PUBLIC SUMMARY DOCUMENT
Product: Plerixafor, solution for injection, 20 mg in 1 mL, 1.2 mL, Mozobil®
Sponsor: Sanofi Aventis Pty Ltd
Date of PBAC Consideration: July 2012

1. Purpose of Application

Re-submission for Section 100 (Highly Specialised Drugs Program) Private Hospital Authority Required and Public Hospital Authority Required (STREAMLINED) listing for:

1. Treatment, in combination with a granulocyte-colony stimulating factor (G-CSF), of lymphoma in patients who require autologous stem cell transplantation and who have failed previous stem cell collection or who are failing a current stem cell collection.
2. Treatment, in combination with a granulocyte-colony stimulating factor (G-CSF), of multiple myeloma in patients who require autologous stem cell transplantation and who have failed previous stem cell collection or who are failing a current stem cell collection.

Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

2. Background

This was the third time plerixafor had been considered by the PBAC.

At its November 2010 meeting, the PBAC rejected a submission seeking a Section 100 (Highly Specialised Drugs Program) listing for use of plerixafor, in combination with granulocyte-colony stimulating factor (G-CSF), in mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL) and multiple myeloma (MM) who meet certain criteria, on the basis of an inappropriate comparator for the first-line indications, uncertain clinical benefit in second-line setting relating to the lack of comparative data, and uncertainty regarding the economic model.

The PBAC agreed that a simple and conservative comparison of costs of mobilisation on a per patient basis should also be provided, rather than a claim of highly uncertain transplant benefits.

At the November 2011 meeting, the PBAC rejected a resubmission seeking a Section 100 (Highly Specialised Drugs Program) listing for use of plerixafor in mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous stem cell transplantation (ASCT) in patients with lymphoma and multiple myeloma who have failed previous stem cell collection attempts (in combination with granulocyte-colony stimulating factor (G-CSF)).

3. Registration Status

Plerixafor was TGA registered on 31 May 2010 for use, in combination with granulocyte-colony stimulating factor (G-CSF) to mobilise haematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma.

4. Listing Requested and PBAC's View

Section 100 listing – Highly Specialised Drug Program
Public Hospital – Authority Required (Streamlined)
Private Hospital – Authority Required
Treatment, in combination with granulocyte-colony stimulating factor (G-CSF) in a patient with lymphoma who requires autologous stem cell transplantation and has failed previous stem cell collection.

Treatment, in combination with granulocyte-colony stimulating factor (G-CSF) in a patient with multiple myeloma who requires autologous stem cell transplantation and has failed previous stem cell collection.

Treatment, in combination with granulocyte-colony stimulating factor (G-CSF) in a patient with lymphoma who requires autologous stem cell transplantation and is failing a current stem cell collection, based upon one of the following:

a. Peripheral blood CD34+ count below the institutional threshold for apheresis on expected morning of first collection.
b. First day apheresis peripheral blood CD34+ yield suboptimal for likely success within 1-2 apheresis.

Treatment, in combination with granulocyte-colony stimulating factor (G-CSF) in a patient with multiple myeloma who requires autologous stem cell transplantation and is failing a current stem cell collection based upon one of the following:

a. Peripheral blood CD34+ count below the institutional threshold for apheresis on expected morning of first collection.
b. First day apheresis peripheral blood CD34+ yield suboptimal for likely success within 1-2 apheresis.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

High dose chemotherapy with autologous stem cell transplantation is a highly effective treatment for patients with haematological malignancies who are fit enough to undergo this form of therapy. Before transplantation can take place, patients must undergo stem cell mobilisation to increase the number of peripheral blood stem cells available for collection and subsequent autologous transplantation. Currently, most patients are mobilised with granulocyte-colony stimulating factor (G-CSF) alone, or G-CSF with chemotherapy.

