NHS England

Evidence review: Plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation

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The content of this evidence review was up-to-date in June 2019. See summaries of product characteristics (SPCs), British national formulary (BNF) or the MHRA or NICE websites for up-to-date information.

Key points

Regulatory status: Plerixafor is used to help dislodge or 'mobilise' stem cells from the bone marrow so they can be released into the blood. Using plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation (HSCT) is an 'off-label' use of this medicine. Plerixafor received a marketing authorisation in July 2009 for use in combination with granulocyte-colony stimulating factor (G-CSF) to enhance mobilisation of stem cells for subsequent autologous HSCT in adults with lymphoma and multiple myeloma whose cells mobilise poorly.

Overview

Autologous HSCT is used to treat various haematological and non-haematological disorders. In autologous transplants, stem cells are removed from a person, stored, and later given back to that same person, rather than using a stem cell donor. Before HSCT is undertaken, 'mobilisation' is needed to dislodge the stem cells from the bone marrow and increase the number of peripheral blood stem cells (PBSC) in the circulating blood flow. The circulating PBSC can then be collected in a procedure called apheresis.

For mobilisation, intravenous chemotherapy and a growth factor (G-CSF) are usually given. However, insufficient cells are collected for autologous transplant in about 10–20% of cases. Plerixafor can be used with G-CSF to increase the amount of PBSC collected. Using plerixafor after unsuccessful PBSC collection is known as **rescue treatment**. Plerixafor has also been used after G-CSF (with or without chemotherapy) in people with a low level of circulating PBSC in the blood on the day of collection. This is known as **pre-emptive treatment**.

NHS England commissions plerixafor for specific haematological cancers (multiple myeloma and lymphoma) in people of any age, and non-haematological solid tumours in people aged 24 years or under. This evidence review considers the effectiveness and safety of plerixafor as a rescue or pre-emptive treatment in stem cell mobilisation for people aged more than 24 years with non-haematological solid tumours who are receiving autologous HSCT. A related evidence review considers plerixafor as a rescue or pre-emptive treatment in stem cell mobilisation for people of any age with haematological tumours (apart from multiple myeloma and lymphoma) or haematological paraneoplastic complications.

This evidence review includes 2 retrospective case series: Horwitz et al. (2012), which studied 21 men with germ cell tumours, and Worel et al. (2012), which studied 33 adults (73%) and children with various non-haematological tumours (mainly germ cell tumours, Ewing sarcomas, Wiscott-Aldrich disease and neuroblastomas).

In the studies, successful mobilisation of cells from the bone marrow was defined as collection of at least 2 million CD34+ cells/kg during treatment with plerixafor plus G-CSF (with or without chemotherapy). CD34+ is the protein expressed on the PBSC that can be detected and measured, allowing the number of stem cells in the blood or the harvest to be counted.

In Horwitz et al. (2012), a median of 3.2 million CD34+ cells/kg were collected. At least 2 million CD34+ cells/kg were collected in 17/21 people (81%) in a median of 2 days. In Worel et al. (2012), a median of 4.1 million CD34+ cells/kg were collected. At least 2 million CD34+ cells/kg were collected in 28/33 people (85%) in a median of 2 days.

In Horwitz et al. (2012), of the 17 people from whom at least 2 million CD34+ cells/kg were collected, 14 (82%) subsequently had HSCT (67% of the total study population [14/21]). In the study by Worel et al. (2012), of the 28 people from whom at least 2 million CD34+ cells/kg were collected, 19 (68%) received a transplant (58% of the total study population [19/33]), of whom 7 had germ cell tumours (all adults), 4 had Wiscott-Aldrich disease (all children), 3 had Ewing sarcomas (age unclear), 1 had neuroblastoma (age unclear) and 4 had other non-haematological diseases (all adults).

Neutrophil and platelet engraftment occurred in all people who received plerixafor and HSCT in the studies (in about 11 days for neutrophils and 3 weeks for platelets). Plerixafor was generally well tolerated and adverse effects were mild and consistent with those listed in the plerixafor summary of product characteristics.

The studies included in this evidence review are observational studies, which are subject to bias and confounding and have many limitations affecting their application to clinical practice. Retrospective case series are subject to recall bias and rely on data being recorded accurately, completely and consistently. Both studies were uncontrolled and, as is usual for rare diseases, had relatively small sample sizes. The dosing regimen used in the studies was consistent with the dosing regimen for the licensed indications for plerixafor, and it was used in combination with G-CSF (with or without chemotherapy). The 2 studies included people both under and over 24 years of age.

In conclusion, the observational studies in this evidence review suggest that plerixafor is effective for stem cell mobilisation in a highly selected population of adults (mainly men) with relapsed or refractory germ cell tumours whose stem cells mobilised poorly. Overall, treatment with plerixafor resulted in enough cells for transplant in about 80% of people with solid tumours (mainly germ cell tumours). Plerixafor treatment resulted in autologous HSCT in about two-thirds of people in the studies, and about three-quarters of those who mobilised at least 2 million CD34+ cells/kg.

The evidence for using plerixafor for stem cell mobilisation in adults with other types of solid tumour is poor and likely to be based on single case reports only, which were outside the scope of this evidence review. Across the studies, about 70% of people had rescue treatment and 30% had pre-emptive treatment. However, results were not reported separately for these subgroups. No evidence was found to determine whether plerixafor is cost-effective for stem cell mobilisation in adults with non-haematological solid tumours undergoing autologous HSCT.

Contents

1. Introduction

Background and current guidance

Haematopoietic stem cell transplantation (HSCT, also known as blood and marrow transplantation) is used to treat various haematological and non-haematological disorders. It is broadly divided into 2 main types: allogeneic and autologous transplantation.

Allogeneic HSCT involves replacing a person's bone marrow stem cells with stem cells from a donor. Autologous transplantation uses the person's own peripheral blood stem cells (PBSC), which are harvested before high-dose chemotherapy is administered. It enables the person to be treated with higher doses of chemotherapy than would be possible without replacing the harvested stem cells afterwards, because the chemotherapy destroys the person's remaining stem cell tissue.

Before an autologous transplant is undertaken, 'mobilisation' is needed to dislodge the haematopoietic stem cells from the bone marrow and increase the number of PBSC in the circulating blood flow. The circulating PBSC can then be collected using a cell separator in a procedure called apheresis. For mobilisation, intravenous chemotherapy and a growth factor called granulocyte-colony stimulating factor (G-CSF) are usually given. This results in successful mobilisation and collection of PBSC in about 80% of people. However, insufficient cells are collected for autologous transplant in about 10–20% of cases. These people are usually offered a second round of stem cell mobilisation and collection using a more intensive chemotherapy regimen. This needs another inpatient admission and more chemotherapy and G-CSF, and has associated adverse effects and costs. Additional attempts at mobilisation are effective only in a small proportion of people (up to 20%).

Plerixafor can be used with G-CSF to increase the amount of PBSC collected (Mozobil summary of product characteristics). In some conditions (such as lymphoma and multiple myeloma), this treatment has been shown to mobilise PBSC in up to 80% of people who previously failed to collect enough cells. Using plerixafor after unsuccessful PBSC collection is known as rescue treatment.

Plerixafor has also been used after G-CSF (with or without chemotherapy) in people with a low level of circulating PBSC in the blood on the day of collection. This is known as pre-emptive treatment. Pre-emptive treatment with plerixafor can improve the number of stem cells mobilising into the blood, avoid a failure of stem cell harvesting, and prevent a second attempt at mobilisation.

NHS England commissions plerixafor for specific haematological cancers (multiple myeloma and lymphoma) in people of any age, and non-haematological solid tumours in people aged 24 years or under. This evidence review considers the effectiveness and safety of plerixafor as a rescue or pre-emptive treatment in stem cell mobilisation for people aged more than 24 years with non-haematological solid tumours who are receiving autologous HSCT. A related evidence review considers plerixafor as a rescue or pre-emptive treatment in stem cell mobilisation for people of any age with haematological tumours (apart from multiple myeloma and lymphoma) or haematological paraneoplastic complications.

See the NHS England clinical commissioning policies on HSCT and plerixafor for stem cell mobilisation for more information.

Product overview

Mode of action

Plerixafor is used to help dislodge or 'mobilise' the stem cells from the bone marrow so they can be released into the blood. It works by blocking the activity of a protein called the CXCR4 chemokine receptor. This protein normally helps to keep stem cells within the bone marrow. By blocking its activity, plerixafor allows the stem cells to be released into the blood, so that they can be collected (Mozobil European public assessment report).

Regulatory status

Plerixafor received a marketing authorisation in July 2009. It is licensed for use in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in adults with lymphoma and multiple myeloma whose cells mobilise poorly (Mozobil summary of product characteristics).

Age over 60 years and/or prior myelosuppressive chemotherapy and/or extensive prior chemotherapy and/or a peak circulating stem cell count of less than 20 stem cells/microlitre, have been identified as predictors of poor mobilisation (Mozobil summary of product characteristics).

Using plerixafor for other indications (including the indications covered by the existing NHS England clinical commissioning policy on plerixafor for stem cell mobilisation and the indications considered in this evidence review) is an 'off-label' use of this medicine. In line with the guidance from the General Medical Council (GMC) on prescribing unlicensed medicines, the prescriber should take full responsibility for determining the needs of the person and whether using plerixafor is appropriate outside its authorised indications. Supporting information and advice is also available from the GMC.

Dosing information

Plerixafor is a solution for subcutaneous injection. G-CSF is used on its own for 4 days before plerixafor is added. Plerixafor is administered 6–11 hours before each apheresis session (when blood is taken and the stem cells are extracted and frozen). It has commonly been used in clinical trials for 2 to 4 (and up to 7) consecutive days. Depending on body weight, the recommended dose of plerixafor for the licensed indications is:

- 20 mg fixed dose or 0.24 mg/kg for people weighing 83 kg or less, and
- 0.24 mg/kg for people weighing more than 83 kg.

The maximum dosage should not exceed 40 mg/day.

2. Methodology

A description of the relevant Population, Intervention, Comparison and Outcomes (PICO) for this review was provided by NHS England's Policy Working Group for the topic (see the literature search terms section for more information). The research questions for this evidence review are:

1. In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT, what is the clinical effectiveness of plerixafor in stem cell mobilisation compared to standard care?
2. In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT, what is the safety of plerixafor in stem cell mobilisation compared to standard care?
3. In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT what is the cost effectiveness of plerixafor in stem cell mobilisation compared to standard care?
4. From the evidence selected, are there any subgroups of people who would gain greater benefit or harm from treatment with plerixafor, in particular pre-emptive treatment or rescue treatment in stem cell mobilisation.

