HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 MARCH 2022

The legally binding text is the original French opinion version

anakinra
KINERET 100 mg/ 0.67 mL solution for injection in pre-filled syringe

New indication

Key points

Unfavourable opinion for reimbursement for the treatment of coronavirus disease 2019 (COVID-19) in adult patients with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) who are at risk of progressing to severe respiratory failure determined by plasma concentration of soluble urokinase plasminogen activator receptor (suPAR) ≥ 6 ng/mL.

Role in the care pathway?

The management of COVID-19 patient is detailed in the French High Council for Public Health (HCSP) report of 28 January 2021 and is based on supportive and preventive treatments:

- Appropriate oxygen therapy,
- Analgesics and antipyretics,
- Prevention of the thrombotic risk,
- Antibacterial antibiotics in the event of arguments in favour of co-infection.

Corticosteroid therapy is an integral component of the standard of care according to national (HCSP) and international (WHO) guidelines.

According to its report of 17 June 2021 concerning the use of IL1 and IL6 receptor antagonists, the HCSP recommends the use of tocilizumab (anti-IL6), in medical units in patients requiring high-flow supplemental oxygen and with a marked inflammatory status (CRP ≥ 75 mg/L) and in the absence of improvement after 48 hours of standard of care therapy including dexamethasone (or an equivalent corticosteroid). However, in critical care units, the HCSP does not recommend the use of tocilizumab in patients requiring invasive mechanical ventilation.

As regards sarilumab (anti-IL6) and anakinra (anti-IL1), the HCSP does not recommend their use irrespective of the situation.

Role of the medicinal product in the care pathway

Based on available data from the SAVE-MORE study, and considering:

- **the modest clinical impact on the improvement of clinical status at 28 days** (assessed using the 11-point WHO scale), **of uncertain scope**, observed in adult patients with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) who are at risk of progressing to severe respiratory failure determined by a suPAR test ≥ 6 ng/mL,
- **the absence of robust data** to date in terms of **morbidity and mortality** (reduction of progression to invasive mechanical ventilation or death),
- **the modest impact on the organisation of care and the care and life pathway** of treated patients (improvement of 1 day for the reduction in the duration of hospitalisation or 4 days for the duration of stay in the ICU),
- **uncertainties concerning the transposability** of the data **to current French practice** in the context of the predominant circulation of the less virulent Omicron variant and the absence of data in immunocompromised patients (a population at high risk of severe COVID-19, excluded from the SAVE-MORE study) for whom the risk of infection not related to COVID-19 could be increased by the use of this immunosuppressive treatment,
- **the non-use in routine practice in France of the suPAR test** to identify patients at risk of progressing to serious forms and who would be eligible for this treatment,
- **the existence of therapeutic alternatives**, in particular tocilizumab in combination with corticosteroid therapy, with a better level of evidence in terms of demonstration of the reduction in mortality and of progression to invasive mechanical ventilation or death (RECOVERY study and WHO meta-analysis).

The Transparency Committee considers that, on the basis of currently available data, KINERET (anakinra) has no role in the care pathway for the management of coronavirus disease 2019 (COVID-19).

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 KINERET (anakinra) is a curative medicinal product.

◗ Although the available data suggested a modest improvement in the patient's clinical status at 28 days based on the WHO Clinical Progression ordinal Scale (primary endpoint of debatable clinical relevance); the Committee considers that the efficacy/adverse effects ratio of KINERET (anakinra) has not currently been adequately established, in the absence of robust data for the reduction in mortality and of progression to invasive mechanical ventilation or death (exploratory analysis in the SAVE-MORE study), which are endpoints of major interest in this clinical context.

◗ There are few therapeutic alternatives (see section 05 clinically relevant comparators), in particular tocilizumab in combination with corticosteroid therapy, with a better level of evidence in terms of demonstration of the reduction in overall mortality and of progression to invasive mechanical ventilation or death in patients not intubated at the time of inclusion (RECOVERY study and WHO meta-analysis).

◗ KINERET (anakinra) has no role in the care pathway for the management of COVID 19 in the absence of robust data and considering the available alternatives, in particular tocilizumab in combination with corticosteroid therapy in the indication considered.

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, well-tolerated medicines in the treatment of severe and critical COVID-19 due to the absence of any available curative treatment,
- the modest clinical impact on the improvement of clinical status at 28 days (assessed using the 11-point WHO scale), of uncertain scope,
- the absence of robust data to date in terms of morbidity and mortality (reduction of progression to invasive mechanical ventilation or death),
- the modest impact on the organisation of care and the care and life pathway of treated patients (improvement of 1 day for the reduction in the duration of hospitalisation or 4 days for the duration of stay in the ICU),
- uncertainties concerning the transposability of the data to current French practice in the context of the predominant circulation of the less virulent Omicron variant and the absence of data in immunocompromised patients (a population at high risk of severe COVID-19, excluded from the SAVE-MORE study) for whom the risk of infection not related to COVID-19 could be increased by the use of an immunosuppressive treatment,
- the non-use in routine practice in France of the suPAR test to identify patients eligible for this treatment,

KINERET (anakinra) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of KINERET (anakinra) is insufficient to justify public funding cover in the MA indication in view of the available alternatives.

The Committee issues an unfavourable opinion for inclusion of KINERET (anakinra) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.