post-autologous HSCT care and management of plerixafor-related reactions and transplant rejection. Service providers need to ensure robust management of plerixafor is in place, including appropriate level of pharmacy supervision, correct storage equipment and audit of plerixafor use.

Equality statement

12. 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.

Links to policies and commissioning statements

13. This policy relates to the following guidance, practices and specification:

- National Institute for Health and Care Excellence (NICE)
  - NICE TA1044
- NHS England
  - Plerixafor for stem cell mobilisation in adults and children 200601P
  - NHS England » Clinical commissioning statement: plerixafor use in patients with transfusion-dependent beta-thalassaemia who are eligible for treatment with exagamglogene autotemcel (ages 12 years and above)

Definitions

Apheresis	The process of withdrawing blood from a donor's body and separating the blood out into different types of cells.
Conditioning	This is a course of treatment that prepares the patient for the transplantation of stem cells. Conditioning usually involves a regimen of high dose chemotherapy and aims to destroy the patient's bone marrow, suppress the immune system and make way for the new stem cells.
HLA matched	Human leukocyte antigen (HLA) typing is a genetic test used to match patients and donors for bone marrow, cord blood or organ transplants.
Mobilisation cycle	Stem cell mobilisation is the process of stimulating stem cells from the bone marrow into the bloodstream so that they can be collected for later reinfusion. One mobilisation cycle is defined as mobilisation plus the completion of all collective attempts at apheresis that may occur in a given time period.

References

1. Esrick, E.B. et al. (2018) ‘Successful hematopoietic stem cell mobilization and apheresis collection using plerixafor alone in sickle cell patients’, Blood Advances, 2(19), pp. 2505–2512. doi:10.1182/bloodadvances.2018016725.

2. Frangoul, H. et al. (2024) ‘Exagamglogene autotemcel for severe sickle cell disease’, New England Journal of Medicine, 390(18), pp. 1649–1662. doi:10.1056/nejmoa2309676.

3. Leonard, A. *et al.* (2021) ‘Disease severity impacts plerixafor-mobilized stem cell collection in patients with sickle cell disease’, *Blood Advances*, 5(9), pp. 2403–2411. doi:10.1182/bloodadvances.2021004232.

4. NICE CKS Sickle Cell Disease: Prevalence (2021) NICE. Available at: https://cks.nice.org.uk/topics/sickle-cell-disease/background-information/prevalence/ (Accessed: 28 February 2024).

5. Medicines & Healthcare Products Regulatory Agency. UK Public Assessment Report. March 2023. Available at: UKPAR for Exacel.pdf . (Accessed: 3 February 2025).

Starting arrangements for all patients

1. The guidance for treatment with exagamglogene autotemcel for patients with sickle cell disease is covered by the NICE technology appraisal NICE TA1044.

Inclusion criteria

2. Patients with a confirmed diagnosis of SCD must meet **all** of the following inclusion criteria to be eligible for treatment with plerixafor. The patient:
    - Must meet all of the eligibility criteria for treatment with exagamglogene autotemcel as outlined in the NICE Technology Appraisal NICE TA1044.
    - Must be managed at a recognised centre commissioned to provide treatment with exagamglogene autotemcel.
    - Consent, patient evaluation and investigations prior to the commencement of the mobilisation procedure must be carried out at a recognised centre commissioned to provide treatment with exagamglogene autotemcel, in accordance with relevant transplant centre policy.

Exclusion criteria

3. Patients who meet **any** of the following exclusion criteria are contraindicated from treatment with plerixafor:
    - Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1 of the SmPC.
    - Plerixafor should not be used in pregnancy. Women of childbearing potential must use effective contraception during treatment with plerixafor.

Plerixafor should be otherwise used in accordance with the SmPC including special warnings and precautions for use.

