INESSS
LE SAVOIR PREND FORME

JUNE 2022

Evaluation of Fibryga™ (human fibrinogen concentrate) – Acquired fibrinogen deficiency

English summary

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

Québec

SUMMARY

Evaluation of Fibryga™ (human fibrinogen concentrate) – Acquired fibrinogen deficiency

Mandate

At the request of the manufacturer, Octapharma Canada Inc., the Institut national d'excellence en santé et en services sociaux (INESSS) evaluated Fibryga™, a human fibrinogen concentrate. This product is indicated "for the treatment of acute bleeding episodes and perioperative prophylaxis in adult and pediatric patients with congenital afibrinogenemia and hypofibrinogenemia" and "as a complementary therapy during the management of uncontrolled severe bleeding in patients with acquired fibrinogen deficiency in the course of surgical interventions". The present evaluation concerns the indication involving acquired fibrinogen deficiency.

Evaluation process

Data from the scientific literature and those provided by the manufacturer were reviewed to document the efficacy, safety and cost-effectiveness of the human fibrinogen concentrate Fibryga™. Contextual and experiential data from the expert consultations are also presented. Lastly, INESSS performed a cost-effectiveness and budget impact analysis.

Sociocultural and populational dimensions

Acquired fibrinogen deficiency, also known as acquired hypofibrinogenemia, is usually caused by the consumptionof coagulation factors following major bleeding. Acquired hypofibrinogenemia can occur unpredictably in adults and children during surgical interventions, major trauma, during the postpartum period, and in certain diseases.

Cryoprecipitate is currently used to compensate for fibrinogen deficiency. It is produced by Héma-Québec by freezing and thawing plasma and contains mainly fibrinogen and other coagulation factors.

The need regarding the treatment of acquired hypofibrinogenemia in the surgical context is limited. However, therapeutic options that allow faster fibrinogen administration without the risk of transmitting infectious agents could offer a certain advantage over the current situation.

Clinical dimension

Efficacy

- The main efficacy and safety data on the treatment of acquired hypofibrinogenemia in the surgical context come from the Canadian study FIBRES, considered to be of good methodological quality, which compared fibrinogen concentrate and cryoprecipitate in cardiac surgery with cardiopulmonary bypass. The results showed that a dose of 4 g of fibrinogen concentrate is noninferior to 10 units of cryoprecipitate for the management of perioperative bleeding in cardiac surgery with extracorporeal circulation.
- A second study, considered to be of low methodological quality, comparing fibrinogen concentrate to cryoprecipitate in cytoreductive surgery for pseudomyxoma peritonei was included. The results of this study suggest that fibrinogen concentrate is noninferior to cryoprecipitate in the management of perioperative bleeding during cytoreductive surgery for pseudomyxoma peritonei. These results support those of the FIBRES study.

Safety

- The safety profile of fibrinogen concentrate is considered acceptable and comparable to that of cryoprecipitate.
- However, the use of cryoprecipitate is still associated with the rare risk of transfusion reactions or its contamination with an emerging pathogen. These risks are considered very low by the experts consulted and do not call into question the use of cryoprecipitate in Québec.

Expert perspective

- The experts note that the FIBRES study's conclusion is that a dose of 4 g of fibrinogen concentrate is noninferior to 10 units of cryoprecipitate in the context of cardiac surgery with extracorporeal circulation. However, these data do not establish that these doses are the minimum quantities needed to treat acquired hypofibrinogenemia.
- The experts consulted consider Québec's blood system to be very safe. The risks of transmission of infectious agents and of transfusion reactions do exist but are extremely rare.
- According to the experts, the faster administration of fibrinogen concentrate by 0.40 h compared to cryoprecipitate in the FORMA-05 study is of the order of what is expected when fibrinogen concentrates are prepared in the operating room compared to those ordered and prepared at the blood bank.

Organizational dimension

- Fibrinogen concentrates could reduce operating room administration times in the event of acquired hypofibrinogenemia if they are distributed in a decentralized manner, if the operating room is adequately equipped, and if the staff is adequately trained.

Economic dimension

Cost-effectiveness analysis

- At the price submitted by the manufacturer, Fibryga™ is a more cost-effective treatment option than the cryoprecipitate currently used in Québec for the treatment of acquired fibrinogen deficiency.

Budget impact analysis

- At the price submitted by the manufacturer, distributing Fibryga™ for the management of acquired hypofibrinogenemia could result in an estimated reduction of $7.4 million in expenditures over the next 3 years.

Deliberation regarding therapeutic value
The members of the Comité scientifique de l'évaluation des médicaments aux fins d'inscription (CSEMI) are of the unanimously opinion that the therapeutic value of the fibrinogen concentrate Fibryga™ is recognized when used as complementary therapy during the management of severe uncontrolled bleeding during surgical interventions in patients with acquired fibrinogen deficiency. **Reasons for the unanimous position** ▪ The members feel that the results of the Canadian study FIBRES are sufficient to recognize the noninferiority of fibrinogen concentrate to cryoprecipitate in the management of bleeding related to acquired hypofibrinogenemia in the context of cardiac surgery with extracorporeal circulation. ▪ The results of the FORMA-05 study support the use of fibrinogen concentrate during surgery other than cardiac surgery with extracorporeal circulation. ▪ The members recognize that fibrinogen concentrate and cryoprecipitate have a similar adverse effect profile. They also feel that the risks of transfusion related reactions and transmission of unknown infectious agents associated with cryoprecipitate are very low. ▪ Fibrinogen concentrate represents an alternative therapeutic option to cryoprecipitate that would address, in part, the health need associated with the management of acquired hypofibrinogenemia in a surgical context, which is considered small. ▪ According to the committee members, the conclusions regarding the therapeutic value of fibrinogen concentrate also apply to the medical conditions in which acquired hypofibrinogenemia is clearly demonstrated.

