INESSS
LE SAVOIR PREND FORME

DECEMBER 2022

KamRAB™ (human rabies immunoglobulin) – Passive and transient postexposure prophylaxis of rabies infection

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Québec

SUMMARY

KamRAB™ (human rabies immunoglobulin) – Passive and transient postexposure prophylaxis of rabies infection

Mandate

At the request of the manufacturer, Kamada Ltd., the Institut national d'excellence en santé et en services sociaux (INESSS) evaluated KamRAB™, a human rabies immunoglobulin (HRIG). This product is indicated" for *passive, transient postexposure prophylaxis (PEP) of rabies infection, when given immediately after contact with a rabid or possibly rabid animal. KamRAB should be administered concurrently with a full course of rabies vaccine*".

Evaluation process

Data from the scientific literature and those provided by the manufacturer were reviewed to document the efficacy, safety and cost-effectiveness of KamRAB™. In addition, experiential and contextual data from expert consultations were mobilized and integrated. Lastly, INESSS performed a cost-effectiveness and budget impact analysis.

Populational dimension

Rabies is an infectious disease caused by a virus transmitted from animals to humans. Although the onset of symptoms ends in death in most cases, only 12 deaths have been reported in Quebec since 1924.

PEP constitutes the standard of care for reducing the risk of infection by the rabies virus in individuals exposed to an infected or possibly infected animal. PEP includes a full vaccination course and the administration of HRIG to reduce the risk of infection until the vaccine takes full effect. In Québec, a clinical algorithm is used to facilitate patient management and guide clinicians in their decision-making. The algorithm indicates whether the exposure to the virus is significant and whether PEP is recommended, based mainly on the type of animal and the risk associated with the geographical area.

Currently, two vaccines and at least one HRIG (HyperRAB™) are available for initiating PEP in patients exposed to the rabies virus. HyperRAB™ is on the *Liste des produits du système du sang du Québec.* Another HRIG, Imogam™, is not used clinically but is available in the event of a supply problem. Apart from the risk of HRIG shortage, which is low, the health need of individuals exposed or possibly exposed to the rabies virus is adequately met.

Clinical dimension

The main efficacy and safety data on the HRIG KamRAB™ come from the phase II/III, randomized, double-blind, comparative, non-inferiority, pivotal study with individuals with no exposure to the rabies virus. This study is considered to be of good methodological quality. The results of a phase IV, single-arm observational study in a rabies-exposed pediatric population were evaluated as well.

Efficacy

- The results of the pivotal study show that the PEP protocol including the HRIG KamRAB™ is non-inferior to that using the HRIG HyperRAB™ in inducing protective humoural immunity against the rabies virus.
- The pharmacokinetic results and the absence of infection reported in the phase IV study support the conclusion of non-inferiority.

Safety

- The safety profile of KamRAB™ is considered satisfactory and similar to that of the comparator HyperRAB™.
- The results of the phase IV study show that the safety profile of the HRIG KamRAB™ in children under 16 years of age is comparable to that observed in adults.

Expert perspective

- In the experts' opinion, the two studies selected are adequate for evaluating the non-inferiority of the HRIG KamRAB™ as part of PEP.
- They feel that the reported efficacy and safety results for KamRAB™ are similar to those for the comparator HyperRAB™.

Organizational dimension

Expert perspective

- With the products currently available in Québec, listing and distributing KamRAB™ would not have an impact on the quality of care and services provided to individuals exposed to the rabies virus.
- According to the experts consulted, adding KamRAB™ to the *Liste des produits du système du sang du Québec* could alleviate potential HRIG shortages.

Economic dimension

Cost-effectiveness analysis

- At the price submitted, KamRAB™ costs almost twice as much as its comparator, HyperRAB™. On the basis of efficacy and safety considered non-inferior to those of its comparator, KamRAB™ is not considered cost-effective.

Budget impact analysis

- If KamRAB™ wins the Héma-Québec call for tenders, its inclusion on the *Liste des produits du système du sang du Québec* could either have no budget impact or result in savings for the healthcare system. This will depend on which product wins the call for tenders.

Deliberation concerning therapeutic value

The members of the Comité scientifique de l'évaluation des médicaments aux fins d'inscription (CSEMI) are of the unanimous opinion that the therapeutic value of KamRAB™ is recognized for the passive, transient postexposure prophylaxis of rabies when administered immediately after contact with a rabid or possibly rabid animal.

Reasons for the unanimous position

- The members are of the opinion that the results of the pivotal study are sufficient for recognizing the non-inferiority of KamRAB™ relative to the HRIG currently distributed in Québec, HyperRAB™. The conclusion of non-inferiority applies to the use of KamRAB™ as part of postexposure prophylaxis including a full rabies vaccination course.

- The members recognize that KamRAB™ and HyperRAB™ share similar adverse effects profiles. However, some members questioned the equivalence of their safety profiles due to the higher frequency of injection site pain with KamRAB™.

- The members recognize that the results of the phase IV study show that the safety profile of KamRAB™ observed in the pediatric population was comparable to that observed in adults, which, they feel, supports the use of this HRIG in children and adolescents.

- The members are of the opinion that the HRIG KamRAB™ constitutes a therapeutic alternative to the other two HRIGs listed that would partially address the health need for individuals exposed or possibly exposed to the rabies virus, which is considered very small.

