AWMSG Secretariat Assessment Report – Limited submission

Plerixafor (Mozobil®) 20 mg/ml solution for injection

Company: Sanofi Aventis

Licensed indication under consideration: For use in combination with granulocyte colony stimulating factor (G-CSF) to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children aged ≥ 1 to <18 years with lymphoma or solid malignant tumours either:

- pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilization with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield, or
- who previously failed to collect sufficient haematopoietic stem cells.

Date of licence extension: 13 May 2019

Comparator(s)

- The current standard of care in the UK for stem cell mobilisation is G-CSF plus chemotherapy. Plerixafor is the first autologous stem cell mobilisation agent licensed for use as an add-on therapy to standard care and will not displace any product already in current practice.

Limited submission details

- The limited submission criteria were met based on a minor licence extension

Clinical effectiveness

- In 2010, plerixafor was recommended by the All Wales Medicines Strategy Group (AWMSG) as an option for restricted use in adults within NHS Wales in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma who have already failed one complete mobilisation attempt.
- Clinical expert opinion sought by the All Wales Therapeutics & Toxicology Centre (AWTTC) agrees that plerixafor is used to aid successful mobilisation of stem cells which is not dependent on the specific cancer diagnosis.
- The evaluation of efficacy is focussed on the data collected within the MOZAIC study, in particular stage 2 of this study. Stage 1 (n=27) was a dose escalation study involving three age cohorts: 2 to <6 years, 6 to <12 years and 12 to <18 years. The plerixafor treatment regimen selected for Stage 2 was the same as that used in adults, 240 micrograms/kg subcutaneous injection the evening prior to apheresis approximately 8 to 12 hours later.

- Stage 2 was an open label, randomised, comparative study of plerixafor in addition to standard regimens (G-CSF ± chemotherapy) (n=30) versus standard regimens alone (n=15). Participants were aged ≥ 1 to <18 years, and the primary efficacy endpoint was successful mobilisation (i.e. the proportion of patients achieving at least a doubling of the PB CD34+ count from the morning of the day preceding the first apheresis day to the morning of apheresis). Apheresis was to occur if the PB CD34+ count, on the scheduled day of apheresis, was ≥2 x 10^6 CD34+ cells/kg. Participants were not required to have already failed one complete mobilisation attempt.
- The proportion of patients with successful mobilisation was significantly greater in the plerixafor plus standard mobilisation arm (80%, 24 of 30 patients) compared to the standard mobilisation only arm (28.6%, 4 of 14 patients) (p=0.0019). The rate of successful mobilisation was similar across age and disease categories in the plerixafor plus standard mobilisation arm.
- Regarding the clinically relevant secondary endpoints, no clear difference was reported between the study arms. The number of patients reaching the threshold of collecting ≥2 x 10^6 CD34+ cells/kg was comparable between the treatment groups (89.7% vs 92.9% for plerixafor plus standard mobilisation and standard mobilisation respectively). However, the median amount of CD34+ cells at baseline was significantly lower in the plerixafor plus standard mobilisation arm and therefore the absolute increase in PB CD34+ count was greater. For both treatment groups the median number of apheresis days needed to collect the threshold number of cells was one. The percentage of patients who proceeded to transplant was higher for the plerixafor plus standard mobilisation arm than for the control arm (76.7% vs 66.7%, respectively), but no data are available regarding reasons for not proceeding to transplant. Exposure to plerixafor did not impact on the outcome of transplantation; all transplanted patients successfully engrafted and durability of engraftment was comparable between the two treatment arms.
- Overall, the Committee for Medicinal Products for Human Use (CHMP) considered that focussing on the potentially low mobilising subjects (based on pre-apheresis PB CD34+ counts), a clinically relevant effect of plerixafor treatment in children (1 to less than 18 years) who are expected to mobilise poorly is sufficiently supported.
- CHMP concluded that the safety of plerixafor added to standard mobilisation in children aged ≥ 1 to <18 years is consistent with that in adults; there were no new safety concerns. There are no long-term safety data.
- The European Medicines Agency granted plerixafor (Mozobil®) orphan status in 2009. AWTTC considers the licensed indication for plerixafor does not exceed the AWMSG ultra-orphan threshold of ≤ 1 in 50,000 in the UK (or ≤ 60 patients in Wales).

Budget impact

- The company estimate that in Year 1 there are six children eligible for stem cell mobilisation and subsequent autologous transplantation in Wales increasing to seven children in Year 5. This is based on population data for Wales and the number of paediatric patients eligible for autologous stem cell transplant in the UK during 2018.
- The company calculates the medicine acquisition cost of plerixafor is £4,883 per patient per year. This is based on the fact each vial is intended for single use only, and the assumption that only one dose of plerixafor is required for successful mobilisation; this was the median number of doses (range: 1.0 to 3.0) administered in the plerixafor plus standard mobilisation arm of the pivotal trial.

- The company also includes sensitivity analysis for two or three doses, highlighting that a maximum three doses of plerixafor per patient is applied as a stopping criteria in the existing NHS England clinical commissioning policy for plerixafor in stem cell mobilisation for paediatrics. If this stopping criteria is also applied in Wales, the cost of plerixafor based on a maximum of three doses at BNF list price is £14,648 per patient/treatment course/year.
- The company assumes that a 100% uptake of plerixafor is likely because there is no alternative corresponding autologous stem cell mobilisation agent.
- Using one vial of plerixafor per patient per treatment course, the company estimates the budget impact to be £29,507 in Year 1 and £34,424 in Year 5; this includes modest net administration costs.
- Clinical expert opinion sought by AWTTC suggests this is likely to be an over estimate as most paediatric patients can be successfully mobilised without the addition of plerixafor to standard mobilisation.
- As plerixafor is an add-on therapy and will not displace any product already in current practice, standard mobilisation regimen costs are not included.

Additional information

- AWTTC is of the opinion that, if recommended, plerixafor (Mozobil®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

Evidence search

Date of evidence search: 30 September 2019
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report**.** Plerixafor (Mozobil®) 20 mg/ml solution for injection**.** Reference number: 3297 January 2020