

**OPINION ON
MEDICINAL
PRODUCTS**

tixagevimab/cilgavimab
EVUSHELD 150 mg/150 mg,
solution for injection
New indication(s)

Adopted by the Transparency Committee on 9 November 2022

SUMMARY

The legally binding text is the original French opinion version

- COVID-19
- Sectors: Community and Hospital

Key points

Approval of reimbursement **subject to susceptibility of the SARS-CoV-2 strain to EVUSHELD (tixagevimab/cilgavimab) and where alternatives cannot be used due to contraindications** for the following indication: “treatment of COVID-19 for adults and adolescents (aged 12 years and over and weighing at least 40 kg), who do not require oxygen supplementation, and who are at an increased risk of progression to a severe form of COVID-19”. Indeed, despite the loss of activity on the Omicron sublineage BA.5, predominant in France at the time of the assessment, which will render its use very marginal or even useless, considering the unpredictability of the epidemic situation and the emergence of more susceptible variants, it is vital to retain access to as many treatment options, including the tixagevimab/cilgavimab association, as possible, even if they may not be deemed to be relevant at the time of assessment.

Therapeutic improvement?

Therapeutic improvement in the care pathway for treatment-susceptible strains of SARS-CoV-2 and where alternatives cannot be used due to contraindications.

Role in therapeutic strategy?

Given the current predominant circulation of the BA.5 sublineage in France (93% of screened tests), the early curative treatment strategy aimed at preventing progression to a severe form in at-risk patients is based on:

- **PAXLOVID (nirmatrelvir/ritonavir), as a first-line approach, regardless of the SARS-CoV-2 variant or sublineage causing the infection;**
- **In the event of contraindication:**
 - **VEKLURY (remdesivir), as an alternative to PAXLOVID (nirmatrelvir/ritonavir) and given the limited activity of EVUSHELD against the Omicron BA.4 and BA.5 sublineages;**
 - **EVUSHELD (tixagevimab/cilgavimab) for patients for whom PAXLOVID (nirmatrelvir/ritonavir) is strictly contraindicated and in cases of renal contraindication or failure access to VEKLURY (remdesivir)^{Erreur ! Signet non défini.} or once again in the context of infection with a documented subvariant for which EVUSHELD retains significant neutralising activity *in vitro*.**

Role of the medicinal product

The Committee deems that EVUSHELD (tixagevimab/cilgavimab) is a potential treatment option, **subject to susceptibility of the SARS-CoV-2 strain to EVUSHELD (tixagevimab/cilgavimab) and where alternatives cannot be used due to contraindications**, for the treatment of COVID-19 for adults and adolescents (aged 12 years and over and weighing at least 40 kg), who do not require oxygen supplementation, and who are at an increased risk of progression to a severe form of COVID-19.

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

The proprietary medicinal product EVUSHELD (tixagevimab/cilgavimab) must be administered at the earliest possible opportunity no later than 7 days following symptom onset (see SPC, “Posology and method of administration” section).

The summary of product characteristics (SPC) and the Risk Management Plan (RMP) must be adhered to.

For pregnant or breastfeeding women, or women of reproductive age not using contraception, this medicinal product must be used in accordance with the SPC.

Special recommendations

The Committee points out that use of anti-COVID-19 treatments does not exempt patients from adhering to control and social distancing measures within the framework of COVID-19 prevention, and that **EVUSHELD (tixagevimab/cilgavimab) is not intended to be used as a substitute for SARS-CoV-2 vaccination.**

The Committee relays the request from patient associations around the need to facilitate access to COVID-19 treatment in community settings.

Due to the rapidly evolving epidemiological context, the Committee would like to see regular updates of the national guidelines in order to adapt the COVID-19 care strategy according to data on the susceptibility of the variants in circulation to the treatments available.