Despite developments in peripheral blood stem cells mobilisation and collection techniques, a proportion of patients can undergo repeated mobilisation attempts and still fail to collect enough cells for stem cell transplantation. These patients are commonly referred to as "failed mobilisers". Although mobilisation protocols can vary between institutions, failed mobilisers are usually defined as those patients who fail to collect the minimum CD34+ cell yield for transplant (2×10^6 CD34+ cells/kg) (Mohty et al., 2011) or those patients who are unable to proceed to apheresis because of low peripheral blood CD34+ cell counts. The respondents to the Sponsor's Australian Treatment Practice Survey provided thresholds of peripheral blood CD 34+ cell counts ranging from 5 to 20 cells/μL to proceed to apheresis.

In general, patients who fail mobilisation tend to be older, more heavily pre-treated and have more extensive disease (Sugrue *et al.*, 2000). The delay in treatment that results from a failure to mobilise further increases the chances of disease progression.

The submission proposed that the place in therapy of plerixafor, in combination with G-CSF, is for the treatment of patients who are failed mobilisers or those who are failing mobilisation (immediate savage) and who will subsequently undergo autologous stem cell transplantation (ASCT) for lymphoma and multiple myeloma patients.

For PBAC's view, see Recommendations and Reasons.

6. Comparator

Granulocyte-colony stimulating factor (G-CSF) 10µg/kg in combination with chemotherapy (ifosfamide + carboplatin + etoposide for lymphoma; and cyclophosphamide for multiple myeloma) was nominated as the comparator.

7. Clinical Trials

The following table outlines the non-randomised studies and observational cohorts presented in the re-submission in failed mobilisers.

Study ID	Protocol title/Publication title	Publication citation
Chemotherapy plus G-CSF and plerixafor plus G-CSF groups		
Pusic (2008) Nov 2010 and Nov 2011	Pusic I, Jiang SY, Landua S, Uy GL, Rettig MP, et al. Impact of Mobilisation and Remobilisation Strategies on Achieving Sufficient Stem Cell Yields for Autologous Transplantation.	Biology of Blood and Marrow Transplantation 2008; 14:1045-1056.
Plerixafor plus G-CSF (± chemotherapy)		
Calandra (2008) Nov 2010 and Nov 2011	Calandra G, McCarty J, Mcguirk J, Tricot G, Crocker SA, et al. AMD3100 plus G-CSF can successfully mobilise CD34+ cells from non-Hodgkin's lymphoma, Hodgkin's disease and multiple myeloma patients previously failing mobilisation with chemotherapy and/or cytokine treatment: Compassionate use data.	Bone Marrow Transplantation 2008; 41:331-338.
Fowler (2009) Nov 2010 and Nov 2011	Fowler CJ, Dunn A, Hayes-Lattin B, Hansen K, Hansen L, et al. Rescue from failed growth factor and/or chemotherapy HSC mobilisation with G-CSF and plerixafor (AMD3100): An institutional experience.	Bone Marrow Transplantation 2009; 43:909-917
Micallef (2009) Nov 2010 and Nov 2011	Genzyme Corporation. A multicenter, randomised, double-blind, placebo-controlled, comparative trial of AMD3100 (240 µg/kg) plus G-CSF (10 µg/kg) versus G-CSF (10 µg/kg) plus placebo to mobilise and collect ≥5 x 10^6 CD34+ cells/kg in non-Hodgkin's lymphoma patients for autologous transplantation – final 12-month clinical study report. Micallef I, Stiff PJ, DiPersio JF, Maziarz RT, McCarty JM, et al. Successful stem cell remobilization using plerixafor (Mozobil) with non-Hodgkin Lymphoma: Results from the plerixafor NHL Phase 3 study rescue protocol.	2008. Biology of Blood and Marrow Transplantation 2009; 15: 1578-86.