The searches for evidence to support the use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous HSCT were undertaken by the NICE Guidance Information Services' team. Results from the literature searches were screened using their titles and abstracts for relevance against the criteria from the PICO. Full text references of potentially relevant evidence were obtained and reviewed to determine whether they met the PICO inclusion criteria for this evidence review. More information can be found in the sections on search strategy and evidence selection.

The NICE evidence summary: process guide (2017) sets out the how the summaries are developed and approved for publication. The included studies are quality assessed using the National Service Framework for Long term Conditions (NSF-LTC) evidence assessment framework as set out in NHS England's Guidance on conducting evidence reviews for Specialised Services Commissioning Products (2016) (see the grade of evidence section for more information).

3. Summary of included studies

Two studies identified from the search are included in this evidence summary. One is a retrospective case series (Horwitz et al. 2012) in men with germ cell tumours and the other is a retrospective case series in people with various non-haematological tumours (including germ cell tumours, Ewing sarcomas, Wiscott-Aldrich disease and neuroblastomas; Worel et al. 2012).

A summary of the included studies is shown in table 1 (see the evidence summary tables for full details).

Table 1 Summary of included studies

Study	Population	Intervention	Primary outcome
Horwitz et al. 2012 Uncontrolled retrospective case series in the US	21 adults (100% male, median age 35 years) with germ cell tumours who were candidates for autologous HSCT and rescue (n=17) or pre-emptive (n=4) treatment with plerixafor[a]	G-CSF 10 microgram/kg per day on days 1 to 4, and plerixafor 0.24 mg/kg per day starting on the evening of day 4 before apheresis on the morning of day 5 Mobilisation and apheresis continued until enough CD34+ cells were collected[b]	Primary outcome not known Main outcome reported: number of CD34+ cells[b] collected
Worel et al. 2012 Uncontrolled retrospective case series in 13 European countries	33 people (79% male, 24 adults [73%], median age 36 years) with non-haematological tumours who were candidates for autologous HSCT and rescue (n=21) or pre-emptive (n=12) treatment with plerixafor[a] Diagnoses were germ cell tumour (n=11, median age 29 years), Ewing sarcoma (n=6, median age 25 years), Wiscott-Aldrich disease (n=5, median age 5 years), neuroblastoma (n=4, median age 5 years), and other (n=7, median age 49 years)	G-CSF 10 microgram/kg per day on days 1 to 4, and plerixafor 0.24 mg/kg per day starting on the evening of day 4 before apheresis on the morning of day 5 Mobilisation and apheresis continued until enough CD34+ cells were collected[b] or for a maximum of 7 days of plerixafor and apheresis	Number of participants collecting more than 2 million CD34+ cells[b]

[a] People from whom insufficient cells were collected during apheresis or who had a low PBSC count following conventional therapy (G-CSF alone or with chemotherapy) and were not considered to have a reasonable chance of enough stem cell collection

[b] Successful mobilisation was defined as collection of a total of at least 2 x 10^6 CD34+ cells/kg during therapy with plerixafor plus G-CSF (with or without chemotherapy). CD34+ is the protein expressed on the PBSC that can be detected and measured, allowing the number of stem cells in the blood or the harvest to be counted

Abbreviations: G-CSF; Granulocyte-colony stimulating factor: HSCT; haematopoietic stem cell transplantation: PBSC; peripheral blood stem cell

Details of the excluded studies are listed in the section on evidence selection.

4. Results

An overview of the results for clinical effectiveness and safety and tolerability can be found in the evidence summary table. The research questions for the evidence review and the key outcomes identified in the scope are discussed in this section.

The grade of evidence for most outcomes is B, although 3 outcomes are graded C (median peak peripheral blood CD34+cell count and median times to neutrophil and platelet engraftment after second transplant).

Clinical effectiveness

1. **In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT, what is the clinical effectiveness of plerixafor in stem cell mobilisation compared to standard care?**

Mobilisation of cells from the bone marrow

Successful mobilisation of cells from the bone marrow was defined as collection of at least 2 million CD34+ cells/kg during treatment with plerixafor plus granulocyte-colony stimulating factor (G-CSF, with or without chemotherapy). CD34+ is the protein expressed on the PBSC that can be detected and measured, allowing the number of stem cells in the blood or the harvest to be counted.

In the study by Horwitz et al. (2012), a median of 3.2 million CD34+ cells/kg (range 0.76 to 15.80 million cells/kg) were collected in 21 men with germ cell tumours. At least 2 million CD34+ cells/kg were collected in 17/21 people (81%) in a median of 2 days (range 1 to 3 days). At least 4 million CD34+ cells/kg were collected in 9/21 people (43%) in a median of 3 days (range 1 to 4 days).

In the study by Worel et al. (2012), a median of 4.1 million CD34+ cells/kg (range 0.9 to 29.5 million cells/kg) were collected in 33 people (73% adults) with various non-haematological tumours. At least 2 million CD34+ cells/kg were collected in 28/33 people (85%) in a median of 2 days (range, 1 to 4 days). This study also reported the peak CD34+ cell count, which was 32 million/litre (range 9 to 250 million/litre) after plerixafor treatment, a 5.3-fold increase compared with baseline (4 million/litre).

It is not reported how big the improvements in the numbers of cells mobilised were compared with baseline or previous mobilisation attempts without plerixafor. Nevertheless, these results suggest that using plerixafor to help mobilise stem cells results in enough cells for transplant in about 80% of adults with solid tumours (mainly men with germ cell tumours).

Autologous HSCT

In the study by Horwitz et al. (2012), of the 17 people from whom at least 2 million CD34+ cells/kg were collected, 14 (82%) subsequently had HSCT (67% of the total study population [14/21]). Three of the men from whom at least 2 million CD34+ cells/kg were collected did not proceed to transplant because of death (n=1) or unknown reasons (n=2), and 2 additional men who did not collect 2 million CD34+ cells/kg had HSCT using pooled stem

cells from an earlier harvest. The first stem cell graft failed in 8/16 men (50%) who then had a second transplant. The second graft did not fail in any of these men.

In the study by Worel et al. (2012), of the 28 people from whom at least 2 million CD34+ cells/kg were collected, 19 (68%) received a transplant (58% of the total study population [19/33]). Of these people, 7 had germ cell tumours (all adults), 4 had Wiscott-Aldrich disease (all children), 3 had Ewing sarcomas (age unclear), 1 had neuroblastoma (age unclear) and 4 had other non-haematological diseases (all adults). It is not reported why 9 people did not proceed to transplant. There were no reports of the first graft failing during this study.

Overall, the studies suggest that using plerixafor to help mobilise stem cells results in HSCT in about two-thirds of adults with solid tumours (mainly men with germ cell tumours), and about three-quarters of those who mobilised at least 2 million CD34+ cells/kg.

Neutrophil and platelet engraftment

In Horwitz et al. (2012), the median time to neutrophil engraftment was 11 days (range 9 to 18 days) in men who had a first stem cell transplant, and the median time to platelet engraftment was 20 days (range 12 to 48 days). The median time to neutrophil engraftment was 10.5 days (range 9 to 12 days) in men who had a second transplant, and the median time to platelet engraftment was 24 days (range 12 to 44 days).

In Worel et al. (2012), the median time to neutrophil engraftment was 11 days (range 9 to 12 days) and the median time to platelet engraftment was 15 days (range 10 to 25 days).

In summary, neutrophil and platelet engraftment occurred in all participants who received plerixafor and HSCT in the studies (in about 11 days for neutrophils and 3 weeks for platelets).

2. From the evidence selected, are there any subgroups of patients who would gain greater benefit or harm from treatment with plerixafor, in particular pre-emptive treatment or rescue treatment in stem cell mobilisation.

Across the studies, about 70% of people had rescue treatment (when insufficient cells are collected) and 30% had pre-emptive treatment (when not enough PBSC are circulating in the blood on the day of collection). However, results were not reported separately for these subgroups and it is not possible to determine whether people receiving rescue or pre-emptive treatment are likely to gain greater benefit or harm from stem cell mobilisation with plerixafor.

3. In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT what is the cost effectiveness of plerixafor in stem cell mobilisation compared to standard care?

No evidence was found to determine whether plerixafor is cost-effective for treating people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT.

Safety and tolerability

4. In people aged over 24 years with non-haematologic solid tumours that can be treated with HSCT and who are scheduled for autologous HSCT, what is the safety of plerixafor in stem cell mobilisation compared to standard care?

Adverse events

In the study by Worel et al. (2012), no treatment-related adverse effects were reported in 33 people with various non-haematological tumours.

In the study by Horwitz et al. (2012), 8/21 men with germ cell tumours (38%) reported 17 adverse events felt to be possibly, probably or definitely related to plerixafor. None of the events were classified as serious. One man experienced chills, which were moderate in severity. All other adverse events were considered mild. They included diarrhoea (n=3), nausea (n=2), injection site reactions (n=3), bone pain (n=2), chills (n=1), neck pain (n=1), lip swelling (n=1), abnormal dreams (n=1), blurred vision (n=1) and fatigue (n=1). These are consistent with adverse effects listed in the plerixafor summary of product characteristics.

According to the plerixafor summary of product characteristics, very common adverse effects seen in at least 1 in 10 people in studies of lymphoma and multiple myeloma are diarrhoea, nausea and injection site reactions. Common adverse effects (in between 1 in 100 and 1 in 10 people) are insomnia, dizziness, headache, vomiting, abdominal pain, stomach discomfort, dyspepsia, abdominal distention, constipation, flatulence, oral hypoaesthesia (reduced sense of touch or sensation), dry mouth, hyperhidrosis, erythema, arthralgia, musculoskeletal pain, fatigue and malaise.

5. Discussion

Evidence strengths and limitations

The studies included in this evidence review are observational studies, which are subject to bias and confounding and have many limitations affecting their application to clinical practice. Retrospective case series are subject to recall bias and rely on data being recorded accurately, completely and consistently. Other limitations of case series include differences in the diagnosis, management and follow up of individual cases, loss to follow up and, potentially, missed cases. This type of study cannot reliably answer the research questions: the results can only be considered hypothesis generating and cannot support any definitive conclusions.

