SUMMARY

Lisocabtagene maraleucel (Liso-cel)

BREYANZI 1.1-70x10^6 cells/mL / 1.1-70x10^6 cells/mL

dispersion for infusion

First assessment

Original French opinion adopted by the Transparency Committee on 20 September 2023

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- Large B-cell lymphomas, including DLBCL, HGBCL, PMBCL and FL3B are life-threatening aggressive non-Hodgkin's lymphomas.
- BREYANZI (lisocabtagene maraleucel) is a curative treatment.
- The efficacy/adverse effects ratio is high.
- There are therapeutic alternatives.
- BREYANZI (lisocabtagene maraleucel) is a second-line treatment for adult patients with diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma (HGBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B), who relapsed within 12 months from completion of, or are refractory to, first-line chemoimmunotherapy.

- **Public health benefit**

Considering:

- the seriousness of the disease and its incidence,
- the partially met medical need,
- the partial response to the identified need, due to:

- a demonstrated additional impact on morbidity of BREYANZI (lisocabtagene maraleucel) compared to a strategy including salvage chemotherapy, high-dose chemotherapy (intensification) then autologous HSCT, but for which the additional impact on mortality has not currently been demonstrated,
- the absence of any demonstrated impact on morbidity and mortality in patients not eligible for autologous haematopoietic stem cell transplantation,
- the lack of demonstrated impact on quality of life,
- the lack of evidence to support an absence of deterioration in the care and/or life pathway, considering, in particular, systematic hospitalisation for the first eight days following infusion and the need for patients to remain near the qualified healthcare facility for at least four weeks after infusion,
- the impact on the organisation of care considering the need for:
  - accreditation of hospitals based on precise criteria,
  - coordination between the various departments of centres authorised to treat patients with CAR-T cells (laboratories, internal pharmacy, clinical departments, etc.),

BREYANZI (lisocabtagene maraleucel) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of BREYANZI (lisocabtagene maraleucel) 1.1-70x10^6 cells/mL/1.1-70x10^6 cells/mL dispersion for infusion is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of BREYANZI (lisocabtagene maraleucel) 1.1-70x10^6 cells/mL/1.1-70x10^6 cells/mL dispersion for infusion 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:

- demonstration of the superiority of BREYANZI (lisocabtagene maraleucel) compared to a treatment sequence composed of salvage immunochemotherapy, potentially followed, in the event of a response, by high-dose chemotherapy (intensification) and autologous HSCT in a randomised phase 3 study (TRANSFORM study) in 184 adult patients with aggressive B-cell NHL, refractory or in relapse within 12 months following completion of first-line therapy and eligible for autologous HSCT, in terms of event-free survival (superiority of liso-cel in terms of EFS compared to the standard of care (HR=0.36; CI95% [0.24; 0.52]; p<0.0001)), complete response rate (higher in the liso-cel group than in the control group, 73.9% vs 43.5%; p<0.0001) and progression-free survival rate (HR=0.40; CI95% [0.26; 0.62]; p<0.0001);
- data from two non-comparative studies, having demonstrated overall response rates of 80.3% (CI95%: 68.2-89.4) and 63% (CI95%: 42.4; 80.6) in patients not eligible for a strategy including autologous HSCT;
- a safety profile marked primarily by haematological (neutropenia, thrombopenia, anaemia) and neurological toxicity (15 to 64% of patients depending on the studies), as well as a cytokine release syndrome (38 to 49% of patients depending on the studies);

and despite:

- the absence of a demonstrated benefit in terms of overall survival in the comparative phase 3 TRANSFORM study, but considering the non-negligible percentage of patients in the standard of care arm having received a CAR-T as third-line therapy following progression or an inadequate response;
- the non-comparative and purely descriptive nature of the studies conducted in patients not eligible for a strategy including autologous HSCT (TRANSCEND PILOT and TRANSCEND-WORLD) leading to uncertainties with respect to the efficacy results observed, but considering the lack of consensus concerning assessment of eligibility or otherwise for autologous HSCT, left to the decision of the physician;
- the small number of patients with the FL3B subtype (one patient in each of the three studies) given the fact that this rare form is treated in the same way as other large B-cell lymphomas;
- the absence of any formal conclusion that can be drawn based on the quality-of-life results;

the Committee deems that BREYANZI (lisocabtagene maraleucel) 1.1-70x10^6 cells/mL/1.1-70x10^6 cells/mL dispersion for infusion provides a moderate clinical added value (CAV III) in the current care pathway, which includes the relevant comparators cited in paragraph 5.2.