Study ID	Protocol title/Publication title	Publication citation
Tricot (2010) Nov 2010 and Nov 2011 (additional data)	Tricot G, Cottler-Fox MH, Calandra G. Safety and efficacy assessment of plerixafor in patients with multiple myeloma proven or predicted to be poor mobilisers, including assessment of tumor cell mobilisation.	Bone Marrow Transplantation 2010; 45:63-68.
Duarte (2011) – Nov 2010 commentary and Nov 2011 submission	Duarte RF, Shaw BE, Marín P, Kottaridis P, Ortiz M, et al. Plerixafor plus granulocyte CSF can mobilize hematopoietic stem cells from multiple myeloma and lymphoma patients failing previous mobilization attempts: EU compassionate use data.	Bone Marrow Transplantation 2011; 46(1): 52-8.
Attolico (2012) Additional	Attolico I, Pavone V, Ostuni A, Rossini B, Musso M, et al. Plerixafor added to chemotherapy plus G-CSF is safe and allows adequate PBSC collection in predicted poor mobiliser patients with multiple myeloma or lymphoma.	Biology of Blood and Marrow Transplantation 2012; 18:241-249.
Basak (2011a) Additional	Basak GW, Knopinska-Posluszny W, Matuszak M, Kisiel E, Hawrylecka D, et al. Hematopoietic stem cell mobilisation with the reversible CXCR4 receptor inhibitor plerixafor (AMD3100) – Polish compassionate use experience.	Annals of Hematology 2011a; 90:557-568.
Cooper (2011) Additional	Cooper DL, Pratt K, Baker J, Medoff E, Conkling-Walsh A, et al. Late afternoon dosing of plerixafor for stem cell mobilisation: a practical solution.	Clinical Lymphoma, Myeloma & Leukemia 2011; 11(3):267-272.
Hübel (2011a) Additional	Hübel K, Fresen MM, Apperley JF, Gabriel IH, Basak GW, et al. European data on stem cell mobilization with plerixafor in non-Hodgkin's lymphoma, Hodgkin's lymphoma and multiple myeloma patients. A subgroup analysis of the European Consortium of stem cell mobilization.	Bone Marrow Transplantation [Article in Press]
Hübel (2011b) Additional	Hübel K, Fresen MM, Theurich S, Lange F, Salwender H, et al. Plerixafor with and without chemotherapy in poor mobilizers: Results from the German compassionate use program.	Bone Marrow Transplantation 2011; 46(8): 1045-1052.
Selleslag (2011) Additional	Selleslag D, Dierickx D, Meers S, Breems DA, Huynh P, et al. Plerixafor in poor stem cell mobilizers: The Belgian compassionate use program.	Acta Clinica Belgica 2011; 66(3): 200-204.
Worel (2011) Additional	Worel N, Rosskopf K, Neumeister P, Kasparu H, Nachbaur D, et al. Plerixafor and granulocyte-colony-stimulating factor (G-CSF) in patients with lymphoma and multiple myeloma previously failing mobilisation with G-CSF with or without chemotherapy for autologous hematopoietic stem cell mobilisation: the Austrian experience on a named patient program.	Transfusion 2011; 51:968-975.
Li (2011) Included in failing mobiliser search	Li J, et al. Effectiveness and cost analysis of "just-in-time" salvage plerixafor administration in autologous transplant patients with poor stem cell mobilization kinetics.	Transfusion 2011; 51(10): 2175-2182.
Basak (2011b) Included in failing mobiliser search	Basak GW, et al, Plerixafor to rescue failing chemotherapy-based stem cell mobilization: It's not too late.	Leukemia and Lymphoma 2011b; 52(9): 1711-1719