The 2 studies in this evidence review included people enrolled in compassionate use programmes for plerixafor. These programmes appear to have had standardised inclusion and exclusion criteria, mobilisation protocols, and prespecified outcomes and methods for data collection. Both studies were multicentre studies and management of participants may have varied across the sites, with the papers reporting that local standards and guidelines were used for procedures, monitoring and follow up. Horwitz et al. (2012) states that 'the compassionate use programme was designed in accordance with good clinical practice. However, as this program was focused on the treatment of individuals rather than an

investigation designed to further drug development, the conduct of the compassionate use programme was not monitored at sites.'

Both studies were uncontrolled and, as is usual for rare diseases, had relatively small sample sizes. Outcome assessment was probably not blinded in the studies. However, most of the outcomes are objective, such as cell counts and transplant success or failure. No statistical analyses were reported.

Both studies are applicable to the population considered in the research questions, although Worel et al. (2012) included children (27%, aged 2 to 12 years) as well as adults (aged 18 to 70 years) and results are not presented for age subgroups. In Horwitz et al. (2012), people were aged 20 to 51 years, meaning neither of the studies included only adults aged over 24 years. Also, neither study included anyone aged over 70 years. Most people in the studies were male (100% in Horwitz et al 2012 and 79% in Worel et al. 2012).

Worel et al. (2012) included people with various non-haematological tumours (mainly germ cell tumours, Ewing sarcomas, Wiscott-Aldrich disease and neuroblastomas) and results are not presented according to disease subgroups. All the participants with germ cell tumours and 'other non-haematological' tumours in Worel et al. (2012) were adults (gender not reported), and all the participants in Horwitz et al. (2012) were adult men with germ cell tumours.

Most participants in both studies had relapsed or refractory disease. Men with germ cell tumours in Horwitz et al. (2012) had received a median of 3 previous lines of chemotherapy before autologous HSCT. The number of previous lines of chemotherapy in people with various non-haematological tumours in Worel et al. (2012) was 0 or 1 in 11 people, 2 or 3 in 18 people and 4 or more in 4 people.

In the study by Worel et al. (2012), 64% of people had rescue treatment with plerixafor and 36% had pre-emptive treatment. In the study by Horwitz et al. (2012), 81% of people had rescue treatment and 19% had pre-emptive treatment. However, results were not reported separately for these subgroups.

The dosing regimen used in the studies was consistent with the dosing regimen for the licensed indications for plerixafor, and it was used in combination with granulocyte-colony stimulating factor (with or without chemotherapy).

No evidence was found to determine whether plerixafor is cost-effective for stem cell mobilisation in adults with non-haematological solid tumours undergoing autologous HSCT.

Other treatments

No other treatments are generally considered at the same stage in the management pathway for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous HSCT.

6. Conclusion

The studies in this evidence review suggest that plerixafor is effective for stem cell mobilisation in a highly selected population of adults (mainly men) with relapsed or refractory

germ cell tumours who were considered ‘poor mobilisers’. Overall, using plerixafor to help mobilise stem cells resulted in autologous HSCT in about two-thirds of people with solid tumours (mainly germ cell tumours) in the studies, and about three-quarters of those who mobilised at least 2 million CD34+ cells/kg. Compared with pre-emptive treatment, there is more evidence for rescue treatment, which about 70% of people in the studies received.

Plerixafor was generally well tolerated and adverse effects were mild and consistent with those listed in the plerixafor summary of product characteristics. Because of the limited evidence for using plerixafor for stem cell mobilisation in adults with non-haematological solid tumours who are receiving autologous HSCT, it is likely that the summary of product characteristics provides the best overview of the adverse effect profile of plerixafor, even for indications outside of the terms of the license.

The evidence for using plerixafor for stem cell mobilisation in adults with other types of solid tumour is poor and likely to be based on single case reports only, which were outside the scope of this evidence review.

7. Evidence summary table

Use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation							
Study Design	**Population characteristics**	**Intervention**	**Outcome measure type**	**Outcome measures**	**Results**	**Quality of Evidence Score**	**Applicability**
Study reference 1: Horwitz et al. 2012							
P1 Primary research using quantitative approaches Noncomparative retrospective case series in the US	Retrospective analysis of data for people who participated in a plerixafor compassionate use program Included 21 adults (100% male, median age 35 years) with germ cell tumours who were candidates for autologous HSCT and rescue (n=17) or pre-emptive (n=4) treatment with plerixafor[a] Participants had received a median of 3 previous lines of chemotherapy before autologous HSCT	G-CSF 10 microgram/kg per day on days 1 to 4, and plerixafor 0.24 mg/kg per day starting on the evening of day 4 before apheresis on the morning of day 5 Mobilisation and apheresis continued until enough CD34+ cells[b] were collected Successful mobilisation was defined as collection of a total of at least 2 x 10^6 CD34+ cells/kg during therapy with plerixafor plus G-CSF (with or without chemotherapy)	Primary outcome not known. Main outcome reported Clinical effectiveness	Median CD34+ cell collection yields after mobilisation with plerixafor plus G-CSF	3.2 x 10^6 cells/kg (range 0.76 to 15.80 x 10^6 cells/kg)	6/10 The research questions are stated but, as the study is a retrospective observational study it is insufficient to reliably answer the questions, and the results can only be considered hypothesis generating and cannot support any definitive conclusions. The methods are clearly described and the results are generalisable to the population	Direct study that focuses on people with the indication and characteristics of interest
			Secondary Clinical effectiveness	Number of participants collecting ≥2 x 10^6 CD34+ cells/kg	17 (81%) 3 people collected more than 2 x 10^6 CD34+ cells/kg but did not proceed to transplant. Of these, 1 person died before transplant and the reason is unknown for 2 people		
			Secondary Clinical effectiveness	Median time to collect ≥2 x 10^6 CD34+ cells/kg	2 days (range 1 to 3 days)		
			Secondary Clinical effectiveness	Number of participants collecting ≥4 x 10^6 CD34+ cells/kg	9 (43%)		

Use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation							
Study Design	**Population characteristics**	**Intervention**	**Outcome measure type**	**Outcome measures**	**Results**	**Quality of Evidence Score**	**Applicability**
			Secondary Clinical effectiveness	Median time to collect ≥4 x 10^6 CD34+ cells/kg	3 days (range 1 to 4 days)	considered in the evidence review	
			Secondary Clinical effectiveness	Number of participants proceeding to first transplant	16 (76%) Includes 2 people who did not collect 2 x 10^6 CD34+ cells/kg but also received cells pooled from previous collections		
			Secondary Clinical effectiveness	Median time to neutrophil engraftment[c] after first transplant	11 days (range 9 to 18 days)		
			Secondary Clinical effectiveness	Median time to platelet engraftment[d] after first transplant	20 days (range 12 to 48 days)		
			Secondary Clinical effectiveness	Number of participants proceeding to second transplant	8 (38%) None of the participants experienced secondary graft failure.		
			Secondary Clinical effectiveness	Median time to neutrophil engraftment[c]	10.5 days (range 9 to 12 days)		

Use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation							
Study Design	**Population characteristics**	**Intervention**	**Outcome measure type**	**Outcome measures**	**Results**	**Quality of Evidence Score**	**Applicability**
				after second transplant			
			Secondary Clinical effectiveness	Median time to platelet engraftment[d] after second transplant	24 days (range 12 to 44 days)		
			Secondary Safety	Adverse events	8 participants (38%) reported 17 adverse events felt to be possibly, probably or definitely related to plerixafor None of the events were classified as serious. One patient experienced chills, which were moderate in severity. All other adverse events were considered mild. They included diarrhoea (n=3), nausea (n=2), injection site reactions (n=3), bone pain (n=2), chills (n=1), neck pain (n=1), lip swelling (n=1), abnormal dreams (n=1), blurred vision (n=1) and fatigue (n=1)		
Critical appraisal summary: Small, uncontrolled, retrospective observational study at high risk of bias and confounding. Highly selected population of poor mobilisers with relapsed or refractory germ cell tumour. Not all participants were aged over 24 years. All were male. No statistical analyses are reported. Results were not reported separately for rescue and pre-emptive treatment							
Study reference 2: Worel et al. 2012							
P1 Primary research using quantitative approaches	Retrospective analysis of data for people who participated in the European plerixafor	G-CSF 10 microgram/kg each morning or 5 micrograms/kg twice daily on days 1 to 4, and plerixafor 0.24 mg/kg per day starting on the evening	Primary Clinical effectiveness	Number of participants collecting ≥2 x 10^6 CD34+ cells/kg	28 (85%) After plerixafor, mobilisation failed in 5 people (15%) who had previously experienced mobilisation failure once (n=4) or twice (n=1)	6/10 The research questions are stated but, as the study is a	Direct study that focuses on people with the indication and

Use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation							
Study Design	**Population characteristics**	**Intervention**	**Outcome measure type**	**Outcome measures**	**Results**	**Quality of Evidence Score**	**Applicability**
Noncomparative retrospective case series in 13 European countries including the UK	compassionate use program 33 people (79% male, median age 26 years, 24 adults [73%, median age 36 years]) with non-haematological tumours who were candidates for autologous HSCT and rescue (n=21) or pre-emptive (n=12) treatment with plerixafor[e]. Of the people undergoing rescue treatment, 14 had 1 failed mobilisation attempt, 6 had 2 failed attempts and 1 had 3 failed attempts Diagnoses were germ cell tumour (n=11, median age 29 years), Ewing sarcoma (n=6, median age 25 years), Wiscott-Aldrich disease (n=5, median age 5 years), neuroblastoma (n=4, median age 5 years),	of day 4 before apheresis on the morning of day 5 Mobilisation and apheresis continued until enough CD34+ cells[b] were collected or for a maximum of 7 days of plerixafor and apheresis Successful mobilisation was defined as collection of a total of at least 2 x 10^6 CD34+ cells/kg during therapy with plerixafor plus G-CSF (with or without chemotherapy)			Results are for adults and children, and all diagnoses combined	retrospective observational study it is insufficient to reliably answer the questions, and the results can only be considered hypothesis generating and cannot support any definitive conclusions. The methods are clearly described and the results are generalisable to the population considered in the evidence review	characteristics of interest
			Secondary Clinical effectiveness	Median CD34+ cell collection yields after mobilisation with plerixafor plus G-CSF	4.1 x 10^6 cells/kg (range 0.9 to 29.5 x 10^6 cells/kg) Result is for adults and children, and all diagnoses combined		
			Secondary Clinical effectiveness	Median peak peripheral blood CD34+cell count	32 x 10^6/L (range 9 to 250 x 10^6/L) A median 5.3-fold increase was seen Result is for adults and children, and all diagnoses combined		
			Secondary Clinical effectiveness	Median time to collect ≥2 x 10^6 CD34+ cells/kg	2 days (range 1 to 4 days) Result is for adults and children, and all diagnoses combined		
			Secondary Clinical effectiveness	Number of participants proceeding to transplant	19/28 people (68%) from whom ≥2 x 10^6 CD34+ cells/kg were collected Result is for adults and children, and all diagnoses combined 7 of these people had germ cell tumours (all adults), 4 had Wiscott-Aldrich disease (all children), 3 had Ewing sarcomas (age unclear), 1 had neuroblastoma (age unclear) and 4 had other non-haematological diseases (all adults)		

