



TRANSPARENCY COMMITTEE

OPINION

22 JULY 2020

treosulfan
TRECONDI 1 g and 5 g powder for solution for infusion

First assessment

► Key points

Favourable opinion for reimbursement in combination with fludarabine as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) in adult patients and in children older than one month and adolescents with malignant diseases.

Unfavourable opinion for reimbursement in combination with fludarabine as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) in adult patients with non-malignant diseases.

► What therapeutic improvement?

In adult patients with malignant diseases: No clinical added value compared to busulfan, in combination with fludarabine as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

In paediatric patients older than one month with malignant diseases: No clinical added value as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

► Role in the care pathway?

The choice of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) depends on numerous criteria, in particular, general health status, the patient's age, comorbidities and the type of blood disease.

There are two types of conditioning treatment, depending on their intensity.

Myeloablative conditioning, which is reserved for patients in good general health, uses various chemotherapy regimens that may include alkylating agents or antimetabolites (cyclophosphamide, busulfan, melphalan, thiotepa, cytarabine), potentially combined with total body irradiation (in the event of a malignant blood disease, in particular). The protocols used are, in particular:

- total body irradiation (TBI) + cyclophosphamide;
- TBI + cytarabine +/- melphalan;
- busulfan + cyclophosphamide, etc.

Reduced intensity conditioning is preferred in adult patients who are elderly, have comorbidities or an impaired general health status insofar as myeloablative conditioning is more toxic. It is based on the use of potent immunosuppressant agents and, in particular, fludarabine with variable combination with other immunosuppressant agents (anti-thymocyte globulin, mycophenolate mofetil), and low doses of chemotherapy (cyclophosphamide, busulfan, aracytine) or low doses of TBI.

Role of the medicinal product in the care pathway

In adults, adolescents and children older than one month with malignant diseases: TRECONDI (treosulfan) in combination with fludarabine constitutes a new treatment option, as a reduced-intensity conditioning regimen prior to allogeneic haematopoietic stem cell transplantation (alloHSCT). It should be noted that in adults, a study demonstrated the non-inferiority of the treosulfan-fludarabine combination versus busulfan-fludarabine in terms of event-free survival after 2 years (primary endpoint). In children, no comparative data versus another conditioning regimen are available.

In adult patients with non-malignant diseases: In the absence of data, TRECONDI (treosulfan) has no role in the therapeutic strategy for this population.

COMMITTEE'S CONCLUSIONS

Clinical benefit

In adult patients with malignant diseases

- ▶ Malignant diseases requiring haematopoietic stem cell transplantation are life-threatening.
- ▶ TRECONDI (treosulfan) is a preparatory (conditioning) treatment prior to curative haematopoietic stem cell transplantation.
- ▶ The efficacy/adverse effects ratio of TRECONDI (treosulfan) is high.
- ▶ There are medicinal and non-medicinal therapeutic alternatives (total body irradiation).
- ▶ TRECONDI (treosulfan) in combination with fludarabine represents a new treatment option, in the same way as reduced-intensity busulfan IV-fludarabine conditioning, as first-line therapy in patients ineligible for myeloablative conditioning, in accordance with the inclusion criteria for the study conducted in adults.

Public health impact

Considering:
the seriousness of the disease,
its incidence,
the partially met medical need,
the absence of additional impact of TRECONDI (treosulfan) on morbidity and mortality
the lack of data on a potential impact on the organisation of care,
the lack of additional response to the identified need,
TRECONDI (treosulfan) is unlikely to have an additional impact on public health.

Given all these elements, the Committee deems that the clinical benefit of TRECONDI (treosulfan) in combination with fludarabine is substantial in adult patients with malignant diseases as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in adult patients with malignant diseases as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

In paediatric patients (older than one month) with malignant diseases

- ▶ Malignant diseases requiring haematopoietic stem cell transplantation are life-threatening.
- ▶ TRECONDI (treosulfan) is a preparatory (conditioning) treatment prior to curative haematopoietic stem cell transplantation.
- ▶ The efficacy/adverse effects ratio of TRECONDI (treosulfan) is high.
- ▶ There are medicinal and non-medicinal therapeutic alternatives (total body irradiation).
- ▶ In the absence of comparative data, the role of TRECONDI (treosulfan) in combination with fludarabine cannot be defined compared to the other conditioning regimens used in paediatric patients. The treosulfan-fludarabine combination constitutes a new treatment option as a conditioning regimen prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) in paediatric patients (older than one month) with malignant diseases.

Public health impact

Considering:
the seriousness of the disease,
its incidence,
the partially met medical need,
the absence of additional impact of TRECONDI (treosulfan) on morbidity and mortality,
the lack of data on a potential impact on the organisation of care,

the lack of additional response to the identified need,
TRECONDI (treosulfan) is unlikely to have an additional impact on public health.

Given all these elements, the Committee deems that the clinical benefit of TRECONDI (treosulfan) in combination with fludarabine is substantial in paediatric patients (older than one month) with malignant diseases as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in paediatric patients (older than one month) with malignant diseases as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

In adult patients with non-malignant diseases

- ▶ Non-malignant diseases requiring haematopoietic stem cell transplantation can be life-threatening.
- ▶ TRECONDI (treosulfan) is a preparatory (conditioning) treatment prior to curative haematopoietic stem cell transplantation.
- ▶ In the absence of data in adult patients with non-malignant diseases, the efficacy/adverse effects ratio of TRECONDI (treosulfan) has not been adequately established.
- ▶ There are medicinal and non-medicinal therapeutic alternatives (total body irradiation).
- ▶ In the absence of data in adult patients with non-malignant diseases, TRECONDI (treosulfan) has no role in the therapeutic strategy for this population.

Public health impact

Considering:
the seriousness of the disease,
its incidence,
the partially met medical need,
the absence of additional impact of TRECONDI (treosulfan) on morbidity and mortality,
the lack of data on a potential impact on the organisation of care,
the lack of additional response to the identified need,
TRECONDI (treosulfan) is unlikely to have an additional impact on public health.

Given all these elements, the Committee deems that the clinical benefit of TRECONDI (treosulfan) in combination with fludarabine is insufficient to justify its funding by the French national health insurance system in adult patients with non-malignant diseases as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in adult patients with non-malignant diseases as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT).

Clinical Added Value

Adult patients with malignant diseases

Considering:
demonstration of the non-inferiority of treosulfan compared to busulfan, both in combination with fludarabine, with no demonstration of superiority, on the event-free survival rate at 2 years (primary endpoint), although the study is associated with several methodological limitations,

the absence of robust data enabling a conclusion to be reached with respect to an improvement in overall survival, quality of life or a better safety of the treosulfan-fludarabine combination compared to the busulfan-fludarabine combination, the Committee considers that TRECONDI in combination with fludarabine provides no clinical added value (CAV V) compared to busulfan in combination with fludarabine as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) in adult patients with malignant diseases.

Paediatric patients older than one month with malignant diseases

Considering:

efficacy and safety data from a phase II descriptive non-comparative study having included 70 paediatric patients and having demonstrated a freedom from transplant-related mortality until day +100 after transplantation of 98.6% (90% CI = [93.4; 99.9]) (primary endpoint), the absence of robust comparative data in terms of improvement in overall survival and data on quality of life, the absence of data comparing treosulfan with the conditioning regimens currently available for paediatric patients, the Committee considers that TRECONDI in combination with fludarabine provides no clinical added value (CAV V) in the therapeutic strategy as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) in paediatric patients older than one month with malignant diseases.