Study ID	Protocol title/Publication title	Publication citation
Shaughnessy (2011) Included in Section D	Shaughnessy P, et al. Cost and Clinical Analysis of Autologous Hematopoietic Stem Cell Mobilization with G-CSF and Plerixafor Compared to G-CSF and Cyclophosphamide.	Biology of Blood and Marrow Transplantation 2011; 17(5): 729-736.
Chemotherapy plus G-CSF		
Majado (2003) Nov 2011	Majado MJ, Gonzalez C, Marin L, Morales A, Moya MR, et al. Second mobilization of peripheral blood progenitor cells in patients with poor first mobilization.	Transplantation Proceedings 2003; 35(5): 2027-8
McKibbin (2007) Nov 2011	McKibbin T, Burzynski J, Greene R, Ochoa-Bayona J, Tsai TW, et al. Paclitaxel and filgrastim for hematopoietic progenitor cell mobilization in patients with hematologic malignancies after failure of a prior mobilization regimen.	Leukemia and Lymphoma 2007; 48(12): 2360-6.
Goterris (2005) Nov 2011	Goterris R, Hernandez-Boluda JC, Teruel A, Gomez C, Lis MJ, Terol MJ, et al. Impact of different strategies of second-line stem cell harvest on the outcome of autologous transplantation in poor peripheral blood stem cell mobilizers.	Bone Marrow Transplantation 2005; 36(10): 847-53.
Attolico (2012) Included in plerixafor plus G-CSF	Attolico I, Pavone V, Ostuni A, Rossini B, Musso M, et al. Plerixafor added to chemotherapy plus G-CSF is safe and allows adequate PBSC collection in predicted poor mobiliser patients with multiple myeloma or lymphoma.	Biology of Blood and Marrow Transplantation 2012; 18:241-249.
Cooper (2011) Included in plerixafor plus G-CSF	Cooper DL, Pratt K, Baker J, Medoff E, Conkling-Walsh A, et al. Late afternoon dosing of plerixafor for stem cell mobilisation: a practical solution.	Clinical Lymphoma, Myeloma & Leukemia 2011; 11(3):267-272.
Basak (2011a) Included in plerixafor plus G-CSF	Basak GW, Knopinska-Posluszny W, Matuszak M, Kisiel E, Hawrylecka D, et al. Hematopoietic stem cell mobilisation with the reversible CXCR4 receptor inhibitor plerixafor (AMD3100) – Polish compassionate use experience.	Annals of Hematology 2011; 90:557-568.
Hübel (2011b) Included in plerixafor plus G-CSF	Hübel K, Fresen MM, Theurich S, Lange F, Salwender H, et al. Plerixafor with and without chemotherapy in poor mobilizers: Results from the German compassionate use program.	Bone Marrow Transplantation 2011; 46(8): 1045-1052.
Selleslag (2011) Included in plerixafor plus G-CSF search	Selleslag D, Dierickx D, Meers S, Breems DA, Huynh P, et al. Plerixafor in poor stem cell mobilizers: The Belgian compassionate use program.	Acta Clinica Belgica 2011; 66(3): 200-204.
Worel (2011) Included in plerixafor plus G-CSF	Worel N, Rosskopf K, Neumeister P, Kasparu H, Nachbaur D, et al. Plerixafor and granulocyte-colony-stimulating factor (G-CSF) in patients with lymphoma and multiple myeloma previously failing mobilisation with G-CSF with or without chemotherapy for autologous hematopoietic stem cell mobilisation: the Austrian experience on a named patient program.	Transfusion 2011; 51:968-975.

Abbreviations: auto-SCT, autologous stem cell transplantation; G-CSF, granulocyte-colony stimulating factor; PB, peripheral blood; PBSC, peripheral blood stem cell collection; USA, United States of America

The following table outlines the non-randomised studies and observational cohorts presented

in the re-submission for immediate salvage of currently failing mobilisers.

