HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
6 APRIL 2022

The legally binding text is the original French opinion version

PF-07321332 / ritonavir
PAXLOVID 150 mg/100 mg film-coated tablets

First assessment

Key points

Favourable opinion for reimbursement in the treatment of coronavirus disease 2019 (COVID-19) in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID-19.

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

What therapeutic improvement?

Therapeutic improvement in the management of the disease.

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 sensitive 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 EPIC-HR clinical study, having demonstrated:

- a beneficial effect on reduction of the risk of progression to a severe form of COVID-19 (COVID-19 related hospitalisation or death from any cause on D28) of 87.8% in patients with onset of symptoms ≤ 5 days before the first dose;
- virological data suggesting a significant reduction in viral load on D5 compared to placebo (around 0.7 $\log_{10}$ copies/mL);
- *in vitro* data suggesting maintenance of the activity of PAXLOVID (PF-07321332/ritonavir) against circulating variants of concern, in particular the Omicron variant;

the Committee considers that PAXLOVID (PF-07321332/ritonavir) may be a therapeutic option in the curative treatment of COVID-19 in adults who do not require supplemental oxygen and who are at high risk for progression to severe COVID-19, as defined by the national guidelines.

Early administration after the onset of symptoms (within 5 days following the onset of symptoms) is an important point.

The Summary of Product Characteristics (SPC) and the Risk Management Plan (RMP) must be complied with due to the numerous drug interactions related to ritonavir, contraindicating its use with numerous medicinal products.

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 PAXLOVID (PF-07321332/ritonavir) 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 sensitivity of circulating variants to available treatments.

Given the major risk of drug interactions related to ritonavir in polymedicated patients, particularly those with risk factors associated with a very high risk of progression to a severe form of the disease (immunosuppression, cancer, chronic kidney disease), the Committee would like prescribers to have access to a prescription aid document or device to facilitate the management of drug interactions.

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 PAXLOVID (PF-07321332/ritonavir) is a curative medicinal product.

◗ The efficacy/adverse effects ratio of this proprietary medicinal product is high, subject to the sensitivity of the SARS-CoV-2 strain and compliance with the special warnings and precautions due to the numerous drug interactions.

◗ There are few therapeutic alternatives: EVUSHELD (tixagevimab/cilgavimab), RONAPREVE (casirivimab/imdevimab), VEKLURY (remdesivir) and XEVUDY (sotrovimab), subject to the sensitivity of the SARS-CoV-2 strain.

◗ This is a first-line treatment for coronavirus disease 2019 (COVID-19) in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID-19.

Public health impact

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 and well-tolerated drugs in the treatment of patients with mild to moderate COVID-19 at high risk for progression to severe COVID-19,
- the fact that PAXLOVID (PF-07321332/ritonavir) 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 progression to severe or critical COVID-19),
- the expected impact on the organisation of care (reduction in hospitalisations),

PAXLOVID (PF-07321332/ritonavir) is likely to have an additional impact on public health, subject to the sensitivity of the SARS-CoV-2 strain.

Considering all these elements, the Committee deems that the clinical benefit of PAXLOVID (PF-07321332/ritonavir) is substantial in the MA indication in the event of a SARS-CoV-2 strain sensitive to the treatment.

The Committee issues a favourable opinion for inclusion of PAXLOVID (PF-07321332/ritonavir) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the marketing authorisation indication and dosages, on condition that the national guidelines in terms of the strategy for the use of curative treatments for COVID-19 are referred to.

◗ **Recommended reimbursement rate: 100%**

Clinical Added Value

Considering:

- the unmet medical need in adult patients with mild to moderate COVID-19 who do not require supplemental oxygen and who are at risk for progression to severe COVID-19;
- the effect size of PAXLOVID (PF-07321332/ritonavir) in terms of a reduction of the risk of progression to a severe form of COVID-19 (COVID-19 related hospitalisation or death from any cause on D28) of 87.8% in patients with onset of symptoms ≤ 5 days before the first dose;
- virological data suggesting a significant reduction in viral load on D5 compared to placebo (around 0.7 $\log_{10}$ copies/mL);
- limited data suggesting a favourable safety profile on condition that the warnings and precautions for use are complied with;
- the ease of use of the medicinal product due to its film-coated tablet form (oral form) mean that it can be used in the ambulatory setting;

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 numerous drug interactions with ritonavir, limiting its use in polymedicated patients,
  - the use of PAXLOVID (PF-07321332/ritonavir) as monotherapy, which could potentially lead to a risk of selection of resistant variants, especially in patients with prolonged viral excretion (immunocompromised);

the Transparency Committee considers that the proprietary medicinal product PAXLOVID (PF-07321332/ritonavir) provides a moderate clinical added value (CAV III) in the treatment of coronavirus disease 2019 (COVID-19) in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID-19.