Use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation							
Study Design	**Population characteristics**	**Intervention**	**Outcome measure type**	**Outcome measures**	**Results**	**Quality of Evidence Score**	**Applicability**
	and other (n=7, median age 49 years) The number of previous lines of chemotherapy was 0 or 1 in 11 participants, 2 or 3 in 18 participants and 4 or more in 4 participants				There were no reports of early or late graft failure during the study.		
			Secondary Clinical effectiveness	Median time to neutrophil engraftment[f] after transplant	11 days (range 9 to 12 days) Result is for adults and children, and all diagnoses combined		
			Secondary Clinical effectiveness	Median time to platelet engraftment[g] after transplant	15 days (range 10 to 25 days) Result is for adults and children, and all diagnoses combined		
			Secondary Safety	Adverse events	No treatment-related adverse effects were reported		
Critical appraisal summary: Small, uncontrolled, retrospective observational study at high risk of bias and confounding. Highly selected population of poor mobilisers. Results for adults (73%) and children are combined, and not all adults were aged over 24 years. 79% of participants were male. Results are not reported separately for individual diagnoses, or for rescue and pre-emptive treatment. No statistical analyses are reported							
[a] People from whom insufficient cells (median 1.35 x 10^6 CD34+ cells/kg) were collected during apheresis or who had a low PBSC count (median 2.43 CD34+ cells/microlitre) following conventional therapy (G-CSF alone [n=14] or with chemotherapy [n=7]) and were not considered to have a reasonable chance of sufficient stem cell collection [b] CD34+ is the protein expressed on the PBSC that can be detected and measured, allowing the number of stem cells in the blood or the harvest to be counted [c] Defined as 3 consecutive days with an absolute neutrophil count of ≥0.5 x 10^9/L or 1 day with a count ≥1 x 10^9/L [d] Defined as the first day when the platelet count is >20 x 10^9/L measured by at least 3 consecutive platelet laboratory values obtained over at least 7 days that show that level was achieved and maintained without platelet transfusion for at least 7 days [e] A failed mobilisation attempt was defined either as a CD34+cell value below 20 x 10^6/L (median 4 x 10^6/L) measured in the peripheral blood before apheresis or as a pooled cell harvest of less than 2.0 x10^6 CD34+ cells/kg in up to 4 apheresis sessions after mobilisation with G-CSF alone (n=21) or combined with chemotherapy(n=12) [f] Defined as the first of 3 consecutive days on which the absolute neutrophil count reached 0.5 x 10^9/L [g] Defined as the first of 3 consecutive days on which the platelet count reached 20 x 10^9/L without platelet transfusion for at least 2 days							
Abbreviations: G-CSF; Granulocyte-colony stimulating factor: HSCT; haematopoietic stem cell transplantation: PBSC; peripheral blood stem cell							

8. Grade of evidence table

Use of plerixafor for stem cell mobilisation in people aged over 24 years with non-haematological solid tumours who are receiving autologous haematopoietic stem cell transplantation					
Outcome Measure	**Reference**	**Quality of Evidence Score**	**Applicability**	**Grade of Evidence**	**Interpretation of Evidence**
Median CD34+ cell collection yields after mobilisation with plerixafor plus G-CSF	Horwitz et al. 2012	6/10	Direct	B	CD34+ is the protein expressed on the PBSC that can be detected and measured. This outcome looks at the number of CD34+ cells that were typically collected after plerixafor was used to help dislodge the stem cells from the bone marrow and increase the amount circulating in the blood, which is known as mobilisation. The median value was used, which is the middle value from the range of results received across all the participants in the study. Successful mobilisation of cells from the bone marrow was defined as collection of at least 2 million CD34+ cells/kg during treatment with plerixafor plus G-CSF (with or without chemotherapy) In a study in 21 men with germ cell tumours, a median of 3.2 million CD34+ cells/kg were collected. In a second study in 33 people (79% male, 73% adults) with various non-haematological tumours (mainly germ cell tumours, Ewing sarcomas, Wiscott-Aldrich disease and neuroblastomas), a median of 4.1 million CD34+ cells/kg were collected It is not reported how big the improvements were compared with baseline or previous mobilisation attempts without plerixafor. However, the median number of CD34+ cells collected was greater than 2 million cells/kg and, therefore, considered successful in both studies Across the studies, about 70% of people had rescue treatment (when insufficient cells are collected) and 30% had pre-emptive treatment (when not enough PBSC are circulating in the blood on the day of collection). Results were not reported separately for these groups. The results of the second study are for adults (73%) and children combined, and all diagnoses combined. The 2 studies included people both under and over 24 years of age. Both studies were small, uncontrolled, retrospective observational studies at high risk of bias and confounding. No statistical analyses were reported
	Worel et al. 2012	6/10	Direct		
Number of participants collecting ≥2 x 10^6 CD34+ cells/kg	Horwitz et al. 2012	6/10	Direct	B	This outcome looks at the number of people in whom at least 2 million CD34+ cells/kg were collected after mobilisation using plerixafor and G-CSF (with or without chemotherapy), meaning they were potentially eligible for HSCT

	Worel et al. 2012	6/10	Direct		In the study in 21 men with germ cell tumours, at least 2 million CD34+ cells/kg were collected in 17 people (81%). In the study in 33 people with various non-haematological tumours, enough cells for transplant were collected in 28 people (85%) These results suggest that using plerixafor to help mobilise stem cells results in enough cells to proceed to HSCT in about 8 out of 10 adults with solid tumours (mainly men with germ cell tumours) Across the studies, about 70% of people had rescue treatment (after insufficient cells were collected) and 30% had pre-emptive treatment (when not enough PBSC were circulating in the blood on the day of collection). Results were not reported separately for these groups. The results of the second study are for adults (73%) and children combined, and all diagnoses combined. The 2 studies included people both under and over 24 years of age. Both studies were small, uncontrolled, retrospective observational studies at high risk of bias and confounding. No statistical analyses were reported
Median peak peripheral blood CD34+cell count	Worel et al. 2012	6/10	Direct	C	This outcome looks at the maximum number of CD34+ cells typically circulating in the peripheral blood after stem cell mobilisation using plerixafor and G-CSF (with or without chemotherapy). The median value was used, which is the middle value from the range of results received across all the participants in the study In the study in 33 people with various non-haematological tumours, the median peak CD34+ cell count was 32 million/litre (range 9 to 250 million/litre) after plerixafor treatment. This was a median 5.3-fold increase compared with baseline (4 million/litre) This suggests that treatment with plerixafor increases the number of CD34+ cells in the circulating peripheral blood, increasing the chance of collecting enough cells for HSCT This result is for adults (73%, not all aged over 24 years) and children, and all diagnoses combined. 64% of people had rescue treatment and 36% had pre-emptive treatment. Results were not reported separately for these groups. The study was small, uncontrolled, and retrospective at high risk of bias and confounding. No statistical analyses were reported
Number of participants proceeding to first transplant	Horwitz et al. 2012	6/10	Direct	B	This outcome looks at the number of people who had HSCT after receiving plerixafor and G-CSF (with or without chemotherapy) In the study in 21 men with germ cell tumours, of the 17 people from whom at least 2 million CD34+ cells/kg were collected, 14 (82%) subsequently had HSCT (67% of the total study population [14/21]). Of the 3 people who did not have HSCT, 1 person died and the reason is unknown for the other 2 people. 2 men who did not collect 2 million CD34+ cells/kg after using plerixafor had HSCT using additional cells pooled from previous collections In the study in 33 people with various non-haematological tumours, of the 28 people from whom at least 2 million CD34+ cells/kg were collected, 19 (68%) had HSCT (58% of the total study population [19/33]). Seven of these people had germ cell tumours (all adults), 4 had Wiscott-Aldrich disease (all children), 3 had Ewing sarcomas (age
	Worel et al. 2012	6/10	Direct		

					unclear), 1 had neuroblastoma (age unclear) and 4 had other non-haematological diseases (all adults). It is not reported why 9 people from whom enough cells were collected did not have HSCT These results suggest that using plerixafor to help mobilise stem cells results in HSCT in about two-thirds of adults with solid tumours (mainly men with germ cell tumours). Of the people who mobilised at least 2 million CD34+stem cells/kg in the studies about three-quarters subsequently had HSCT Across the studies, about 70% of people had rescue treatment and 30% had pre-emptive treatment. Results were not reported separately for these groups. The results of the second study are for adults (73%) and children combined, and all diagnoses combined. The 2 studies included people both under and over 24 years of age. Both studies were small, uncontrolled, retrospective observational studies at high risk of bias and confounding. No statistical analyses were reported
Median time to neutrophil engraftment after first transplant	Horwitz et al. 2012	6/10	Direct	B	This outcome looks at the number of days for the number of neutrophils (a type of white blood cell) to recover and reach a set level (generally 0.5 x 10^9/L on 3 consecutive days) after HSCT (known as engraftment). The median value was used, which is the middle value from the range of results received across all the participants in the study The neutrophils engrafted after about 11 days in both studies (range 9 to 18 days in the study in 21 men with germ cell tumours and 9 to 12 days in the study in 33 people with various non-haematological tumours). Specialists consider that this appears clinically satisfactory Across the studies, about 70% of people had rescue treatment and 30% had pre-emptive treatment. Results were not reported separately for these groups. The results of the second study are for adults (73%) and children combined, and all diagnoses combined. The 2 studies included people both under and over 24 years of age. Both studies were small, uncontrolled, retrospective observational studies at high risk of bias and confounding. No statistical analyses were reported
	Worel et al. 2012	6/10	Direct		
Median time to platelet engraftment after first transplant	Horwitz et al. 2012	6/10	Direct	B	This outcome looks at the number of days for the number of platelets (a type of blood cell involved in blood clotting) to recover and reach a set level (generally 20 x 10^9/L without platelet transfusion on 3 consecutive days) after HSCT (known as engraftment). The median value was used, which is the middle value from the range of results received across all the participants in the study The platelets engrafted after about 20 days (range 12 to 48 days) in the study in 21 men with germ cell tumours and 15 days (range 10 to 25 days) in the study in 33 people with various non-haematological tumours. Specialists consider that this appears clinically satisfactory Across the studies, about 70% of people had rescue treatment and 30% had pre-emptive treatment. Results were not reported separately for these groups. The results of the second study are for adults (73%) and children combined, and all diagnoses combined. The 2 studies included people both under and over 24 years of age. Both
	Worel et al. 2012	6/10	Direct		

