HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
15 JUNE 2022

The legally binding text is the original French opinion version

tixagevimab/cilgavimab
EVUSHELD 150 mg/150 mg solution for injection

First assessment

Key points

Favourable opinion for reimbursement **in the event of a susceptible SARS-CoV-2 strain**, for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg with immune deficiency related to a disease or treatments and demonstrating no or low response to a complete vaccination regimen in accordance with current guidelines OR not eligible for vaccination and at increased risk for severe COVID-19.

What therapeutic improvement?

Therapeutic improvement in the management of the disease, in the event of a SARS-CoV-2 strain susceptible to the treatment.

Role in the care pathway?

Currently, vaccination combined with protective measures are the main pillars in the management of COVID-19, in order to prevent infection with SARS-CoV-2 and the development of symptomatic COVID-19 that may potentially progress towards a severe form of the disease.

However, recent studies have shown that approximately 50% of immunocompromised individuals (depending on the type of immunosuppression) having received a complete vaccination regimen were seronegative after the third dose of vaccine. Furthermore, in view of the emergence of new variants of concern (which may be less susceptible to currently available vaccines), other preventive and curative antiviral treatments that can help reduce the risk of developing severe forms of the disease, hospitalisations and deaths, constitute an additional weapon to that of vaccination in order to effectively fight the pandemic, particularly in individuals demonstrating no or low response to vaccination.

Role of the medicinal product in the care pathway

Based on available data from the PROVENT clinical trial, having demonstrated:

- a beneficial effect in terms of an approximately 80% reduction in the incidence of virologically confirmed (positive nasopharyngeal RT-qPCR test) symptomatic SARS-CoV-2 infection, occurring after injection and prior to day 183 following injection of the investigational treatment;
- *in vitro* data suggesting a maintained activity of EVUSHELD (tixagevimab/cilgavimab) against Omicron subvariant BA.2 (currently the dominant subvariant in France, 98.6% of screened tests);

the Committee considers that EVUSHELD (tixagevimab/cilgavimab) could be a therapeutic option, providing that the SARS-CoV-2 strain is susceptible to the tixagevimab/cilgavimab combination, for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg with immune deficiency related to a disease or treatments and demonstrating no or low response to a complete vaccination regimen in accordance with current guidelines OR not eligible for vaccination and at increased risk for severe COVID-19.

Refer to the national guidelines in terms of the strategy for the use of prophylactic and curative treatments for COVID-19.

It should be noted that guidelines on the conditions for use of anti-COVID-19 treatments will soon be issued by the ANRS-MIE or the DGS (Ministry of Health).

The Summary of Product Characteristics (SPC) and the Risk Management Plan (RMP) must be complied with.

The use of this medicinal product in pregnant or breast-feeding women, or in women of childbearing potential not using contraception must comply with the SPC.

Special recommendations

The Committee highlights the fact that the use of anti-COVID-19 treatments does not dispense with the need for patients to comply with protective and physical distancing measures in the context of control of COVID-19 and that **EVUSHELD (tixagevimab/cilgavimab) is not intended to be used as a substitute for vaccination against SARS-CoV-2**.

The Committee endorses the requests of patient associations relative to the need to facilitate access to COVID-19 treatment in the non-hospital setting.

Due to the rapidly evolving epidemic context, the Committee would like to see regular updating of national guidelines in order to adapt the management strategy for COVID-19 based on data on the susceptibility of circulating variants to available treatments.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ SARS-CoV-2 is an acute viral disease that is potentially life-threatening, primarily in its severe form, following complications. It is a major public health problem of global concern due to its contagiousness, its severity and its impact on healthcare system organisation and, in particular, intensive care units.

◗ The proprietary medicinal product EVUSHELD (tixagevimab/cilgavimab) is a preventive medicinal product.

◗ The efficacy/adverse effects ratio of this proprietary medicinal product is high, subject to the susceptibility of the SARS-CoV-2 strain.

◗ There is a therapeutic alternative: RONAPREVE (casirivimab/imdevimab), subject to the susceptibility of the SARS-CoV-2 strain. However, in the Omicron variant context, there are no therapeutic alternatives due to a total loss of activity of RONAPREVE (casirivimab/imdevimab) against this variant.

◗ This is a first-line treatment for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg:

- with immune deficiency related to a disease or treatments and demonstrating no or low response[Erreur ! Signet non défini.] to a complete vaccination regimen in accordance with current guidelines;
- OR not eligible for vaccination and at increased risk for severe COVID-19.

Public health benefit

Considering:

- the severity, contagiousness and impact on the organisation of care, particularly in intensive care units, and the Public Health Emergency of International Concern (PHEIC);
- the major medical need to have access to effective, well-tolerated medicines in the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older:
  - with immune deficiency related to a disease or treatments and demonstrating no or low response-[Erreur ! Signet non défini.] to a complete vaccination regimen in accordance with current guidelines;
  - OR not eligible for vaccination and at increased risk for severe COVID-19;
- the fact that EVUSHELD (tixagevimab/cilgavimab) provides a partial response to the identified medical need due to a demonstrated additional impact on morbidity and mortality and on the care and life pathway of treated patients (reduction in the incidence of virologically confirmed symptomatic SARS-CoV-2 infection);
- the expected impact on the organisation of care (reduction in hospitalisations);

EVUSHELD (tixagevimab/cilgavimab) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of EVUSHELD (tixagevimab/cilgavimab) is substantial in the MA indication in the event of a SARS-CoV-2 strain susceptible to the treatment.

The Committee issues a favourable opinion for inclusion of EVUSHELD (tixagevimab/cilgavimab) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the marketing authorisation indication in the event of a SARS-CoV-2 strain susceptible to the treatment, at the recommended dosages, on condition that the national guidelines in terms of the strategy for the use of prophylactic treatments for COVID-19 are referred to.

- **Recommended reimbursement rate: 65%**

Clinical Added Value

Considering:

- the inadequately met need for the prevention of SARS-CoV-2 infections in patients demonstrating no or low response to a complete vaccination regimen in accordance with current guidelines and belonging to one of subgroups at very high risk of severe COVID-19, as defined by the ANRS-MIE, or not eligible for vaccination and at increased risk for severe COVID-19;
- the effect size of EVUSHELD (tixagevimab/cilgavimab) in terms of an approximately 80% reduction in the incidence of virologically confirmed (positive nasopharyngeal RT-qPCR test) symptomatic SARS-CoV-2 infection, occurring after injection and prior to day 183 following injection of the investigational treatment;
- limited data suggesting a favourable safety profile in clinical trials, provided the special warnings and precautions for use are complied with concerning the identified risks: hypersensitivity (including anaphylaxis), cardiovascular and/or thrombo-embolic events (in particular myocardial infarction), clinically significant coagulation disorders;
- the long half-life of EVUSHELD (tixagevimab/cilgavimab) enabling a long protection duration following the prophylactic administration of a single dose of the combination;

And despite:

- uncertainties concerning the transposability of the available data to clinical practice and the current epidemic context, due to the absence of clinical efficacy data relative to the Omicron variant (less virulent) and in patients at very high risk of progression to a severe form of the disease (immunosuppression, cancer, chronic kidney disease),

the Transparency Committee considers that, in the event of a susceptible SARS-CoV-2 strain, the proprietary medicinal product EVUSHELD (tixagevimab/cilgavimab) provides a moderate clinical added value (CAV III) in the care pathway for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg with immune deficiency related to a disease or treatments and demonstrating no or low response to a complete vaccination regimen in accordance with current guidelines OR not eligible for vaccination and at increased risk for severe COVID-19.