OPINION ON MEDICINAL PRODUCTS

remdesivir

VEKLURY 100 mg,

powder for solution for dilution for infusion

New indication(s)

Adopted by the Transparency Committee on 4 January 2023

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement subject to susceptibility of the SARS-CoV-2 strain to remdesivir, in recommended cohorts and for patients for whom PAXLOVID (nirmatrelvir/ritonavir) treatment is not optimal particularly on account of contraindications or resistance, in the following indication: "*treatment of COVID-19 disease for adults and paediatric patients (weighing at least 40 kg), who do not require oxygen therapy and who are at an increased risk of progression to a severe form of COVID-19*".

Therapeutic improvement?

No therapeutic improvement in the care pathway.

Role in therapeutic strategy?

Given the current predominant circulation of Omicron BA.5 and its sublineages, in particular BQ.1.1 (94% of screened tests) in France resulting in updating of the national guidelines, the early curative treatment strategy aimed at preventing progression to a severe form in at-risk patients is based on (see DGS-Urgent No. 2022-86 of 22/12/2022):

- **PAXLOVID (nirmatelvir/ritonavir), as a first-line approach, regardless of the SARS-CoV-2 variant or sublineage causing the infection, particularly from 65 years of age regardless of vaccination status and any comorbidities;**
- **in cases of contraindication to PAXLOVID (nirmatrelvir/ritonavir) particularly associated with drug interactions AND in the absence of any renal contraindication, VEKLURY (remdesivir), as a second-line approach on account of continued in vitro efficacy regardless of the variant.**

Note that monoclonal antibodies are no longer recommended in the current epidemic context. However, in its opinion of 19 December 2022, COVARS stated that sotrovimab (XEVUDY) may be discussed in cases of contraindication to PAXLOVID (nirmatrelvir/ritonavir).

Role of the medicinal product

Despite the many clinical uncertainties around the efficacy of VEKLURY (remdesivir) in a context of very rapidly evolving therapeutic strategies, the role of VEKLURY (remdesivir) has been defined with regard to its potential utility for certain patients at a very high risk of progression to a severe form of COVID-19.

The Committee deems that VEKLURY (remdesivir) could represent a therapeutic option in the treatment of adult and paediatric patients (weighing at least 40 kg) who do not require oxygen therapy and who are at an increased risk of progression to a severe form of COVID-19 **only in the case of SARS-CoV-2 strains susceptible to remdesivir, in recommended cohorts and for patients for whom PAXLOVID (nirmatrelvir/ritonavir) treatment is not optimal particularly on account of contraindications or resistance.**

Additional data are needed and expected to establish, with a superior level of evidence. the efficacy, adverse effects and risks of VEKLURY (remdesivir) in the marketing authorisation indication.

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

The Committee points out that limited data are available in kidney and liver failure patients, and in pregnant women.

Use of VEKLURY (remdesivir) must be accompanied by close clinical monitoring considering the possible adverse reactions at the time of injection (particularly arterial hypotension) and kidney function and liver function follow-up (information lacking in the context of the RMP).

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 **VEKLURY (remdesivir) 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

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 VEKLURY (remdesivir) is a curative antiviral treatment.
- The efficacy/adverse effect ratio of this proprietary medicinal product is poorly defined to date. However, the limited data (PINETREE study) suggest a low clinical benefit, in adult and paediatric patients (weighing at least 40 kg) who do not require oxygen therapy and who are at an increased of progression to a severe form of COVID-19, subject to susceptibility of the SARS-CoV-2 strain.
- Few alternative medications are available, particularly the antiviral proprietary medicinal product PAXLOVID (nirmatrelvir/ritonavir), subject to susceptibility of the SARS-CoV-2 strain.
- VEKLURY (remdesivir) could represent a therapeutic option in the treatment of adult and paediatric patients (weighing at least 40 kg) who do not require oxygen therapy and who are at an increased risk of progression to a severe form of COVID-19 only in the case of SARS-CoV-2 strains susceptible to remdesivir, in recommended cohorts and where PAXLOVID (nirmatrelvir/ritonavir) cannot be used on account of contraindications or resistance.

➔ 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,
- the limited clinical data in methodological (early discontinuation of inclusions) and structural (inclusion of unvaccinated and mildly immunocompromised patients) terms suggesting an impact of VEKLURY (remdesivir) on reducing morbidity-mortality and on delivery of care (reduction of risk of COVID-19-related hospitalisation or all-cause deaths at D28),
- the lack of robust data capable of supporting an impact of VEKLURY (remdesivir) on reducing nasopharyngeal viral load and on improving quality of life of COVID-19 patients,

in view of the data currently available, VEKLURY (remdesivir) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of VEKLURY (remdesivir) is low subject to susceptibility of the SARS-CoV-2 strain to remdesivir, in recommended cohorts and where patients PAXLOVID (nirmatrelvir/ritonavir) treatment is not optimal particularly on account of contraindications or resistance, in the marketing authorisation indication.

This assessment shows the continuing significant uncertainty around the efficacy and safety of VEKLURY (remdesivir) in a context of very rapidly evolving therapeutic strategies and the public health need.

The Committee approves inclusion in the list of proprietary medicinal products approved for community use in the indication and at the dosages of the marketing authorisation, in recommended cohorts and for patients for whom PAXLOVID (nirmatrelvir/ritonavir) treatment is not optimal particularly on account of contraindications or resistance.

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 VEKLURY (remdesivir) in terms of relative reduction of the risk of COVID-19-related hospitalisations or all-cause deaths at D28 of 87% (primary outcome measure; PINETREE study);
- the acceptable safety profile;

But considering:

- evidence of efficacy only on the risk of hospitalisation with few events in the placebo group (5.4% hospitalisations and 0% deaths) indicating a low-risk population,
- the numerous methodological limitations (including a risk of overestimating the treatment effect associated with the premature discontinuation of patient inclusions; 562 patients included of the 1264 patients envisaged),
- uncertainties around the transposability of the findings of the clinical study (unvaccinated and slightly at-risk patients) to clinical practice in the current epidemic context, on account of the lack of clinical efficacy data on the Omicron variant;
- the lack of evidence of an impact on symptom improvement and patient deterioration (need for oxygen therapy or admission to intensive care unit or death);
- the lack of evidence of an impact to date on reducing the nasopharyngeal viral load casting doubt on the proof of concept,

the Committee deems that VEKLURY (remdesivir) provides no clinical added value (**CAV V**) in the treatment of adult and paediatric patients (weighing at least 40 kg) who do not require oxygen therapy and who are at an increased of progression to a severe form of COVID-19, subject to susceptibility of the SARS-CoV-2 strain to remdesivir, in recommended cohorts and for patients for whom PAXLOVID (nirmatrelvir/ritonavir) treatment is not optimal particularly on account of contraindications or resistance.