Study ID	Protocol title/ Publication title	Publication citation
Plerixafor plus G-CSF		
Basak (2011a) Additional, also failed mobiliser search	Basak GW, Knopinska-Posluszny W, Matuszak M, Kisiel E, Hawrylecka D, et al. Haemotopoietic stem cell mobilisation with the reversible CXCR4 receptor inhibitor plerixafor (AMD3100) – Polish compassionate use experience.	Annals of Haemotology 2011a; 90:557-568.
Basak (2011b) Additional	Basak GW, Mikala G, Koristek Z, Jaksic O, Basic-Kinda S, et al for the Central and Eastern European Leukemia Group (CELG). Plerixafor to rescue failing chemotherapy-based stem cell mobilization: it's not too late.	Leukemia & Lymphoma 2011b; 52(9):1711-1719.
Cooper (2011) Additional, also failed mobiliser search	Cooper DL, Baker J, Medoff E, Foss F, Seropian SE, et al. Late afternoon dosing of plerixafor for stem cell mobilization: a practical solution.	Clinical Lymphoma, Myeloma and Leukemia 2011; 11(3):267-272.
D'Addio (2011) Additional	D'Addio A, Curti A, Worel N, Douglas K, Motta MR, et al. The addition of plerixafor is safe and allows adequate PBSC collection in multiple myeloma and lymphoma patient's poor mobilizers after chemotherapy and G-CSF.	Bone Marrow Transplantation 2011; 46:356-363.
Li (2011) Additional	Li J, Hamilton E, Vaughn L, Graiser M, Renfroe H, et al. Effectiveness and cost analysis of "just-in-time" salvage plerixafor administration in autologous transplant patients with poor stem cell mobilization kinetics.	Transfusion 2011; 51:2175-2182.
Tricot (2010) Nov 2011	Tricot G, Cottler-Fox MH, Calandra G. Safety and efficacy assessment of plerixafor in patients with multiple myeloma proven or predicted to be poor mobilisers, including assessment of tumor cell mobilisation.	Bone Marrow Transplantation 2010; 45:63-68.

Abbreviations: G-CSF, granulocyte-colony stimulating factor; HD, Hodgkin disease; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; PBSC, peripheral blood stem cell collection

For PBAC's view, see Recommendations and Reasons.

8. Results of Trials

The re-submission presented the proportion of patients achieving the minimum number of CD34+ cells required for transplant ($\geq 2 \times 10^6$ CD34+ cells/kg), referred to as "mobilisation success rate," as the first outcome. This was the key outcome used in the economic evaluation. The re-submission presented mobilisation success rates based on no pooling ("unpooled") and pooling cells from other collections ("pooled").

The re-submission argued that only a very small proportion of patients' cells were pooled, based on the Australian Treatment Practice Survey. Consequently, the re-submission claimed that mobilisation success rates from pooled cells are not representative of the vast majority of Australian clinical practice and "undermines" the relevance of the pooled efficacy results seen in chemo-mobilisation studies.

The Australian Treatment Practice Survey interview guide does not anchor the question

relating to the proportion of patients in whom pooling of cells occurs to those who have failed previous mobilisation attempt(s). Therefore, the apparently "small" proportion of patients in whom pooling of cells occurs may also be a reflection that many patients successfully mobilise sufficient cells, thus pooling of cells is not necessary. The majority of the responding transplant centres (88%) report pooling of cells.

The PBAC has previously considered that results obtained by application of the minimum threshold to the pooled cell numbers is more applicable to Australian clinical practice, as pooling of cells is standard practice in Australia. Therefore, the submission base case assumes all cells are "pooled" for all patients in all the Australian centres.

The submission presented a summary of the mobilisation success rates (patients receiving $\geq 2x10^6$ $CD34^+$ cells/kg) in failed mobilisers.

For the plerixafor studies, the proportion of patients who successfully mobilise ranged from 59% to 100% for the overall population. The re-submission claimed that the results were "generally consistent." However, the PBAC noted that there were substantial variations in the mobilisation success rates for the overall population, and for the different diagnoses.

For chemo-mobilisation studies, the proportions of patients who successfully mobilise ranged from 26% to 51% without pooling (unpooled); and from 53% to 76% with pooling (pooled) for the overall population.

