

May 13, 2020

Sylvie Bouchard
Direction de l'évaluation des médicaments et des technologies à des fins de remboursement
INESSS
2535, boulevard Laurier, 5e étage Québec
G1V 4M3

Dear Mme Bouchard,

On behalf of Quebeckers and all Canadians living with acquired thrombotic thrombocytopenic purpura (aTTP), Answering TTP Foundation is writing to express our profound shock and dismay at the INESSS' "Do not list" recommendation for caplacizumab (Cabliivi) in the Régie de l'assurance maladie Québec (RAMQ) Public Prescription Drug Insurance Plan. We are shocked because the recommendation appears to ignore the fact that aTTP is a rare, immediately life-threatening event. ATTP is characterized by small blood clots causing damage to organs and a precipitous drop in platelets. ATTP can affect people of all ages, but usually women at the average age of 40¹ (working age with a young family). The only method of treatment is an arduous and time consuming series of in-hospital full volume (and sometimes more) plasma exchange procedures over multiple weeks or months. This experience starts suddenly, it is traumatic and not without side-effects. Nearly half of all Canadian respondents to our survey said that they spent more than three weeks (and up to 12-week plus) in hospital. Those are the patients who were lucky enough to survive. For up to 20% of patients, the current therapy fails and they die.

Specific concerns

Perhaps the review committee did not fully comprehend the enormous challenge of rescuing the patient with plasma exchange following a TTP crisis.

Plasma exchange must be administered as soon as possible; unfortunately, initial treatment is too often delayed because the Emergency Room (or General Practitioner) often does not immediately recognize the rare disease episode of aTTP and/or the patient must be transferred to a facility with the capability of plasma exchange. Delays to treatment increase risk of life threatening thrombotic events which further complicate treatment and lead to a higher risk of death.

Plasma exchange and immunosuppression therapy may be the gold standard treatment for aTTP but it is not a targeted therapy and it is not without serious side-effects. Plasma exchange is arduous and time-consuming exchange of a patient's entire volume of blood plasma (or more) through an invasive central line that remains fixed for the duration of treatment. The very real and long term health challenges of TTP have been identified in survivors including a high prevalence of PTSD and depression². Our survey of the TTP Community revealed that, on average, patients required more than 20 plasma exchange treatments

¹ [J Thromb Haemost.](#) 2005 Jul;3(7):1432-6.

² [Thromb Res.](#) 2017 Mar;151:51-56. doi: 10.1016/j.thromres.2017.01.003. Epub 2017 Jan 6.

to achieve remission following a crisis. A single plasma exchange treatment typically takes over three hours, so this means that the average TTP patients can spend 60 hours undergoing this treatment or more for a single TTP crisis. The time spent in hospital is typically 3 to 12 weeks; and too often, even longer.

We are dismayed because we cannot understand how INESSS could have concluded that Cablivi's "therapeutic value is not recognized". Across numerous reviews of rare disease therapies, INESSS has been able to make appropriate assessments applying a rare disease framework to clinical trial data coming from early stage, small, and short duration clinical trials. Indeed, INESSS has been uniquely able to appreciate disease-specific outcomes, in this case, the superiority of a composite endpoint, namely TTP-related death, recurrence of TTP episode, or major thromboembolic event. How could INESSS have failed, in this case, to agree with the regulator's judgment of overall therapeutic value, not just for high-risk patients not responding to plasma exchange and immunosuppression therapy, but for all those diagnosed with aTTP.

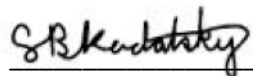
NEW - Cablivi for aTTP in the time of COVID-19

We appreciate that INESSS did not have the current COVID-19 crisis as a reference during assessment of Cablivi. However, we urge INESSS to consider the added value of a therapy that can shorten the time in hospital and reduce the likelihood of recurrence for a life-threatening condition that requires hospitalization and plasma. The added value of caplacizumab during this pandemic to shorten hospital stays of vulnerable immunosuppressed patients in TTP crisis is outlined in the April 15, 2020 update from the America Society of Hematology³.

In conclusion, we urge INESSS to reconsider its recommendation "not to list" Cablivi and to make it available to every aTTP who would qualify for therapy.

The Foundation would appreciate any information you may provide. I look forward to your reply.

Sincerely,



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CC: Danielle McCann, QC Minister of Health
Trevor Richter, Director, CADTH Common Drug Review and Optimal Use

³ www.hematology.org/covid-19/covid-19-and-ttp