



TRANSPARENCY COMMITTEE SUMMARY 8 SEPTEMBER 2021

The legally binding text is the original French opinion version

***sodium chloride, potassium chloride, magnesium chloride hexahydrate,
calcium chloride dihydrate, histidine, histidine hydrochloride monohydrate,
tryptophan, mannitol, α -cetoglutaric acid***

PERISOC cardioplegia solution/organ preservation solution

First assessment

► Key points

Favourable opinion for reimbursement:

- in cardioplegia during cardiac surgery;
- in the protection of organs during surgical procedures in a bloodless field (heart, kidney, liver);
- for the preservation of donor organs for transplantation: perfusion and cold preservation (heart, kidney, liver, pancreas).

► What therapeutic improvement?

No clinical added value in the therapeutic strategy in each of the indications.

► Role in the care pathway?

Cardioplegia during cardiac surgery

The choice of cardioplegia solution used during cardiac surgery depends on two main factors: the type of surgery performed (in particular, the clamping time associated with the surgery), as well as the centre's practices and the local protocols in place. Practices vary from one cardiac surgery unit to another.

For crystalloid cardioplegia, the choice of solution depends primarily on the clamping time.

The use of cardioplegia techniques with blood or a crystalloid solution such as PLEGISOL requires re-administration every 20 to 30 minutes.

Role of the medicinal product in the care pathway

Like certain crystalloid or blood cardioplegia solutions, PERISOC can be used as a first-line option for cardioplegia. The benefit of PERISOC lies in its single-dose administration. This benefit can be useful for complex and/or lengthy cardiac surgery procedures. The aortic clamping time can thus be prolonged without the need to repeat the cardioplegia injection.

Protection of organs during surgical procedures in a bloodless field (heart, kidney, liver)

There are no guidelines concerning the protection of organs during surgical procedures in a bloodless field. However, in the surgical context, organ protection is essential.

Role of the medicinal product in the care pathway

In the same way as solutions for organ preservation, the role of organ protection solutions like PERISOC is to maintain the viability of the organ ex vivo, in the best condition possible, throughout the surgical procedure. Like the other solutions, PERISOC is a first-line medicinal product.

Preservation of donor organs for transplant: perfusion and cold preservation (heart, kidney, liver, pancreas)

In the transplantation context, organ preservation is a critical phase. The role of solutions for organ preservation is to maintain the viability of the organ ex vivo, in the best possible condition, during transportation from the donor to the recipient, with a view to ensuring optimal transplantation success. The 2020 European kidney transplantation guidelines indicate that University of Wisconsin and HTK solution are equally effective and are standard for multi-organ or single kidney harvesting procedures. According to these guidelines, "the characteristics of HTK are its low viscosity, low potassium concentration and low cost. University of Wisconsin solution has been the standard static cold preservation solution for the procurement of liver, kidney, pancreas, and intestine. [...]. HTK and UW retained a greater capacity to preserve endothelial structure and pH buffering function during warm ischaemia in comparison to MHCS and Celsior, especially in DCD donors."

Role of the medicinal product in the care pathway

Like University of Wisconsin solution, PERISOC should be used as a first-line option to protect donor organs for transplantation.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

Cardioplegia during cardiac surgery

- ▶ The purpose of cardioplegia is to stop the heart and halt its perfusion throughout the duration of the surgical procedure, offering optimal myocardial protection during heart or chest surgery, until activity is resumed. The conditions in which cardioplegia is required represent serious situations that may be life-threatening to the patient, either immediately or following complications.
- ▶ This is a preventive treatment: the role of the cardioplegia solution is to maintain optimal viability of the organ.
- ▶ The efficacy/adverse effects ratio of PERISOC is high.
- ▶ There are therapeutic alternatives (crystalloid solutions and blood cardioplegia solutions).
- ▶ PERISOC is a first-line medicinal product in the event of cardioplegia during cardiac surgery, irrespective of clamping time.

Public health impact

Considering:

- the seriousness of the conditions requiring cardioplegia,
 - the prevalence of these conditions,
 - the met medical need in cardiac surgery procedures,
 - the lack of an additional response to the identified need in the absence of any demonstrated impact on morbidity and mortality, quality of life or the care pathway,
- PERISOC is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of PERISOC is substantial in cardioplegia during cardiac surgery.