Starting criteria

4. The targeted $CD34^+$ collection is $\geq 15x10^6$ cells/kg at mobilisation required for manufacturing of exagamglogene autotemcel in order to achieve a minimum target dose of $3x10^6$ $CD34^+$ cells/kg.
5. One mobilisation cycle is defined as mobilisation plus the completion of all collective attempts at apheresis that occur from Day 1 to Day 3 (inclusive):
    - On Day 1 of mobilisation, subjects should receive plerixafor 2-3 hours before the start of apheresis (dosing regimens are set out in the 'Dosing' section of this commissioning statement). Prior to apheresis, a $CD34^+$ count should be taken, and the treating Transplant Consultant will determine if this is sufficient to proceed.
    - On Day 2, patients should be given a further dose of subcutaneous plerixafor and an attempt at harvesting made the following day if the repeat $CD34^+$ is sufficient.
    - On Day 3 of apheresis, if further cell harvest for backup cells is required, a further dose of plerixafor alone should be administered. 2×10^6 $CD34^+$ cells/kg are required as backup for rescue therapy in the event of a non-neutrophil engraftment with exagamglogene autotemcel. No collection of cells for manufacturing should occur on the day of backup cell

rescue therapy collection. The administration of a 3rd dose of plerixafor for the collection of backup cells is generally only required as part of the 1st mobilisation cycle.

- **For patients who require more than two mobilisation and apheresis cycles:**
    - For these patients, clinical teams should email the National Haemoglobinopathy Panel Stem Cell Transplant/Cellular Therapy Operational Group informing the Group of the need for more than two mobilisation cycles. Based on limited trial evidence, this is likely to be limited to an extremely small number of patients.
    - Subsequent mobilisation cycles will likely only require a schedule up to and including Day 2 (e.g. a maximum of two doses of plerixafor per subsequent mobilisation cycle), assuming sufficient backup cells have been obtained in 1st mobilisation cycle.
- 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.

Stopping criteria

- A maximum of 3 doses of plerixafor are permitted per mobilisation cycle.

Dosing

Plerixafor

- Plerixafor should be administered at a dose of 0.24mg/kg by subcutaneous injection 2-3 hours before the start of each apheresis.
- The body weight used in the calculation of dosing should be taken within 5 days before Day 1 of mobilisation.

The use of plerixafor as outlined in this NHS England commissioning statement is off-label. Trust Policy regarding off-label use of medicines should apply.

For further information on plerixafor dosing prior to treatment with exagamglogene autotemcel in SCD please see Annex B and refer to the UK Public Assessment Report.

Monitoring

Patients should be monitored in a transplant unit and receive supportive care according to standard practices for patients undergoing haematopoietic stem cell transplantation.

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.

Effective from

The commissioning statement is effective from the date of publication. This commissioning statement will be reviewed in line with any updates to the NICE technology appraisal for

exagamglogene autotemcel use in patients with SCD.

Recommendations for governance and data collection

The use of the plerixafor will be subject to the NHS England prior approval (Blueteq) system.

The use of plerixafor in the context of this commissioning statement is off-label. 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 these assurance processes.

Plerixafor for HSCT mobilisation for **treatment with exagamglogene autotemcel** in adults and children under this policy will be commissioned and funded by NHS England Specialised Commissioning under **commissioning** arrangements for the provision of **treatment with exagamglogene autotemcel.** 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 Colony Forming Units (CFU) following plerixafor.
- Number of collection days required to obtain sufficient cells for indicated Peripheral Blood Stem Cell Transplantation (PBSCT).
- Time to neutrophil and platelet engraftment following PBSCT to assess the quality of the stem cell harvested.

Full dosing chart

SCD[1],[2]	**Mobilisation + Days of Apheresis**						
	Day 1	Day 2	Day 3[3]	-	-	-	-
Plerixafor[4],[5]	X	X	X				

Information in the Full Dosing Chart supplied by Vertex Pharmaceuticals Incorporated, Boston, MA

[1] Frangoul H, et al. *N Engl J Med* 2021;384(3):252-260. (protocol)
[2] Data on file. Vertex Pharmaceuticals Incorporated, Boston, MA
[3] The third day of apheresis is reserved ONLY for collection of backup cells. No collection of cells for manufacturing should occur on that day.
[4] Plerixafor will be administered only if apheresis is planned for that day
[5] Administered 2-3 hours before planned apheresis