

# National Horizon Scanning Centre

## Plerixafor (Mozobil) for stem cell mobilisation in non- Hodgkin's lymphoma

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This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

## **Plerixafor (Mozobil) for stem cell mobilisation in non-Hodgkin's lymphoma**

### **Target group**

- Non-Hodgkin's lymphoma (NHL) – undergoing autologous transplantation

### **Technology description**

Plerixafor (Mozobil, AMD 3100) is a first in class CXCR4 antagonist that mobilises stem cells from the bone marrow increasing their numbers in peripheral blood. Plerixafor blocks the CXCR4 chemokine receptor and its cognate ligand SDF-1 $\alpha$ , which are involved in the retention of stem cells in bone marrow. As plerixafor is a release factor and not a growth factor it does not initiate differentiation of haematopoietic stem cells.

Plerixafor is administered by subcutaneous injection at 240  $\mu$ g/kg in combination with a granulocyte-colony stimulating factor (G-CSF) prior to autologous stem cell transplant.

Plerixafor is also in clinical trials for stem cell mobilisation in multiple myeloma.

### **Innovation and/or advantages**

Plerixafor is the first in class and has the potential to reduce the number of apheresis sessions required and increase the number of patients reaching minimum cell-yield target who can proceed to transplantation.

### **Developer**

Genzyme Therapeutics.

### **Place of use**

- |   |   |  |
|---|---|--|
| <input type="checkbox"/> Home care e.g. home dialysis                         | <input type="checkbox"/> Community or residential care e.g. district nurses, physio           | <input type="checkbox"/> Primary care e.g. used by GPs or practice nurses    |
| <input type="checkbox"/> Secondary care e.g. general, non-specialist hospital | <input checked="" type="checkbox"/> Tertiary care e.g. highly specialist services or hospital | <input type="checkbox"/> Emergency care e.g. paramedic services, trauma care |
| <input type="checkbox"/> General public e.g. over the counter                 | <input type="checkbox"/> Other:   |  |

### **Availability, launch or marketing dates, and licensing plans:**

The company anticipate a licence application in the EU in Q1/2 2008. Plerixafor has been granted orphan drug status in the EU and US.

### **NHS or Government priority area:**

This topic relates to the NHS Cancer Plan.

### **Relevant guidance**

- NICE cancer service guideline. Haemato-oncology. October 2003<sup>1</sup>.
- NICE technology appraisal. Rituximab for the treatment of follicular lymphoma. 2006<sup>2</sup>.
- NICE technology appraisal. Rituximab for aggressive non-Hodgkin's lymphoma. 2003<sup>3</sup>.
- NICE technology appraisal. Rituximab for recurrent or refractory stage III or IV follicular non-Hodgkin's lymphoma. 2002 (currently being reviewed)<sup>4</sup>.
- British Committee for Standards in Haematology. Guidelines on the diagnosis and therapy: nodal non-Hodgkin's Lymphoma. 2002<sup>5</sup>.

- British Committee for Standards in Haematology. Guidelines on the use of colony-stimulating factors in haematological malignancies. 2003<sup>6</sup>.

### Clinical need and burden of disease

In 2005 there were 8,841 new cases of NHL registered in England and Wales, with 3,929 deaths<sup>7</sup>. In 2006 there were 395 autologous peripheral blood stem cell transplants undertaken in patients with NHL in the UK<sup>8</sup>. It is unclear what proportion of patients undergoing autologous transplantation would benefit from plerixafor.

### Existing comparators and treatments

- Recombinant human granulocyte-colony-stimulation factor (G-CSF): used either alone prior to autologous transplantation or after myelosuppressive chemotherapy.
  - Filgrastim (Neupogen)
  - Lenograstim (Granocyte)

### Efficacy and safety

There are many published or registered case series and/or small non-randomised, open label trials of plerixafor, but only 3 randomised trials:

Trial name or code	AMD3100-3101; NCT00203610 Phase III	AMD3100-C201; NCT00396266 Phase II (NHL or MM)	First trial in patients (NHL or MM)
Sponsor	Genzyme	Genzyme	-
Status	Unpublished <sup>9</sup>	Ongoing – no longer recruiting	Published <sup>10</sup>
Location	USA and Canada	Canada	USA
Design	Randomised, controlled, double-blind	Open-label, uncontrolled	Randomised, cross-over, proof-of-concept
Participants in trial	N=298; NHL; undergoing haematopoietic stem cell transplant. Randomised to G-CSF (10 µg/kg/day) with plerixafor (240 µg/kg) or G-CSF with placebo.	N=23; NHL or multiple myeloma (MM); undergoing autologous transplant. Plerixafor (240 µg/kg) and G-CSF (10 µg/kg/day) prior to apheresis for up to 5 consecutive days.	N=25; MM or NHL in complete or partial remission; undergoing autologous transplant. Randomised to G-CSF with plerixafor or G-CSF alone; 2-week washout before cross-over.
Follow-up	12 months post transplantation	12 months following transplant	-
Primary outcome	Target mobilisation threshold of ≥ 5 million CD34+ cells/kg in four or fewer apheresis sessions.	Safety	Average CD34+ cells/kg per day of apheresis; total number of CD34+ cells/kg.
Secondary outcomes	≥ 2 million CD34+ cells/kg in four or fewer apheresis sessions; engraftment of stem cells; graft durability to 100 days.	≥2-fold increase in circulating CD34+ cells; time to engraftment of stem cells.	≥ 2 million CD34+ cells/kg collected
Key results	Primary endpoint: 59% on plerixafor with G-CSF compared with 20% on placebo with G-CSF achieved primary endpoint (p<0.0001).	-	More CD34+ cells were collected after plerixafor with G-CSF, than with G-CSF alone. In 84% of cases plerixafor with G-CSF produced a