The submission presented a summary of the mobilisation success rates for currently failing mobilisers receiving immediate salvage plerixafor achieving $\geq 2x10^6$ $CD34^+$ cells/kg.

The proportion of plerixafor-treated currently failing mobilisers who successfully mobilise ranged from 71% to 100%.

The re-submission claimed that the only alternative that had existed before the advent of plerixafor was to allow the patient to fail and re-attempt mobilisation after a rest period of at least one month. The re-submission also stated that in a small of number of patients, ancestim (human stem cell factor) may have been added, or the dose of G-CSF increased. The re-submission stated that the clinicians interviewed noted that the majority of patients still do not collect enough cells using these strategies and the attempt is abandoned. The Australian Treatment Practice Survey appears to anchor questions relating to immediate salvage to patients with a suboptimal yield on the first day only.

For PBAC's view, see Recommendations and Reasons.

The re-submission presented new toxicity data in failed mobilisers (Attolico 2012, Hübel 2011b and Worel 2011); and immediate salvage patients (Cooper 2011, D'Addio 2011, and Li 2011). The re-submission also presented a brief summary of the fifth Periodic Safety Update Report (PSUR). No additional safety data were presented for chemo-mobilisation.

The most common adverse events reported in the trials and studies as associated with plerixafor plus G-CSF include gastrointestinal disorders (diarrhoea, nausea), injection site reactions (erythema, pruritis) and dizziness. There was one report of fever of unknown origin reported in patients undergoing plerixafor plus chemo-mobilisation Attolico (2012).

For chemo-mobilisation, there were reports of febrile neutropenia leading to hospitalisation, anaemia (some requiring transfusion), and thrombocytopenia in McKibben (2007). One patient developed sepsis resulting in death. The dose of paclitaxel used in McKibben (2007) is higher than the maximum dose recommended in the product information.

No new safety issues were identified during the reporting period of the fifth PSUR.

9. Clinical Claim

The re-submission stated that plerixafor, administered in conjunction with G-CSF can be an effective means to salvage patients who had previously failed standard mobilisation attempts, or are in the process of failing a current attempt.

For PBAC's view, see Recommendations and Reasons.

10. Economic Analysis

A cost-effectiveness analysis was presented in the submission based on data from non-randomised (often single arm) and observational studies, using the proportion of patients successfully mobilised as the outcome.

The PBAC considered that the claimed incremental cost per additional patient achieving successful mobilisation for multiple myeloma less than $15,000 for failed mobilisers, and less (though in the same range) for immediate salvage were highly uncertain.

For PBAC's view, see Recommendations and Reasons.

11. Estimated PBS Usage and Financial Implications

An epidemiological approach was taken in estimating the extent of use and financial implications in the re-submission.

The likely number of vials dispensed per year was estimated in the submission to be <10,000 in Year 5, at an estimated net cost per year to the PBS of less than $10 million in Year 5.

For PBAC's view, see Recommendations and Reasons.

12. Recommendation and Reasons

The PBAC noted that the proposed restriction had been revised in the current re-submission to specify the inclusion of patients who are failing a current stem cell collection (i.e. immediate rescue), as well as patients who have failed previous stem cell collection. The PBAC agreed that it was important that the restriction include a definition of the patient groups, including CD34+ thresholds, and noted that proposed definitions had been provided in the sponsor's pre-PBAC response.

The PBAC noted that the current re-submission presented an additional proposed clinical management algorithm for patients failing a current stem cell collection attempt. This algorithm was based on Herbert et al (2011), which the PBAC previously had noted was likely to be representative of Australian clinical practice.