Committee's conclusions

Actual Clinical Benefit

- SARS-CoV-2 disease is an acute viral disease, which is potentially life-threatening primarily in its severe form, after complications. It is a major global public health problem due to its transmissibility, severity, and impact on healthcare system organisation, in particular in relation to intensive care units.
- The proprietary medicinal product EVUSHELD (tixagevimab/cilgavimab) is a curative medicinal product.
- The efficacy/adverse effect ratio of this proprietary medicinal product is significant, subject to susceptibility of the SARS-CoV-2 strain and where alternatives cannot be used due to contraindications.
- Few alternative medications are available: PAXLOVID (nirmatrelvir/ritonavir), VEKLURY (remdesivir), RONAPREVE (casirivimab/imdevimab), and XEVUDY (sotrovimab) subject to SARS-CoV-2 strain susceptibility.
- It is a treatment option, **subject to susceptibility of the SARS-CoV-2 strain to the tixagevimab/cilgavimab association and where alternatives cannot be used due to contraindications**, for the treatment of COVID-19 for adults and adolescents (aged 12 years and over and weighing at least 40 kg), who do not require oxygen supplementation, and who are at an increased risk of progression to a severe form of COVID-19.

→ Public health benefit

Considering:

- the severity, transmissibility, impact on the delivery of care, in particular intensive care units, and the Public Health Emergency of International Concern (PHEIC),
- the major medical need for effective and well-tolerated medicinal products for the treatment of patients suffering from mild to moderate COVID-19 and at a high risk of progression to a severe form of COVID-19,
- that EVUSHELD (tixagevimab/cilgavimab) provides a partial response to the identified medical need on account of evidence of an additional impact on morbidity-mortality (reduction in COVID-19-related hospital admissions and deaths), and on the care and life pathway of treated patients (reduction in progression to a severe or critical form of COVID-19),
- an expected impact on the delivery of care (reduction of hospital admissions),

EVUSHELD (tixagevimab/cilgavimab) is likely to have an additional impact on public health subject to susceptibility of the SARS-CoV-2 strain.

Considering all of these elements, the Committee deems the actual clinical benefit of EVUSHELD (tixagevimab/cilgavimab) to be significant for the marketing authorisation indication in the case of treatment-susceptible SARS-CoV-2 strains, and where alternatives cannot be used due to contraindications.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the marketing authorisation indication and at the marketing authorisation dosages, subject to the national guidelines in terms of the strategy of the use of curative COVID-19 treatments.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- the unmet medical need among patients not requiring oxygen therapy due to COVID-19, and who are at a high risk of progression to a severe form of the disease in a context of limited clinical data to date with the various treatments available, an evolving epidemic context, monoclonal antibody susceptibility in respect of circulating variants and any future variants of SARS-CoV-2 in France, and problems accessing these treatments around the country;
- the effect size of EVUSHELD in terms of reducing progression to a severe form of COVID-19 or all-cause death on D29 by 50.5% among patients with symptoms ≤ 7 days before the first dose (TACKLE study); limited data suggesting a favourable safety profile in clinical studies, subject to adherence to warnings and precautions for use in respect of identified risks: hypersensitivity (including anaphylaxis), cardiovascular and/or thromboembolic events (especially myocardial infarction), clinically significant clotting disorders;

And despite:

- the lack of clinical data from seropositive or vaccinated subjects, and severely immunocompromised subjects;
- the uncertainties around the transposability of the clinical study findings to clinical practice and the current epidemic context, on account of the lack of clinical efficacy data on the Omicron variant (BA.5 sublineage currently predominant in France) for which the current *in vitro* data suggest a loss of neutralising activity which should render its use marginal or even useless in practice;
- the lack of comparative data between the different curative strategies available due to concomitant development;

the Transparency Committee deems that the proprietary medicinal product EVUSHELD (tixagevimab/cilgavimab) provides, **for susceptible SARS-CoV-2 strains and where alternatives cannot be used due to contraindications**, moderate clinical added value (**CAV III**) for the therapeutic care strategy for adults and adolescents (aged 12 years and over and weighing at least 40 kg), who do not require oxygen supplementation, and who are at an increased risk of progression to a severe form of COVID-19.

EVUSHELD 150 mg/150 mg, 9 November 2022
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