Original French opinion adopted by the Transparency Committee

The legally binding text is the original French opinion version

SUMMARY

melphalan

PHELINUN 50 mg/10 ml and 200 mg/40 ml

powder and solvent for concentrate for solution for infusion

Inclusion on list

Hybrid

Adopted by the Transparency Committee on 12 March 2025

Summary of opinion

Favourable opinion for reimbursement only in "High-dose of PHELINUN used alone or in combination with other cytotoxic medicinal products and/or total body irradiation is indicated in the treatment of:

- **multiple myeloma;**
- **malignant lymphoma (Hodgkin, non-Hodgkin lymphoma);**
- **acute lymphoblastic and myeloblastic leukaemia;**
- **childhood neuroblastoma.**

PHELINUN in combination with other cytotoxic medicinal products is indicated as reduced intensity conditioning (RIC) treatment prior to allogeneic haematopoietic stem cell transplantation (allo-HSCT) in malignant haematological diseases in adults.

PHELINUN in combination with other cytotoxic medicinal products is indicated as conditioning regimen prior to allogeneic haematopoietic stem cell transplantation in haematological diseases in the paediatric population as:

- **Myeloablative conditioning (MAC) treatment in case of malignant haematological diseases;**
- **RIC treatment in case of non-malignant haematological diseases."**

Unfavourable opinion for reimbursement in the other situations covered by the MA indication.

Transparency Committee's Conclusions

Clinical Benefit

Multiple myeloma

- Multiple myeloma is a serious, life-threatening disease.
- This is a curative treatment.
- The efficacy/adverse effects ratio is high.
- There are medicinal alternatives.
- This is a first-line medicinal product in the treatment of multiple myeloma in symptomatic patients over 65 years of age.

- **Public health benefit**

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Malignant lymphoma (Hodgkin, non-Hodgkin lymphoma)

- Malignant lymphomas are serious, life-threatening diseases.
- This is a curative treatment.
- The efficacy/adverse effects ratio is high.
- There are medicinal alternatives.
- This is a first-line medicinal product in the treatment of malignant lymphoma.

- **Public health benefit**

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Acute lymphoblastic and myeloblastic leukaemia

- Acute lymphoblastic and myeloblastic leukaemias are serious, life-threatening diseases.
- This is a curative treatment.
- The efficacy/adverse effects ratio of these medicinal products is high.
- There are medicinal alternatives.
- This is a first-line medicinal product in the treatment of acute lymphoblastic and myeloblastic leukaemia.

- **Public health benefit**

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Childhood neuroblastoma

- Childhood neuroblastoma is a serious, life-threatening disease.
- This is a curative treatment.
- The efficacy/adverse effects ratio is high.

- There are medicinal alternatives.
- Melphalan is a therapeutic option in the treatment of childhood neuroblastoma.

Public health benefit

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Ovarian cancer

- Advanced ovarian cancer is a serious, life-threatening disease.
- This is a curative treatment.
- The efficacy/adverse effects ratio is low.
- There are medicinal alternatives.
- In view of the current guidelines for the treatment of advanced ovarian cancer, these medicinal products have no role in the therapeutic strategy.

Public health benefit

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Mammary adenocarcinoma

- Metastatic mammary adenocarcinoma is a serious, life-threatening disease.
- This is a curative treatment.
- The efficacy/adverse effects ratio is low.
- There are therapeutic alternatives.
- In view of the current guidelines for the treatment of metastatic breast cancer, these medicinal products have no role in the therapeutic strategy.

Public health benefit

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) in malignant haematological diseases in adults

- Malignant diseases requiring allogeneic haematopoietic stem cell transplantation can be life-threatening.
- This is a preparatory (conditioning) treatment prior to curative haematopoietic stem cell transplantation.
- The efficacy/adverse effects ratio has not been adequately established.
- Medicinal and non-medicinal alternatives are available.
- This is a treatment option as an RIC protocol prior to allogeneic haematopoietic stem cell transplantation. In the absence of sufficiently robust comparative data, the role of PHELINUN cannot be defined compared to the other RIC protocols used in malignant haematological diseases in adults.

➔ **Public health benefit**

Considering:

- the seriousness of the disease and its incidence,
- the partially met medical need,
- the lack of response to the identified need given:
  - the lack of evidence of an additional impact on morbidity and mortality and on quality of life,
  - the lack of evidence of an additional impact on the organisation of care,

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) in haematological diseases in the paediatric population

➔ Malignant diseases requiring allogeneic haematopoietic stem cell transplantation can be life-threatening.

➔ This is a preparatory (conditioning) treatment prior to curative haematopoietic stem cell transplantation.

➔ The efficacy/adverse effects ratio has not been adequately established.

➔ Medicinal and non-medicinal alternatives are available.

➔ This is a treatment option as a MAC protocol prior to allogeneic haematopoietic stem cell transplantation. In the absence of sufficiently robust comparative data, the role of PHELINUN cannot be defined compared to the other MAC protocols used in malignant haematological diseases in the paediatric population.