Data from 10 new studies for plerixafor plus G-CSF were presented in this re-submission. Two studies (Basak, 2011a and Cooper, 2011) provide data for both failed mobilisers and immediate salvage of currently failing mobilisers. Five studies (Attolico, 2012; Hübel, 2011a; Hübel, 2011b; Selleslag, 2011; and Worel, 2011) are included for failed mobilisers and three studies are included for immediate salvage of currently failing mobilisers (Basal, 2011b; D'Addio, 2011; and Li, 2011). As previously, the PBAC noted that the evidence presented in the re-submission to support the requested listings is derived from non-randomised studies (often data from one arm of the study) and observational cohorts and that these studies may be subject to bias (e.g. selection bias) and confounding. The PBAC noted that in particular there was a paucity of data to inform the effectiveness of the comparator, and that new data were unlikely to become available.

Based on the data available, the PBAC considered that the claim of efficacy over the comparator was reasonable, but that the magnitude of the benefit remained uncertain. The PBAC noted that the incremental benefit, in terms of mobilisation success rates for failed mobilisers, of plerixafor (74%) over the comparator (53%) was smaller than the benefit claimed in previous submissions. Given the difficulties with constructing a comparison using the available data, the PBAC considered that this may represent the best estimate that can be made of the actual benefit of plerixafor treatment.

The PBAC considered that the incremental cost per additional patient achieving successful mobilisation for lymphoma of between $15,000 - $45,000 for failed mobilisers and less than $15,000 for immediate salvage were high and uncertain.

The PBAC also considered that the incremental cost per additional patient achieving successful mobilisation for multiple myeloma of less than $15,000 for failed mobilisers and for immediate salvage were highly uncertain. While the base case ICERs presented in the submission were lower than for lymphoma, the PBAC noted that they were largely driven by inappropriate cost-offsets. The PBAC considered that the cost of febrile neutropenia applied in the submission was inappropriately high, and noted that this cost is significantly higher than the cost applied in the November 2011 re-submission which they had also considered an over-estimate. The PBAC noted that the Lingaratnam et al 2011 paper, from which the cost had been sourced, included some inappropriate AR-DRGs in the costing for febrile neutropenia (for example A08A: Auto bone marrow transplantation with catastrophic complication or comorbidity). The PBAC also considered that the inclusion of cost-offsets for the administration of G-CSF in the submission was inappropriate, and agreed that no cost-offset should be included for the administration of G-CSF. The PBAC also noted the assumption in the model that, without plerixafor, no patients in the immediate salvage group successfully mobilised, and considered this assumption unreasonable.

The PBAC considered that the assumption of a first-line mobilisation failure rate of 30% was poorly justified and unreasonably high, and that the submission's estimates of patient numbers and total expenditure had therefore been overestimated.

The PBAC noted that an updated price proposal was presented in the current re-submission but considered that further adjustments would be necessary for the incremental costs to be acceptable.

The PBAC noted the proposal for a risk share arrangement in the submission, and agreed that a risk share arrangement would be appropriate, but did not consider that the proposal in the submission would adequately manage the considerable risk of leakage into treatment of patients who were not actually failing mobilisation. This was of particular concern to the PBAC as the cost-effectiveness of plerixafor is dependent on being able to target treatment to the most appropriate patients. Further, this meant that it is important that the details of any restriction be finalised prior to any possible PBAC recommendation for listing. The PBAC also considered that the proposed cap on expenditure was too high, given that the patient numbers had been overestimated.

The PBAC noted from the sponsor's Pre-Sub-Committee Response that there were a number of benefits stated by the Australian specialists to be associated with plerixafor which have not been accounted for in the re-submission. Whilst the PBAC agreed that many of these benefits might be realised with plerixafor treatment, and would be used by individual hospitals or treatment centres in determining whether to administer plerixafor on a patient by patient basis, it is difficult to account for these benefits in the context of the PBS.

The PBAC therefore rejected the submission on the basis of high and uncertain cost-effectiveness.

Recommendation:
Reject

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

Although Sanofi is disappointed by the PBAC's decision, Sanofi remains committed to working with the PBAC to resolve their remaining concerns. Sanofi will continue to pursue the listing of Mozobil on the PBS for those lymphoma and multiple myeloma patients undergoing stem cell mobilisation.