					studies were small, uncontrolled, retrospective observational studies at high risk of bias and confounding. No statistical analyses were reported
Number of participants proceeding to second transplant	Horwitz et al. 2012	6/10	Direct	B	This outcome looks at the number of people who needed a second HSCT after the first was unsuccessful and the stem cell graft failed In the study in 21 men with germ cell tumours, 8 men (38%) received a second HSCT because the stem cell graft failed. None of the men experienced secondary graft failure. There were no reports of early or late failure of the first graft during the study in 33 people with various non-haematological tumours Across the studies, about 70% of people had rescue treatment and 30% had pre-emptive treatment. Results were not reported separately for these groups. The results of the second study are for adults (73%) and children combined, and all diagnoses combined. The 2 studies included people both under and over 24 years of age. Both studies were small, uncontrolled, retrospective observational studies at high risk of bias and confounding. No statistical analyses were reported
	Worel et al. 2012	6/10	Direct		
Median time to neutrophil engraftment after second transplant	Horwitz et al. 2012	6/10	Direct	C	This outcome looks at the number of days for the number of neutrophils to recover and reach a set level (generally 0.5 x 10^9/L on 3 consecutive days) after the second HSCT. The median value was used, which is the middle value from the range of results received across all the participants in the study The neutrophils engrafted in about 10.5 days (range 9 to 12 days) in the study in 21 men with germ cell tumours. Specialists consider that this appears clinically satisfactory In the total study population, 81% of people had rescue treatment and 19% had pre-emptive treatment. Results were not reported separately for these groups. Not all participants were aged over 24 years. The study was a small, uncontrolled, retrospective observational study at high risk of bias and confounding. No statistical analyses were reported
Median time to platelet engraftment after second transplant	Horwitz et al. 2012	6/10	Direct	C	This outcome looks at the number of days for the number of platelets to recover and reach a set level (generally 20 x 10^9/L without platelet transfusion on 3 consecutive days) after the second HSCT. The median value was used, which is the middle value from the range of results received across all the participants in the study The platelets engrafted after about 24 days (range 12 to 44 days) in the study in 21 men with germ cell tumours. Specialists consider that this appears clinically satisfactory In the total study population, about 81% of people had rescue treatment and 19% had pre-emptive treatment. Results were not reported separately for these groups. Not all participants were aged over 24 years. The study was a

					small, uncontrolled, retrospective observational study at high risk of bias and confounding. No statistical analyses were reported
Adverse events	Horwitz et al. 2012	6/10	Direct	B	This outcome looks at the number of people using plerixafor who had adverse events during the study. These may or may not have been side effects been caused by the study treatment No treatment-related adverse effects were reported in the study in 33 people with various non-haematological tumours. In the study in 21 men with germ cell tumours, 8 men (38%) reported 17 adverse events felt to be possibly, probably or definitely related to plerixafor. None of the events were classified as serious. 1 man experienced chills, which were moderate in severity. All other adverse events were considered mild. They included diarrhoea (n=3), nausea (n=2), injection site reactions (n=3), bone pain (n=2), chills (n=1), neck pain (n=1), lip swelling (n=1), abnormal dreams (n=1), blurred vision (n=1) and fatigue (n=1). These are consistent with adverse effects listed in the plerixafor summary of product characteristics Across the studies, about 70% of people had rescue treatment and 30% had pre-emptive treatment. Results were not reported separately for these groups. The results of the second study are for adults (73%) and children combined, and all diagnoses combined. The 2 studies included people both under and over 24 years of age. Both studies were small, uncontrolled, retrospective observational studies at high risk of bias and confounding. No statistical analyses were reported
	Worel et al. 2012	6/10	Direct		
Abbreviations: G-CSF; Granulocyte-colony stimulating factor: HSCT; haematopoietic stem cell transplantation: PBSC; peripheral blood stem cell					

9. Literature search terms

P –Population and indication Describe the relevant population and indication provided previously including if necessary disease severity or duration, previous treatment, new or recurrent symptoms, any specific co-morbidities and other population factors (for example, age range). Add details of any subgroups or stratifications for which separate evidence may be required.	Adults with non-haematologic solid tumours that can be treated with autologous HSCT who have received either chemotherapy + G-CSF or G-CSF alone and who have a low peripheral blood CD34+ cell count [people aged over 24 years primarily, studies which include people aged over 18 years are acceptable]
I – Intervention Describe the intervention details provided previously including if necessary details of treatment, mode of delivery, size/frequency/duration of dose, position of intervention in treatment pathway (e.g. first/second line/salvage) and any background / concomitant medication	Plerixafor (as EITHER a rescue OR pre-emptive treatment) [Subgroups of interest: a rescue OR pre-emptive treatment]
C – Comparators What is/are the main alternative/s to compare with the intervention being considered? Describe the comparator details provided previously including if necessary details of treatment, mode of delivery, size/frequency/duration of dose, position of intervention in treatment pathway (e.g. first/second line/salvage) and any background / concomitant medication	No plerixafor treatment A further round of G-CSF +/- chemotherapy

O – Outcomes
 	
Outcomes should be patient focused and relate to those detailed in the PPP and the Research Questions covering clinical effectiveness, safety and cost effectiveness as required.
 	
Examples will be topic specific but might include intermediate or short-term outcomes; mortality; morbidity; quality of life; treatment complications; adverse effects; rates of relapse; late morbidity and re-admission; return to work, physical and social functioning, resource use.
	Critical to decision-making:
	
	• clinical effectiveness, for example:
	  ○ number of patients collecting sufficient stem cells to be eligible for transplant
	  ○ total CD34+cell count (x10^6/kg) in harvest of patients receiving plerixafor
	  ○ number of patients meeting target peripheral blood CD34+ thresholds and proceeding to apheresis
	  ○ number of days of apheresis
	  ○ number of patients proceeding to transplant
	  ○ median number of days to neutrophil and platelet engraftment
	• adverse effects of plerixafor
	• mortality
	
	Important to decision-making:
	
	cost effectiveness of plerixafor

Inclusion criteria	
Study design	Systematic reviews, randomised controlled trials, controlled clinical trials, cohort studies. If no higher level quality evidence is found, case series can be considered.
Language	English only
Patients	Human studies only
Age	All ages
Date limits	2009-2019
Exclusion criteria	

Publication type	Conference abstracts, non-systematic reviews, narrative reviews, commentaries, letters and editorials
Study design	Case reports, resource utilisation studies
Abbreviations: G-CSF; Granulocyte-colony stimulating factor: HSCT; Haematopoietic stem cell transplantation	

10. Search strategy

Database search strategies

Database: Medline
Platform: Ovid
Version: 1946 to March 18 2019
Search date: 19/03/2019
Number of results retrieved: 361
Search strategy:
1 (plerixafor* or amd 3100 or amd3100 or mozobil* or jm 3100 or jm3100 or sdzsid 791 or sdzsid791 or sid 791 or sid791).tw. (1477)
2 Hematopoietic Stem Cell Mobilization/ (3956)
3 Hematopoietic Stem Cell Transplantation/ (37906)
4 Hematopoietic Stem Cells/ (40574)
5 ((autologous or autogenous or autogeneic) adj2 stem* adj2 (mobilization or mobilisation*)).tw. (65)
6 (auto-sct or autosct).tw. (320)
7 (hematopoietic adj2 stem* adj2 (mobilization or mobilisation*)).tw. (362)
8 2 or 3 or 5 or 6 or 7 (40589)
9 1 and 8 (458)
10 animals/ not humans/ (4524962)
11 9 not 10 (387)
12 limit 11 to ed=20090101-20190321 (361)

Database: Medline in-process
Platform: Ovid
Version: 1946 to March 18 2019
Search date: 19/03/2019
Number of results retrieved: 5
Search strategy: see Medline above

Database: Medline epubs ahead of print
Platform: Ovid
Version: March 18, 2019
Search date: 19/03/2019
Number of results retrieved: 6
Search strategy: see Medline above

Database: Medline daily update
Platform: Ovid
Version: March 2018
Search date: 19/03/2019
Number of results retrieved: 1
Search strategy see Medline above

Database: Embase
Platform: Ovid
Version: 1980 to 2019 Week 11
Search date: 19/03/2019
Number of results retrieved: 703
Search strategy:

1 Plerixafor/ (4463)
2 (plerixafor* or amd 3100 or amd3100 or mozobil* or jm 3100 or jm3100 or sdzsid 791 or sdzsid791 or sid 791 or sid791).tw. (4675)
3 1 or 2 (5339)
4 stem cell mobilization/ (7055)

5 Hematopoietic Stem Cell Transplantation/ (34977)
6 Hematopoietic Stem Cell/ (54231)
7 ((autologous or autogenous or autogeneic) adj2 stem* adj2 (mobilization or mobilisation*)).tw. (199)
8 (auto-sct or autosct).tw. (1129)
9 (hematopoietic adj2 stem* adj2 (mobilization or mobilisation*)).tw. (711)
10 4 or 5 or 6 or 7 or 8 or 9 (91815)
11 3 and 10 (1915)
12 nonhuman/ not (human/ and nonhuman/) (4321121)
13 11 not 12 (1724)
14 limit 13 to dc=20090101-20190321 (1621)
15 limit 14 to english language (1601)
16 (letter or editorial).pt. (1599576)
17 (conference abstract or conference paper or conference proceeding or "conference review").pt. (4067509)
18 16 or 17 (5667085)
19 15 not 18 (703)

Database: Cochrane Library – incorporating Cochrane Database of Systematic Reviews (CDSR); CENTRAL
Platform: Wiley
Version:
CDSR – Issue 3 of 12, March 2019
CENTRAL – Issue 3 of 12, March 2019
Search date: 19/03/2019
Number of results retrieved:
CDSR – 1
CENTRAL – 37.

