HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 MARCH 2022

The legally binding text is the original French opinion version

imlifidase
IDEFIRIX 11 mg powder for concentrate for solution for infusion

First assessment

Key points

Favourable opinion for the reimbursement in the desensitisation treatment of highly sensitised adult kidney transplant patients with positive crossmatch against an available deceased donor, with use to be reserved for patients unlikely to be transplanted under the current available kidney allocation system, including prioritisation programmes for highly sensitised patients.

What therapeutic improvement?

Therapeutic improvement in the management of the disease.

Role in the care pathway?

In highly sensitised adult kidney transplant patients with positive crossmatch against an available deceased donor, the objective of HLA desensitisation is to eliminate as many anti-HLA antibodies from the plasma as possible in order to make transplantation possible.

Desensitisation is currently based on protocols using apheresis and/or medicinal products used off-label. However, this technique is relatively little used due to its limitations:
- Desensitisation protocols are not standardised and there is no consensus relating to this subject. They are considered on a case-by-case basis depending on the management strategies specific to each transplant unit,
- The medicinal products used in the protocols have no MA in this indication (B-cell depleting agents (mainly rituximab), immunomodulatory therapies (intravenous immunoglobulins [Ig IV]))
- It requires repeated doses for several weeks or months prior to transplantation before a transplant can be considered,
- It does not always enable a sufficient reduction in antibodies to allow transplantation,
- It can cause serious adverse effects (bleeding risk, risk of infection for apheresis techniques, risk of infection for immunomodulators).

These protocols are almost exclusively used for live donor kidney transplants since they are impossible to implement urgently to achieve crossmatch conversion from positive to negative in the event of a deceased donor transplant. In some cases, a desensitisation protocol can be put in place while awaiting a deceased donor transplant for which the crossmatch is “acceptable”. However, this is very rarely done in practice given a moderate and transient efficacy.

Role of the medicinal product in the care pathway

The proprietary medicinal product IDEFIRIX (imlifidase) is a first-line treatment in the desensitisation strategy for highly sensitised adult kidney transplant patients. In accordance with its marketing authorisation, its use is reserved for patients with positive crossmatch against an available deceased donor and unlikely to be transplanted under the current available kidney allocation system, including prioritisation programmes for highly sensitised patients.

In the absence of comparative data in patients eligible for these experimental desensitisation techniques, despite the low prevalence in the event of deceased donor transplant, the role of imlifidase compared to these techniques should be determined on the basis of the patient’s profile and available efficacy and safety data.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ The clinical condition in question is serious and life-threatening and results in a deterioration in the patient's quality of life. Highly sensitised patients awaiting a kidney transplant can spend their entire lives dependent on dialysis in the absence of a compatible donor, exposing them to a higher risk of morbidity and mortality than the general population and to a significant deterioration in their quality of life.
◗ The proprietary medicinal product IDEFIRIX (imlifidase) is a preventive treatment against transplant rejection.
◗ The efficacy/adverse effects ratio of imlifidase is high.
◗ There are currently no validated therapeutic alternatives in the treatment of highly sensitised adult kidney transplant patients with positive crossmatch against an available deceased donor (see section 05). However, in certain eligible patients, non-standardised desensitisation protocols using plasma exchange and/or medicinal products used off-label can be put in place.
◗ IDEFIRIX (imlifidase) is a first-line treatment in the desensitisation strategy for highly sensitised adult kidney transplant patients. In the absence of comparative data in patients eligible for these experimental desensitisation techniques, despite the low prevalence in the event of deceased donor transplant, the role of imlifidase compared to these techniques should be determined on the basis of the patient's profile and available efficacy and safety data.

Public health benefit

Considering:

- the seriousness of the disease,
- the partially met medical need for patients eligible for the experimental desensitisation techniques currently used and the unmet medical need for patients not eligible for these techniques,
- the partial response to the identified need given:
    - the expected additional impact on morbidity and mortality, although the available data is currently very limited,
    - despite the absence of demonstration of a benefit in terms of quality of life,
- the expected additional impact on the patient's care and/or life pathway, given the administration conditions (one to two injections within a maximum interval of 24 hours, with rapid crossmatch conversion from positive to negative enabling transplantation) compared to existing desensitisation protocols for a low proportion of patients who would be eligible, or compared to the absence of any alternative for the majority of patients, resulting in continuation of kidney dialysis,

IDEFIRIX (imlifidase) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of IDEFIRIX (imlifidase) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and at the MA dosages.

Clinical Added Value

Considering:

- efficacy data on pre-transplantation crossmatch conversion to negative (n=17/19) and on graft survival (n=16/18) in a six-month, phase II, open-label study (study 06) in highly sensitised patients not having responded to desensitisation treatment or not eligible for desensitisation treatment due to their anti-HLA antibody levels,
- the medical need to have access to effective and well-tolerated medicinal products, simplifying the care and life pathway of patients, in a context in which desensitisation protocols are rarely proposed in the event of deceased-donor transplants, given a moderate and transient efficacy and their complexity in terms of organisation and the long-term risk of infection they entail,
- the imlifidase administration conditions (one to two injections within a maximum interval of 24 hours), enabling rapid crossmatch conversion from positive to negative,

And despite:

- uncertainties with respect to the efficacy and safety of imlifidase in the MA population and long-term maintenance of graft survival beyond 6 months, in view of the clinical data from non-comparative studies conducted over a period of six months, on low numbers of patients (46 patients in total), having included a broader patient population than that targeted in the MA, with intermediate follow-up data after three years for a limited number of patients,
- the prolongation in cold ischaemia time in the event of a deceased donor, due to the time required for crossmatching after administration of imlifidase, which increases the risk of delayed graft function as a result of acute tubular necrosis, leading to lower graft survival.

The Committee considers that IDEFIRIX (imlifidase) provides a moderate clinical added value (CAV III) in the care pathway for the desensitisation treatment of highly sensitised adult kidney transplant patients with positive crossmatch against an available deceased donor and unlikely to be transplanted under the current available kidney allocation system, including prioritisation programmes for highly sensitised patients.