Deliberation regarding all the criteria

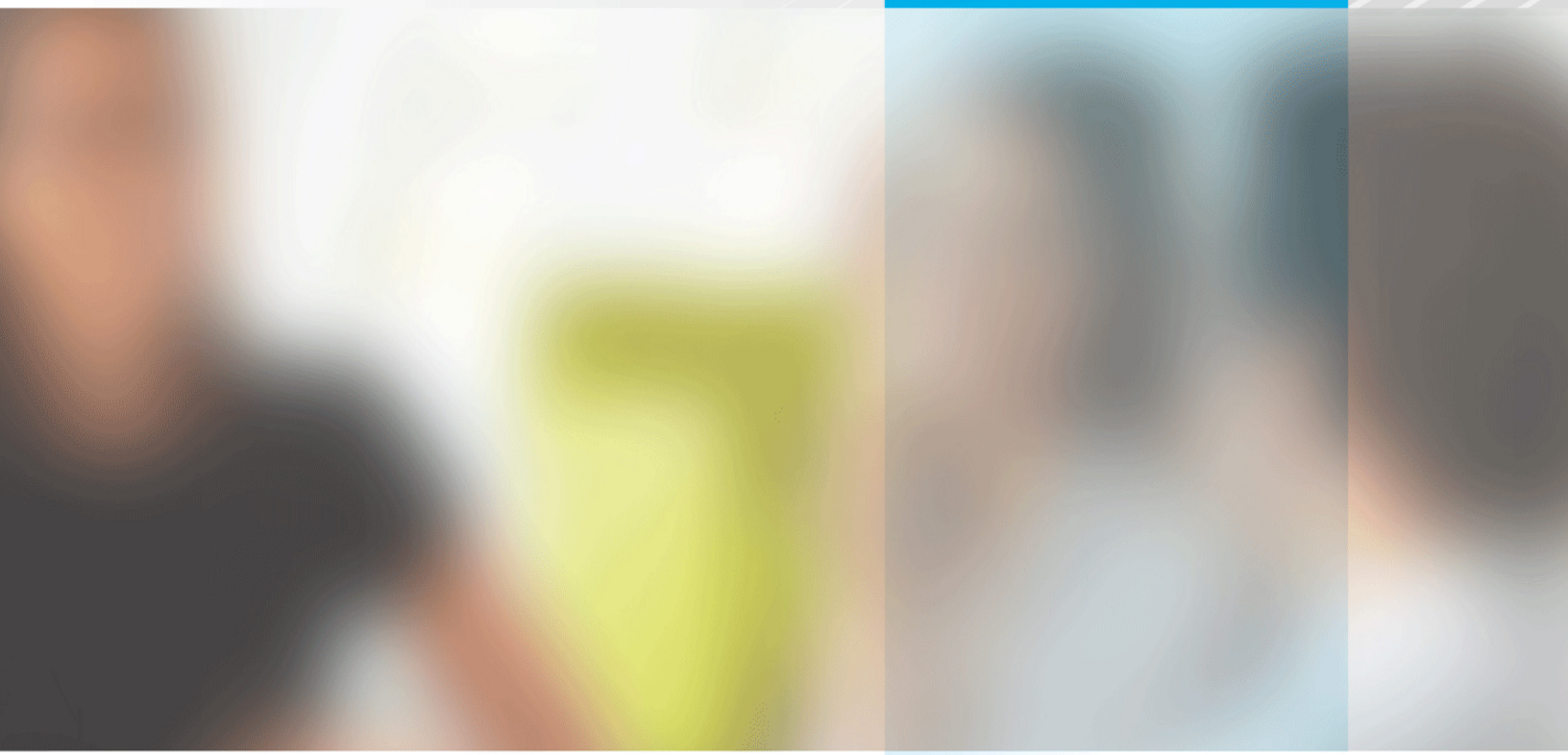
The members of the Comité scientifique de l'évaluation des médicaments aux fins d'inscription (CSEMI) are of the unanimously opinion that the fibrinogen concentrate Fibryga™ should be added to the *Liste des produits du système du sang du Québec* as complementary therapy during the management of severe uncontrolled bleeding during surgical interventions in patients with acquired fibrinogen deficiency.

Reasons for the unanimous position

- The members recognize the noninferior therapeutic value of fibrinogen concentrate relative to cryoprecipitate for the management of perioperative bleeding in patients with acquired hypofibrinogenemia.
- At the price submitted by the manufacturer, Fibryga™ is a more cost-effective treatment option than the cryoprecipitate currently distributed in Québec.
- The members note that the use of cryoprecipitate is associated with wastage. They stated that blood is a precious and limited resource that should be used judiciously by the health-care system. Any reduction in blood product wastage should therefore be valued.
- Distributing Fibryga™ for the management of acquired hypofibrinogenemia would result in an estimated $7.4 million in cost savings in the health-care facility budget over the next 3 years.
- The members believe that fibrinogen concentrate has the potential to reduce administration times in surgical context if it is prepared in the operating room instead of the blood bank. However, they add that the impact of faster administration of fibrinogen concentrate has not been investigated.

INESSS's recommendation concerning Fibryga™

In light of the available data, INESSS recommends that the fibrinogen concentrate Fibryga™ be added to the *Liste des produits du système du sang du Québec* as complementary therapy during the management of severe uncontrolled bleeding during surgical interventions in patients with acquired fibrinogen deficiency.



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