Deliberation concerning all the aspects

The members of the Comité scientifique de l'évaluation des médicaments aux fins d'inscription (CSEMI) unanimously agree that the HRIG KamRAB™ should be added to the *Liste des produits du système du sang du Québec* for concurrent use with vaccination for the passive, transient postexposure prophylaxis of rabies, when administered immediately after contact with a rabid or possibly rabid animal.

Reasons for the unanimous position

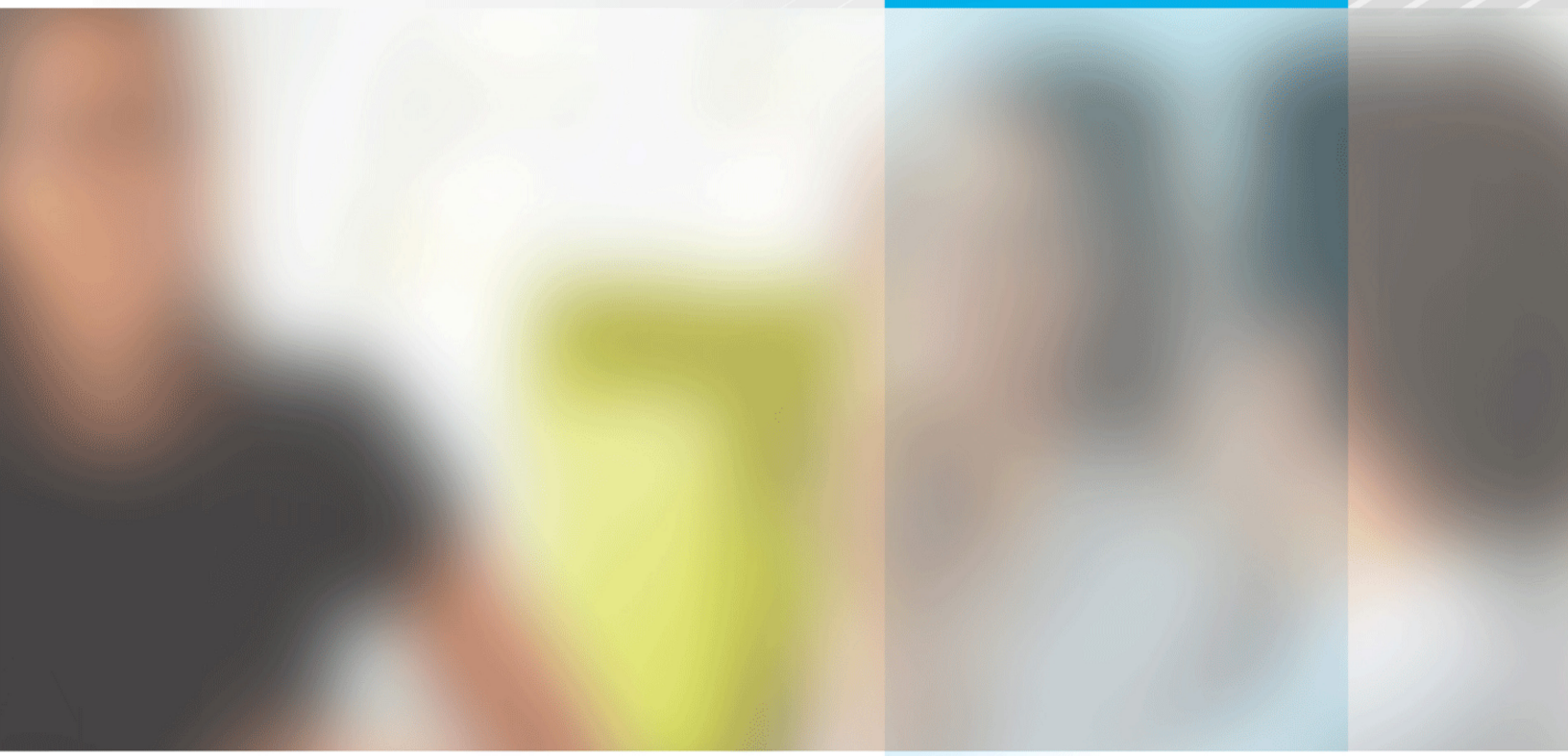
- The members recognize the non-inferior therapeutic value of the HRIG KamRAB™ relative to HyperRAB™ when used concurrently with vaccination in the context of rabies PEP.
- All the dimensions considered, the members feel that KamRAB™ constitutes a therapeutic alternative with a non-incremental value relative to the other currently available HRIGs.
- The members believe that adding KamRAB™ to the *Liste des produits du système du sang du Québec* could address potential HRIG shortages, although they acknowledge that the risk is low.
- The members are of the opinion that, in a call-for-tenders context, adding KamRAB™ to the *Liste des produits du système du sang du Québec* could generate savings for the healthcare system.

INESSS's recommendation regarding KamRAB™

In light of the available data, INESSS recommends that the HRIG KamRAB™ be added to the *Liste des produits du système du sang du Québec* for concurrent use with vaccination for the passive, transient postexposure prophylaxis of rabies in individuals exposed or possibly exposed to the virus.

Note concerning the recommendation

From a distributive justice perspective, coverage of KamRAB™ for the requested indication would be a responsible, fair and equitable decision, provided the cost of using it does not exceed the cost of the other HRIGs in the next call for tenders.



Siège social

2535, boulevard Laurier, 5e étage
Québec (Québec) G1V 4M3
418 643-1339

Bureau de Montréal

2021, avenue Union, 12e étage, bureau 1200
Montréal (Québec) H3A 2S9
514 873-2563
inesss.qc.ca

Institut national d'excellence en santé et en services sociaux
Québec