	Secondary endpoint: 87% on plerixafor with G-CSF compared with 47% on placebo with G-CSF achieved secondary endpoint (p<0.0001).		daily increase in CD34+ cells/kg of more than 50%. Patients with NHL mobilised a median of 4.4-fold more cells with plerixafor.
Expected reporting date	Results to be presented to American Society of Hematology in Dec 2007.	Trial commenced Jan 2005	N/A
Adverse effects	Plerixafor was well tolerated; most common adverse effects were mild gastrointestinal effects and injection site redness.	-	No serious adverse events were felt related to plerixafor. Most common milder adverse events associated with plerixafor were diarrhoea, injection site redness and nausea.

### Estimated cost and cost impact

The cost of plerixafor is not yet known. The cost of available G-CSF is:

Drug	Dose	Cost of course <sup>a</sup>
Filgrastim	1 MU/kg daily for 5-7 days	£545 to £763
Lenograstim	1.28 MU/kg for 4-6 days	£815 to ££1,223

### Potential or intended impact – speculative

#### Patients

- |  |  |   |
|--|--|---|
| <input checked="" type="checkbox"/> Reduced morbidity: Increased numbers of patients reaching cell yield target who may proceed to transplantation | <input checked="" type="checkbox"/> Reduced mortality or increased survival: Increased numbers of patients reaching cell yield target who may proceed to transplantation | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers: Fewer transfusions |
| <input type="checkbox"/> Quicker, earlier or more accurate diagnosis or identification of disease  | <input type="checkbox"/> Other:  | <input type="checkbox"/> Non identified   |

#### Services

- |  |  |   |
|--|--|---|
| <input type="checkbox"/> Increased use   | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input checked="" type="checkbox"/> Decreased use: reduced numbers of blood transfusions and hospital days | <input type="checkbox"/> Other:                          | <input type="checkbox"/> Non identified             |

#### Costs

- |  |  |   |
|--|--|---|
| <input type="checkbox"/> Increased unit cost compared to alternative         | <input type="checkbox"/> Increased costs: more patients coming for treatment   | <input type="checkbox"/> Increased costs: capital investment needed |
| <input checked="" type="checkbox"/> New costs: Additional mobilisation agent | <input checked="" type="checkbox"/> Savings: Potential reduced numbers of apheresis, blood transfusions and hospital days. | <input type="checkbox"/> Other:                                     |

<sup>a</sup> Costs from BNF 53, March 2007. Average weight adult 67.5kg.

## References

- <sup>1</sup> National Institute for Clinical Excellence. Cancer Service Guideline. Improving outcomes in haemato-oncology cancer. October 2003.
- <sup>2</sup> National Institute for Health and Clinical Excellence. Rituximab for the treatment of follicular lymphoma. Technology Appraisal 110. September 2006.
- <sup>3</sup> National Institute for Clinical Excellence. Rituximab for aggressive non-Hodgkin's lymphoma. Technology Appraisal 65. September 2003.
- <sup>4</sup> National Institute for Health and Clinical Excellence. Rituximab for recurrent or refractory stage III or IV follicular non-Hodgkin's lymphoma. Technology Appraisal 37. 2002
- <sup>5</sup> Cullen M., Dixon A., Goldstone A. *et al.* British Committee for Standards in Haematology Guidelines on diagnosis and therapy: Nodal non-Hodgkin's Lymphoma. The Haemato-Oncology Task Force of British Committee for Standards in Haematology, August 2002.
- <sup>6</sup> British Committee for Standards in Haematology. Guidelines on the use of colony-stimulating factors in haematological malignancies. *British Journal of Haematology*, 2003;125:22-33.
- <sup>7</sup> Cancer Research UK. Non-Hodgkin lymphoma: Cancer Stats Information. Available at: <http://info.cancerresearchuk.org/cancerstats/types/nhl> [accessed 18/10/07].
- <sup>8</sup> British Society of Blood and Marrow Transplants. BSBMT Data Registry: 2006 activity data by indication. Available at: <http://www.bsbmt.org> [accessed 13<sup>th</sup> September 2007].
- <sup>9</sup> Genzyme Corp. Genzyme announces phase 3 trial of Mozobil in non-Hodgkin's lymphoma meet primary endpoint. Press release, July 19<sup>th</sup> 2007. Available at: <http://www.genzyme.com/corp/media/GENZ%20PR-071907.asp> [accessed 13/09/07].
- <sup>10</sup> Flomenberg N, Devine SM, DiPersio JF *et al.* The use of AMD3100 plus G-CSF for autologous hematopoietic progenitor cell mobilization is superior to G-CSF alone. *Blood* 2005; 106(5):1967-1874.

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