#1 MeSH descriptor: [Hematopoietic Stem Cell Mobilization] this term only 287
#2 MeSH descriptor: [Hematopoietic Stem Cell Transplantation] this term only 1086
#3 MeSH descriptor: [Hematopoietic Stem Cells] this term only 269
#4 ((((autologous or autogenous or autogeneic) Near/2 stem* Near/2 (mobilization or mobilisation*)))):ti,ab,kw 22
#5 (((auto-sct or autosct))):ti,ab,kw 77
#6 (((hematopoietic Near/2 stem* Near/2 (mobilization or mobilisation*)))):ti,ab,kw 318
#7 (plerixafor* or amd 3100 or amd3100 or mozobil* or jm 3100 or jm3100 or sdzsid 791 or sdzsid791 or sid 791 or sid791):ti,ab,kw 134
#8 #1 or #2 or #3 or #4 or #5 or #6 1515
#9 #7 and #8 37

Database: HTA
Platform: CRD
Version: From 31 March 2018, the HTA database remains available, but CRD are no longer adding new records to it
Search date: 19/03/2019
Number of results retrieved: 6
Search strategy: plerixafor* or amd 3100 or amd3100 or mozobil* or jm 3100 or sdzsid 791or sid 791

Trials registry search results

Clinicaltrials.gov
Search date: 12 March 2019
Number of results retrieved: 75
Search strategy: Plerixafor or Mozibil AND stem cell

11. Evidence selection

A single literature search was conducted for 2 related evidence summaries looking at plerixafor for mobilisation in people receiving autologous HSCT for solid tumours or haematological tumours (excluding multiple myeloma and lymphoma) and haematological paraneoplastic complications. The search identified 797 references after duplicates were removed (see search strategy for full details). These references were screened using their titles and abstracts and 85 references were obtained and assessed for relevance. Of these, 2 references are included in this evidence summary on solid tumours and 1 reference is included in the evidence summary on haematological tumours and haematological paraneoplastic complications. The remaining 82 references were excluded and are listed in the following table.

Study	Reason for exclusion
Aabideen, Kanakkande, Anoop, Parameswaran, Ethell, Mark E. et al. (2011) The feasibility of plerixafor as a second-line stem cell mobilizing agent in children. Journal of pediatric hematology/oncology 33(1): 65-7	Study includes children with solid tumours
Abhyankar, S., DeJarnette, S., Aljitawi, O. et al. (2012) A risk-based approach to optimize autologous hematopoietic stem cell (HSC) collection with the use of plerixafor. Bone marrow transplantation 47(4): 483-7	Study includes population with MM and/or lymphoma
Abusin, G. A., Abu-Arja, R. F., Gingrich, R. D. et al. (2013) An algorithm for utilizing peripheral blood CD34 count as a predictor of the need for plerixafor in autologous stem cell mobilization - Cost-effectiveness analysis. Journal of Clinical Apheresis 28(4): 293-300	Study combines various populations
Avramova, Boryana E., Yordanova, Maya N., Konstantinov, Dobrin N. et al. (2011) Successful mobilization of peripheral blood stem cells in children with cancer using plerixafor (Mozobil) and granulocyte-colony stimulating factor. Drug design, development and therapy 5: 407-9	Study includes children with solid tumours
Azar, Nabih, Ouzegdouh, Maya, Choquet, Sylvain et al. (2018) Impact of plerixafor (mozobil) on hospital efficiency: A single center experience. Journal of clinical apheresis 33(1): 5-13	Study combines various populations
Baertsch, M. A., Kriegsmann, K., Pavel, P. et al. (2018) Platelet Count before Peripheral Blood Stem Cell Mobilization Is Associated with the Need for Plerixafor But Not with the Collection Result. Transfusion Medicine and Hemotherapy 45(1): 24-31	Study combines various populations
Basak, G. W., Mikala, G., Koristek, Z. et al. (2011) Plerixafor to rescue failing chemotherapy-based stem cell mobilization: It's not too late. Leukemia and Lymphoma 52(9): 1711-1719	Study includes population with MM and/or lymphoma

Study	Reason for exclusion
Basak, Grzegorz W., Jaksic, Ozren, Koristek, Zdenek et al. (2011) Identification of prognostic factors for plerixafor-based hematopoietic stem cell mobilization. American journal of hematology 86(7): 550-3	Study includes population with MM and/or lymphoma
Bitan, Menachem, Eshel, Rinat, Sadot, Efraim et al. (2016) Combined plerixafor and granulocyte colony-stimulating factor for harvesting high-dose hematopoietic stem cells: Possible niche for plerixafor use in pediatric patients. Pediatric transplantation 20(4): 565-71	Study includes children with solid tumours
Boulad, F., Shore, T., van Besien, K. et al. (2018) Safety and efficacy of plerixafor dose escalation for the mobilization of cd34+ hematopoietic progenitor cells in patients with sickle cell disease: Interim results. Haematologica 103(5): 770-777	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Cappellari, Roberta, D'Anna, Marianna, Avogaro, Angelo et al. (2016) Plerixafor improves the endothelial health balance. The effect of diabetes analysed by polychromatic flow cytometry. Atherosclerosis 251: 373-380	Not a relevant study design
Cardenoux, Charlotte, Demeocq, Francois, Kanold, Justyna et al. (2010) Pegfilgrastim plus AMD 3100 for stem-cell mobilization in children. Pediatric blood & cancer 55(4): 769	Not a relevant study design
Chambon, Fanny, Merlin, Etienne, Rochette, Emmanuelle et al. (2013) Mobilization of hematopoietic stem cells by plerixafor alone in children: a sequential Bayesian trial. Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis 49(3): 453-8	Study includes children with solid tumour
Chen, A. I., Bains, T., Murray, S. et al. (2012) Clinical experience with a simple algorithm for plerixafor utilization in autologous stem cell mobilization. Bone marrow transplantation 47(12): 1526-9	Study combines various populations
De Blasio, Angelo, Rossi, Luigi, Zappone, Elisabetta et al. (2013) Plerixafor and autologous stem cell transplantation: impressive result in a chemoresistant testicular cancer patient treated with high-dose chemotherapy. Anti-cancer drugs 24(6): 653-7	Not a relevant study design
de Greef, G. E., Braakman, E., van der Holt, B. et al. (2019) The feasibility and efficacy of subcutaneous plerixafor for mobilization of peripheral blood stem cells in allogeneic HLA-identical sibling donors: results of the HOVON-107 study. Transfusion 59(1): 316-324	Does not contain a population of people undergoing autologous HSCT treated with plerixafor

Study	Reason for exclusion
Dhakal, B., D'Souza, A., Arce-Lara, C. et al. (2015) Superior efficacy but higher cost of plerixafor and abbreviated-course G-CSF for mobilizing hematopoietic progenitor cells (HPC) in AL amyloidosis. Bone marrow transplantation 50(4): 610-2	Not rescue or pre-emptive treatment
Dhakal, Binod, Strouse, Christopher, D'Souza, Anita et al. (2014) Plerixafor and abbreviated-course granulocyte colony-stimulating factor for mobilizing hematopoietic progenitor cells in light chain amyloidosis. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 20(12): 1926-31	Not rescue or pre-emptive treatment
Dunn, D., Vikas, P., Jagasia, M. et al. (2012) Plerixafor in AL amyloidosis: improved graft composition and faster lymphocyte recovery after auto-SCT in patient with end-stage renal-disease. Bone marrow transplantation 47(8): 1136-7	Not a relevant study design
Dvorak, Christopher C., Horn, Biljana N., Puck, Jennifer M. et al. (2014) A trial of plerixafor adjunctive therapy in allogeneic hematopoietic cell transplantation with minimal conditioning for severe combined immunodeficiency. Pediatric transplantation 18(6): 602-8	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Emir, Suna, Demir, Haci Ahmet, Aksu, Tekin et al. (2014) Use of plerixafor for peripheral blood stem cell mobilization failure in children. Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis 50(2): 214-8	Study includes children with solid tumours
Esrick, E. B., Manis, J. P., Daley, H. et al. (2018) Successful hematopoietic stem cell mobilization and apheresis collection using plerixafor alone in sickle cell patients. Blood Advances 2(19): 2505-2512	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Fadini, Gian Paolo, Fiala, Mark, Cappellari, Roberta et al. (2015) Diabetes Limits Stem Cell Mobilization Following G-CSF but Not Plerixafor. Diabetes 64(8): 2969-77	Study includes population with MM and/or lymphoma
Fowler, C. J., Dunn, A., Hayes-Lattin, B. et al. (2009) Rescue from failed growth factor and/or chemotherapy HSC mobilization with G-CSF and plerixafor (AMD3100): an institutional experience. Bone marrow transplantation 43(12): 909-17	Study includes population with MM and/or lymphoma