➔ **Public health benefit**

Considering:

- the seriousness of the disease and its incidence,
- the partially met medical need,
- the lack of response to the identified need given:
  - the lack of evidence of an additional impact on morbidity and mortality and on quality of life,
  - the lack of evidence of an additional impact on the organisation of care,

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) in non-malignant haematological diseases in the paediatric population

➔ Non-malignant diseases requiring allogeneic haematopoietic stem cell transplantation can be life-threatening.

➔ This is a preparatory (conditioning) treatment prior to curative haematopoietic stem cell transplantation.

➔ The efficacy/adverse effects ratio has not been adequately established.

➔ Medicinal and non-medicinal alternatives are available.

➔ This is a treatment option as an RIC protocol prior to allogeneic haematopoietic stem cell transplantation. In the absence of sufficiently robust comparative data, the role of PHELINUN cannot

be defined compared to the other RIC protocols used in non-malignant haematological diseases in the paediatric population.

➔ Public health benefit

Considering:

- the seriousness of the disease and its incidence,
- the partially met medical need,
- the lack of response to the identified need given:
  - the lack of evidence of an additional impact on morbidity and mortality and on quality of life,
  - the lack of evidence of an additional impact on the organisation of care,

PHELINUN (melphalan) is unlikely to have an additional impact on public health in this indication.

Considering all of these elements, the Committee deems that the clinical benefit of PHELINUN 50 mg/10 ml and 200 mg/40 ml (melphalan) is:

- **substantial only in "High-dose of PHELINUN used alone or in combination with other cytotoxic medicinal products and/or total body irradiation is indicated in the treatment of:**
  - **multiple myeloma;**
  - **malignant lymphoma (Hodgkin, non-Hodgkin lymphoma);**
  - **acute lymphoblastic and myeloblastic leukaemia;**
  - **childhood neuroblastoma."**
- **low only in the indication "PHELINUN in combination with other cytotoxic medicinal products is indicated as reduced intensity conditioning (RIC) treatment prior to allogeneic haematopoietic stem cell transplantation (allo-HSCT) in malignant haematological diseases in adults.**

  PHELINUN in combination with other cytotoxic medicinal products is indicated as conditioning regimen prior to allogeneic haematopoietic stem cell transplantation in haematological diseases in the paediatric population as:
  - **Myeloablative conditioning (MAC) treatment in case of malignant haematological diseases;**
  - **RIC treatment in case of non-malignant haematological diseases."**
- **insufficient in the treatment of ovarian cancer and mammary adenocarcinoma to justify public funding in view of the alternatives available in the other MA situations.**

The Committee issues the following opinions:

- **a favourable opinion for inclusion of PHELINUN 50 mg/10 ml and 200 mg/40 ml (melphalan) in the list of covered drugs for inpatients approved for use only within the scope retained and at the MA dosages.**
- **an unfavourable opinion for inclusion of PHELINUN 50 mg/10 ml and 200 mg/40 ml (melphalan) in the list of covered drugs for inpatients approved for use in the treatment of ovarian cancer and mammary adenocarcinoma.**

Clinical Added Value

Reimbursable indications shared with the reference medicinal product

In the treatment of multiple myeloma, malignant lymphoma, acute lymphoblastic and myeloblastic leukaemia and childhood neuroblastoma, these proprietary medicinal products are hybrids that do not provide any clinical added value (CAV V) compared to the proprietary medicinal products containing melphalan already listed.

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) in malignant haematological diseases in adults

Considering:

- the available data, predominantly observational, retrospective and with a low level of evidence,
- the absence of sufficiently robust comparative data enabling the effect size of conditioning protocols using melphalan to be estimated compared to the other RIC protocols available, used in this indication,
- and the partially met medical need,

the Committee deems that PHELINUN 50 mg/10 ml and 200 mg/40 ml (melphalan) provides no clinical added value (CAV V) compared to the RIC protocols available.

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) in haematological diseases in the paediatric population

Considering:

- the available observational, retrospective data and their low level of evidence,
- the absence of sufficiently robust comparative data enabling the size effect of conditioning protocols using melphalan to be estimated compared to the other MAC protocols available, used in malignant haematological diseases in the paediatric population,
- and the partially met medical need,

the Committee deems that PHELINUN 50 mg/10 ml and 200 mg/40 ml (melphalan) provides no clinical added value (CAV V) compared to the MAC protocols available in the paediatric population.

Allogeneic haematopoietic stem cell transplantation (allo-HSCT) in non-malignant haematological diseases in the paediatric population

Considering:

- observational, retrospective, non-comparative data and their low level of evidence,
- the absence of sufficiently robust comparative data enabling the effect size of RIC protocols using melphalan to be estimated compared to the other RIC protocols available, used in non-malignant haematological diseases in the paediatric population,

- and the partially met medical need,

the Committee deems that PHELINUN 50 mg/10 ml and 200 mg/40 ml (melphalan) provides no clinical added value (CAV V) compared to the RIC protocols available in the paediatric population.