Protection of organs during surgical procedures in a bloodless field (heart, kidney, liver)

- ▶ The conditions for which a surgical procedure in a bloodless field with organ protection is required represent serious situations that may be life-threatening to the patient either immediately or following complications.
- ▶ This is a preventive treatment: the role of the protection solution is to maintain the optimal viability of the organ.
- ▶ The efficacy/adverse effects ratio of PERISOC is high.
- ▶ There are therapeutic alternatives (in particular Ringer's lactate solutions).
- ▶ PERISOC is a first-line medicinal product in the protection of organs during surgical procedures in a bloodless field (heart, kidney, liver).

Public health impact

Considering:

- the seriousness of conditions requiring the protection of organs during surgical procedures in a bloodless field,
 - the prevalence of these conditions,
 - the met medical need in surgical procedures in a bloodless field,
 - the lack of an additional response to the identified need in the absence of any demonstrated impact on morbidity and mortality, quality of life or the care pathway,
- PERISOC is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of PERISOC is substantial in the protection of organs during surgical procedures in a bloodless field (heart, kidney, liver).

Preservation of donor organs for transplantation: perfusion and cold preservation (heart, kidney, liver, pancreas)

- ▶ Organ transplantation is a last-resort treatment in the event of end-stage failure of a vital organ. In this transplantation procedure, organ preservation is one of the critical phases.
- ▶ This is a preventive treatment: the role of the preservation solution is to maintain the optimal viability of the organ.
- ▶ The efficacy/adverse effects ratio of PERISOC is high.
- ▶ There are therapeutic alternatives, in particular other preservation solutions with medicinal product or medical device status.
- ▶ PERISOC is a first-line medicinal product in the event of perfusion and cold preservation of heart, liver, kidney and pancreas organs during a transplantation procedure.

Public health impact

Considering:

- the vital need represented by recourse to transplantation,
 - the number of transplant procedures performed in France in 2019, with 5,508 transplants concerning the target organs of PERISOC,
 - the met medical need,
 - the lack of an additional response to the identified need in the absence of any demonstrated impact on morbidity and mortality, and on the care pathway,
- PERISOC is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of PERISOC is substantial in the preservation of donor organs for transplant: perfusion and cold preservation (heart, kidney, liver, pancreas).

Clinical Added Value

Cardioplegia during cardiac surgery

Considering:

- the absence of robust data demonstrating an advantage of PERISOC in terms of efficacy and safety compared to the alternatives;
- the medical need met by the medicinal and non-medicinal alternatives currently available, including BRETSCHEIDER with the same qualitative and quantitative composition as PERISOC;

the Transparency Committee considers that PERISOC provides no clinical added value (CAV V) in the current care pathway for cardioplegia.

Protection of organs during surgical procedures in a bloodless field (heart, kidney, liver)

Considering:

- demonstration in a study of the efficacy and safety of CUSTODIOL compared to Ringer's lactate solution in terms of protection against ischemic kidney damage (primary endpoint) in patients having undergone an open surgical repair of a thoraco-abdominal aortic aneurysm;

but taking into account:

- the medical need met by the medicinal and non-medicinal alternatives currently available, including CUSTODIOL with the same qualitative and quantitative composition as PERISOC;

the Transparency Committee considers that PERISOC provides no clinical added value (CAV V) in the current care pathway for the protection of organs during surgical procedures in a bloodless field.

Preservation of donor organs for transplant: perfusion and cold preservation (heart, kidney, liver, pancreas)

Considering:

- the absence of demonstration of an advantage of CUSTODIOL, a proprietary medical device with the same composition as PERISOC, in terms of efficacy and safety compared to the other preservation solutions, particularly on transplant survival at 1 year (liver, kidney, pancreas) in a review of the literature and a meta-analysis;
- the absence of data in this indication concerning the protection of donor hearts for transplantation;
- the medical need met by the medicinal and non-medicinal alternatives currently available, including CUSTODIOL with the same qualitative and quantitative composition as PERISOC;

the Transparency Committee considers that PERISOC provides no clinical added value (CAV V) in the current care pathway for the preservation of donor organs for transplant.