Study	Reason for exclusion
Galli, Monica, Lessi, Federica, Rambaldi, Alessandro et al. (2015) Mobilization of peripheral blood hematopoietic stem cells by granulocyte-colony stimulating factor and plerixafor in patients with cardiac AL amyloidosis. Amyloid : the international journal of experimental and clinical investigation : the official journal of the International Society of Amyloidosis 22(4): 259-60	Not rescue or pre-emptive treatment
Garcia-Escobar, I., Parrilla, L., Ortega, L. M. et al. (2014) Clinical experience with plerixafor as a mobilization regimen for autologous peripheral blood stem cell transplantation in patients with refractory germ cell tumors. Molecular and Clinical Oncology 2(6): 923-926	Not a relevant study design
Ghobadi, Armin, Fiala, Mark A., Ramsingh, Giridharan et al. (2017) Fresh or Cryopreserved CD34+-Selected Mobilized Peripheral Blood Stem and Progenitor Cells for the Treatment of Poor Graft Function after Allogeneic Hematopoietic Cell Transplantation. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 23(7): 1072-1077	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Green, Michael M. B., Chao, Nelson, Chhabra, Saurabh et al. (2016) Plerixafor (a CXCR4 antagonist) following myeloablative allogeneic hematopoietic stem cell transplantation enhances hematopoietic recovery. Journal of hematology & oncology 9(1): 71	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Gregory, Kelly M.; Rao, Kamakshi V.; Armistead, Paul M. (2010) Plerixafor dosing and administration in a patient with dialysis-dependent renal failure. The Annals of pharmacotherapy 44(12): 2028-30	Not a relevant study design
Greil, Christine, Kiote-Schmidt, Chrissoula, Fink, Geertje et al. (2017) Successful peripheral blood stem cell mobilization with a cost-efficient single fixed-dose plerixafor schedule in poor mobilizers. Leukemia & lymphoma 58(8): 1849-1858	Study combines various populations
Hamid, A. A., Markt, S. C., Vicier, C. et al. (2019) Autologous Stem-Cell Transplantation Outcomes for Relapsed Metastatic Germ-Cell Tumors in the Modern Era. Clinical Genitourinary Cancer 17(1): 58	Not a relevant study design
He, Shun, Chu, Jianhong, Vasu, Sumithira et al. (2014) FLT3L and plerixafor combination increases hematopoietic stem cell mobilization and leads to improved transplantation outcome. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 20(3): 309-13	Not a relevant study design

Study	Reason for exclusion
Hong, Kyung Taek, Kang, Hyoung Jin, Kim, Nam Hee et al. (2012) Successful mobilization using a combination of plerixafor and G-CSF in pediatric patients who failed previous chemomobilization with G-CSF alone and possible complications of the treatment. Journal of hematology & oncology 5: 14	Study includes children with solid tumours
Horwitz, M. E., Chute, J. P., Gasparetto, C. et al. (2012) Preemptive dosing of plerixafor given to poor stem cell mobilizers on day 5 of G-CSF administration. Bone marrow transplantation 47(8): 1051-5	Study includes population with MM and/or lymphoma
Hsieh, Matthew M. and Tisdale, John F. (2018) Hematopoietic stem cell mobilization with plerixafor in sickle cell disease. Haematologica 103(5): 749-750	Not a relevant study design
Hubel, K., Fresen, M. M., Salwender, H. et al. (2011) Plerixafor with and without chemotherapy in poor mobilizers: results from the German compassionate use program. Bone marrow transplantation 46(8): 1045-52	Study includes population with MM and/or lymphoma
Jaiswal, Sarita Rani, Bhakuni, Prakash, Joy, Aby et al. (2018) Impact of Single-Dose Plerixafor as an Adjunct to Granulocyte Colony-Stimulating Factor-Based Peripheral Blood Stem Cell Mobilization on the Graft Composition and Outcome for T Cell-Replete Haploidentical Peripheral Blood Stem Cell Transplantation with Post-Transplantation Cyclophosphamide: A Comparative Study. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 24(3): 542-548	Not a relevant study design
Jantunen, E. and Fruehauf, S. (2011) Importance of blood graft characteristics in auto-SCT: implications for optimizing mobilization regimens. Bone marrow transplantation 46(5): 627-35	Study includes population with MM and/or lymphoma
Kamdar, M., Abebe, S., Gonzalez Fontal, G. R. et al. (2017) Administration of plerixafor for peripheral blood CD34+ stem cell content of less than 30 x 10-6/L for autologous stem cell mobilization leads to decreased apheresis days and increased total yield. Bone marrow transplantation. Conference: 43rd annual meeting of the F society for blood and marrow transplantation. France 52(supplement1): 39	Conference abstract
Karponi, Garyfalia, Psatha, Nikoletta, Lederer, Carsten Werner et al. (2015) Plerixafor+G-CSF-mobilized CD34+ cells represent an optimal graft source for thalassemia gene therapy. Blood 126(5): 616-9	Does not contain a population of people undergoing autologous HSCT treated with plerixafor

Study	Reason for exclusion
Kaul, E., Shah, G., Chaulagain, C. et al. (2014) Plerixafor and G-CSF for autologous stem cell mobilization in AL amyloidosis. Bone marrow transplantation 49(9): 1233	Not rescue or pre-emptive treatment
Kobold, S., Isernhagen, J., Hubel, K. et al. (2011) Plerixafor is effective and safe for stem cell mobilization in heavily pretreated germ cell tumor patients. Bone marrow transplantation 46(8): 1053-6	Not a relevant study design
Kosmas, Christos, Athanasopoulos, Aggelos, Dimitriadis, George et al. (2014) Plerixafor added to G-CSF-supported paclitaxel-ifosfamide-cisplatin salvage chemotherapy enhances mobilization of adequate numbers of hematopoietic stem cells for subsequent autografting in hard-to-mobilize patients with relapsed/refractory germ-cell tumors: a single-center experience. Anti-cancer drugs 25(7): 841-7	Not a relevant study design
Lagresle-Peyrou, C., Lefrere, F., Magrin, E. et al. (2018) Plerixafor enables safe, rapid, efficient mobilization of hematopoietic stem cells in sickle cell disease patients after exchange transfusion. Haematologica 103(5): 778-786	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Leotta, S., Poidomani, M., Mauro, E. et al. (2011) AMD3100 for urgent PBSC mobilization and allogeneic transplantation from a normal donor after failed marrow harvest. Bone marrow transplantation 46(2): 314-6	Not a relevant study design
Lessi, Federica, Marson, Piero, Colpo, Anna et al. (2016) Spontaneous splenic rupture following stem cell mobilization with G-CSF and plerixafor in AL amyloidosis. Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis 54(2): 256-8	Not a relevant study design
Lidonnici, Maria Rosa, Aprile, Annamaria, Frittoli, Marta Claudia et al. (2017) Plerixafor and G-CSF combination mobilizes hematopoietic stem and progenitors cells with a distinct transcriptional profile and a reduced in vivo homing capacity compared to plerixafor alone. Haematologica 102(4): e120-e124	Not a relevant study design
Liesveld, J. (2015) Plerixafor: Potential role in acute leukemia therapy. Expert Opinion on Orphan Drugs 3(4): 467-475	Review article but not a systematic review
Liu, T., Li, X., You, S. et al. (2016) Effectiveness of AMD3100 in treatment of leukemia and solid tumors: From original discovery to use in current clinical practice. Experimental Hematology and Oncology 5(1): 19	Review article but not a systematic review

Study	Reason for exclusion
Lopez-Castano, F., Manresa, P., Diaz, V. et al. (2019) Comparison and cost analysis of three protocols for mobilization and apheresis of haematopoietic progenitor cells. Journal of Clinical Apheresis	Study includes population with MM and/or lymphoma
Maschan, A. A., Balashov, D. N., Kurnikova, E. E. et al. (2015) Efficacy of plerixafor in children with malignant tumors failing to mobilize a sufficient number of hematopoietic progenitors with G-CSF. Bone marrow transplantation 50(8): 1089-91	Study includes children with solid tumours
Mehdizadeh, M., Hajifathali, A., Tabarraee, M. et al. (2013) Plerixafor in the treatment of stem cell mobilization failure; first experience in Iran. Iranian Journal of Pharmaceutical Research 12(suppl): 185-187	Study includes population with MM and/or lymphoma
Micallef, I. N., Jacobsen, E. D., Shaughnessy, P. et al. (2013) G-CSF plus plerixafor (Mozobil) to mobilize hematopoietic stem cells in patients with thrombocytopenia or leukopenia prior to auto-SCT. Bone marrow transplantation 48(2): 303-4	Study includes population with MM and/or lymphoma
Milone, Giuseppe and Tripepi, Giovanni (2014) Algorithms for early identification of poor mobilization and for on-demand use of plerixafor in patients mobilized by chemotherapy and granulocyte-colony stimulating factor. Leukemia & lymphoma 55(3): 725-6	Not a relevant study design
Miltiadous, Constantinos, Dimitriadis, Georgios K., Roditis, Pavlos et al. (2017) Plerixafor mobilization of peripheral blood hematopoietic progenitors to support further high-dose chemotherapy cycles in a patient with germ-cell tumor relapsing after previous tandem high-dose chemotherapy and hematopoietic cell transplantation: report of a case. Anti-cancer drugs 28(2): 237-241	Not a relevant study design
Modak, Shakeel, Cheung, Irene Y., Kushner, Brian H. et al. (2012) Plerixafor plus granulocyte-colony stimulating factor for autologous hematopoietic stem cell mobilization in patients with metastatic neuroblastoma. Pediatric blood & cancer 58(3): 469-71	Study includes children with solid tumours
Mohty, M., Drillat, P., Grouin, J. M. et al. (2017) Addition of plerixafor to G-CSF is useful to achieve efficient collection even in very poor mobilizers: hope for patients with diminished hematopoietic function. Bone marrow transplantation 52(7): 1049-1050	Not a relevant study design
Naithani, Rahul, Sachdeva, Mansi, Rai, Reeta et al. (2016) Plerixafor for Hematopoietic Stem Cell Mobilization in Children With Neuroblastoma.	Study includes children with solid tumours

Study	Reason for exclusion
Experimental and clinical transplantation : official journal of the Middle East Society for Organ Transplantation 14(3): 358-9	
O'Hara, V. J. D., Karr, A. H., Srivastava, S. et al. (2014) Experience with plerixafor for hematopoietic cell mobilization in nine patients with germ cell tumors. Pharmacotherapy 34(1): 85-88	Not rescue or pre-emptive treatment
Saure, Christian, Weigelt, Christian, Schroeder, Thomas et al. (2010) Plerixafor enables successful hematopoietic stem cell collection in an extensively pretreated patient with testicular cancer. Acta haematologica 124(4): 235-8	Not a relevant study design
Schroeder, Mark A., Rettig, Michael P., Lopez, Sandra et al. (2017) Mobilization of allogeneic peripheral blood stem cell donors with intravenous plerixafor mobilizes a unique graft. Blood 129(19): 2680-2692	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Selleslag, D., Dierickx, D., Breems, D. A. et al. (2011) Plerixafor in poor stem cell mobilizers: the Belgian Compassionate Use Program. Acta clinica Belgica 66(3): 200-4	Study includes population with MM and/or lymphoma
Sevilla, Julian, Schiavello, Elisabetta, Madero, Luis et al. (2012) Priming of hematopoietic progenitor cells by plerixafor and filgrastim in children with previous failure of mobilization with chemotherapy and/or cytokine treatment. Journal of pediatric hematology/oncology 34(2): 146-50	Study includes children with solid tumours
Sheppard, Dawn, Bredeson, Christopher, Allan, David et al. (2012) Systematic review of randomized controlled trials of hematopoietic stem cell mobilization strategies for autologous transplantation for hematologic malignancies. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 18(8): 1191-203	Study includes population with MM and/or lymphoma
Shimizu, N., Sakaida, E., Ohwada, C. et al. (2012) Mobilization of PBSCs in poor mobilizers with POEMS syndrome using G-CSF with plerixafor. Bone marrow transplantation 47(12): 1587-8	Not a relevant study design
Son, Meong Hi, Kang, Eun Suk, Kim, Dong Hwan et al. (2013) Efficacy and toxicity of plerixafor for peripheral blood stem cell mobilization in children with high-risk neuroblastoma. Pediatric blood & cancer 60(8): E57-9	Study includes children with solid tumours

Study	Reason for exclusion
Spoerl, Silvia, Peter, Robert, Wascher, Dagmar et al. (2017) Patients' outcome after rescue plerixafor administration for autologous stem cell mobilization: a single-center retrospective analysis. Transfusion 57(1): 115-121	Study includes population with MM and/or lymphoma
Srinivasan, Ashok, Panetta, John C., Cross, Shane J. et al. (2014) Phase I study of the safety and pharmacokinetics of plerixafor in children undergoing a second allogeneic hematopoietic stem cell transplantation for relapsed or refractory leukemia. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 20(8): 1224-8	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Tanhehco, Yvette C., Adamski, Jill, Sell, Mary et al. (2010) Plerixafor mobilization leads to a lower ratio of CD34+ cells to total nucleated cells which results in greater storage costs. Journal of clinical apheresis 25(4): 202-8	Study includes population with MM and/or lymphoma
Teusink, Ashley, Pinkard, Susan, Davies, Stella et al. (2016) Plerixafor is safe and efficacious for mobilization of peripheral blood stem cells in pediatric patients. Transfusion 56(6): 1402-5	Study includes children with solid tumours
Toledano, Helen, Yahel, Anat, Cohen, Ian J. et al. (2010) Successful mobilization, harvest and transplant of peripheral blood stem cells using AMD3100 and G-CSF following high dose craniospinal irradiation for medulloblastoma in a young child. Pediatric blood & cancer 54(4): 613-5	Study includes children with solid tumours
Tuffaha, Haitham and Abdel-Rahman, Fawzi Abdel-Latif (2010) Successful stem-cell mobilization and transplantation using plerixafor in a patient with a germ cell tumor. Hematology/oncology and stem cell therapy 3(4): 203-5	Not a relevant study design
Veeraputhiran, Muthu, Jain, Tania, Cronin, Simon et al. (2014) Successful hematopoietic stem cell collection in patients who fail initial plerixafor mobilization for autologous stem cell transplant. Journal of clinical apheresis 29(6): 293-8	Study includes population with MM and/or lymphoma
Vettenranta, Kim; Mottonen, Merja; Riikonen, Pekka (2012) The use of plerixafor in harvesting autologous stem cells in the pediatric setting. Pediatric blood & cancer 59(1): 197-8	Study includes children with solid tumours
Vishnu, Prakash, Roy, Vivek, Paulsen, Athena et al. (2012) Efficacy and cost-benefit analysis of risk-adaptive use of plerixafor for autologous hematopoietic progenitor cell mobilization. Transfusion 52(1): 55-62	Study includes population with MM and/or lymphoma

Study	Reason for exclusion
Vives, S., Sancho, J. M., Almazan, F. et al. (2012) Plerixafor plus G-CSF in combination with chemotherapy for stem cell mobilization in a pediatric patient with Ewing's sarcoma. Journal of Clinical Apheresis 27(5): 260-262	Study includes children with solid tumours
Worel, Nina, Fritsch, Gerhard, Agis, Hermine et al. (2017) Plerixafor as preemptive strategy results in high success rates in autologous stem cell mobilization failure. Journal of clinical apheresis 32(4): 224-234	Study includes population with MM and/or lymphoma
Yannaki, E., Papayannopoulou, T., Jonlin, E. et al. (2012) Erratum: "hematopoietic stem cell mobilization for gene therapy of adult patients with severe beta-Thalassemia: Results of clinical trials using G-CSF or plerixafor in splenectomized and nonsplenectomized subjects" (Molecular Therapy (2012) 20 (230-238) DOI: 10.1038/mt.2011.195). Molecular Therapy 20(2): 469	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Yannaki, E., Papayannopoulou, T., Jonlin, E. et al. (2011) Hematopoietic Stem Cell Mobilization for Gene Therapy of Adult Patients With Severe beta-Thalassemia: Results of Clinical Trials Using G-CSF or plerixafor in Splenectomized and Nonsplenectomized Subjects. Molecular Therapy	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Yannaki, Evangelia, Karponi, Garyfalia, Zervou, Fani et al. (2013) Hematopoietic stem cell mobilization for gene therapy: superior mobilization by the combination of granulocyte-colony stimulating factor plus plerixafor in patients with beta-thalassemia major. Human gene therapy 24(10): 852-60	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Yannaki, Evangelia, Papayannopoulou, Thalia, Jonlin, Erica et al. (2012) Hematopoietic stem cell mobilization for gene therapy of adult patients with severe beta-thalassemia: results of clinical trials using G-CSF or plerixafor in splenectomized and nonsplenectomized subjects. Molecular therapy : the journal of the American Society of Gene Therapy 20(1): 230-8	Does not contain a population of people undergoing autologous HSCT treated with plerixafor
Yuan, Shan, Wang, Shirong, Salhotra, Amandeep et al. (2014) Plerixafor to the rescue: boosting peripheral blood stem cell mobilization in patients previously treated with hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate, cytarabine (Hyper-CVAD) chemotherapy. Leukemia & lymphoma 55(7): 1557-62	Study includes population with MM and/or lymphoma
Abbreviations: G-CSF; Granulocyte-colony stimulating factor: HSCT; haematopoietic stem cell transplantation: MM, multiple myeloma	

References for the 3 most clinically impactful studies were submitted with the Preliminary Policy Proposition. These are listed in the following table with the evidence selection decision:

Study	Comment
Worel N, Apperley J, Basak G, Douglas K, Gabriel I, et al. (2012). European data on stem cell mobilization with plerixafor in patients with nonhematologic disease: an analysis of the European consortium of stem cell mobilization. Transfusion 52, pp 2395- 2400	Included in this evidence summary
Horwitz M, Long, Holman P, Libby E, Calandra G, Schriber J. (2012). Efficacy and safety of hematopoietic stem cell remobilization with plerixafor +G-CSF in adult patients with germ cell tumours. Bone Marrow Transplantation, 47, 1287-1286	Included in this evidence summary
Jaimovich G, Castro M, Ostriz B, Fernandez M, Silveyra D, Campestri R. (2016). Plerixafor, cyclophosphamide and G-CSF and blood cell mobilization in a patient with acute promyelocytic leukaemia. Journal of Clinical Apheresis, 32, pp 592-593	Excluded: not a relevant study design

12. Related NICE guidance and NHS England clinical policies

NHS England has published clinical commissioning policies on haematopoietic stem cell transplantation and plerixafor for stem cell mobilisation. NICE has not issued any guidance on plerixafor for stem cell mobilisation.

13. Terms used in this evidence summary

Abbreviations

Term	Definition
G-CSF	Granulocyte-colony stimulating factor
HSCT	Haematopoietic stem cell transplantation
PBSC	Peripheral blood stem cells

Medical definitions

Term	Definition
Allogeneic stem cell transplant	A procedure in which a person receives haematopoietic stem cells (cells from which all blood cells develop) from a genetically similar donor
Apheresis	The name given to the flow of the person's blood through the cell separator during which the stem cells (PBSC) are separated and collected into a separate container in which they can then be frozen for later use
Autologous stem cell transplant	The process of high-dose chemotherapy followed by infusion of the harvested stem cells which will repopulate the bone marrow and allow the recovery of the person's blood counts
CD34+ cell	The protein expressed on the stem cells (PBSC) that can be detected and measured, allowing the number of stem cells in the blood or the harvest to be counted
Haematological	Relating to the blood and blood forming tissues
Haematopoietic stem cells	Cells in the bone marrow that can develop into different types of blood cells
Haematopoietic stem cell transplantation	Blood and bone marrow transplantation
Lymphoma	A cancer that affects cells of the immune system called 'lymphocytes'
Myeloma	A cancer that affects the bone marrow
Neutrophil	The most common type of white blood cell
Peripheral blood stem cells	Stem cells in the circulating blood flow, rather than in the bone marrow
Platelet	A type of blood cell that helps blood clot
Pre-emptive treatment	Use of plerixafor when there is a low level of circulating PBSC on the day of planned collection
Rescue treatment	Use of plerixafor with high-dose G-CSF when a previous attempt at mobilisation has failed to collect enough PBSC
Solid tumours	Solid tumours may be benign (not cancer), or malignant (cancer). Different types of solid tumours are named for the type of cells that form them. Examples of solid tumours are sarcomas, carcinomas, and lymphomas. Leukaemias (cancers of the bone marrow and blood) generally do not form solid tumours
Stem cell harvest	Collection of the stem cells (PBSC) from the blood using a cell separator machine
Stem cell mobilisation	A process to dislodge the stem cells from the bone marrow and increase the amount circulating in the blood from where they can be collected

14. References

Horwitz ME, Long G, Holman P et al. (2012) Efficacy and safety of hematopoietic stem cell remobilization with plerixafor+G-CSF in adult patients with germ cell tumors. Bone marrow transplantation 47(10): 1283-6

Mozobil European public assessment report

Mozobil summary of product characteristics

NHS England Clinical Commissioning Policy Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised January 2015

NHS England Clinical Commissioning Policy Use of Plerixafor for Stem Cell Mobilisation (updated to include paediatrics) August 2016

Worel N, Apperley JF, Basak GW et al. (2012) European data on stem cell mobilization with plerixafor in patients with nonhematologic diseases: an analysis of the European consortium of stem cell mobilization. Transfusion 52(11): 2395-400