CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

CAPLACIZUMAB (CABLIVI)

Sanofi-aventis Canada Inc.

Indication: For the treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP) in combination with plasma exchange (PE) and immunosuppressive therapy (IST).

December 1, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0736-000
Brand name (generic)	Cablivi (Caplacizumab)
Indication(s)	treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP) in combination with plasma exchange (PE) and immunosuppressive therapy.
Organization	Canadian Association of Apheresis Nurses
Contact information[a]	Name: Megan Buchholz, RN

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

The Canadian Association of Apheresis Nurses is a network of over 350 healthcare providers who aspire to advance apheresis medicine for patients and practitioners through education, evidence-based practice, research, and advocacy. We are the front line nurses that spend countless hours caring for our aTTP patients and providing life-saving treatments.

CADTH's decision to reject funding for Caplacizumab has disappointed the Apheresis Nursing community. **We do not agree with the committee's recommendation.** Statistics has shown that the demographics that is often afflicted with aTTP are primarily young women, most in their childbearing years. The women that are admitted to ICU are mothers that are separated from their small children for weeks at a time. The financial burden placed upon these families and the psychological trauma the children endure, displaced from their mothers, is devastating.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

We believe it does not. In our clinical experience, we do find most aTTP patients achieve remission with standard of care treatment, **but not all and everyone should deserve a chance at having access to a life-saving drug.** I recall a significant event of a 19-year-old patient to illustrate my point. They were a basketball star with a future so bright, diagnosed with aTTP after collapsing at home. After receiving all conventional treatments, they died in front of us from a massive heart attack. Another case was a mother of 4, a nurse and primary care giver at home to her severally autistic daughter. She died because Caplacizumab wasn't available to her. Recently I was called into work at 2 am in the morning to treat an aTTP patient having her 5th relapse. She's a mother of 3 and again despite SOC and Rituximab remained refractory and was rapidly declining neurologically. Thankfully we managed to get Caplacizumab on a compassionate basis and she stabilized, and the access to this drug most definitely saving her life. Lastly, a 21-year-old who was receiving plasmapheresis for 15 days consecutively, got up to use the bathroom before treatment suffered with aphasia when she's returned back to bed due to a stroke. These that I have highlighted are the patients that are in desperate need of this drug.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐

	No	☒
The recommendation highlights trial bias, but the stakeholder feedback has clearly demonstrated real world evidence of this drug's efficacy. In my personal experience, and my 14 years in Apheresis, I have cared for nearly 200 patients with aTTP. Our hospital was one of initial centers that participated in the Hercules trial and we recruited 5 aTTP patients, all of whom were young women. All 5 women received the drug and all 5 were off the PLEX machine within 5-6 treatments, out of ICU faster in a shorter time period, and discharged from hospital sooner; moreover, reducing their length of stay. I have seen firsthand that the drug works and because of Caplacizumab, **these women have their lives back without damage to their brains, kidneys or hearts.** In my extensive clinical practice and experience, I have seen that this drug works and I have seen the worst that can happen from this disease. aTTP is a rare but catastrophic hematological emergency that despite the current standard of care in Canada, will take the lives of our patients. We, the Apheresis Nurses of Canada, plead with CADTH to reconsider their decision and keep in mind about the patient's that I have highlighted above, that are no longer with us, or unable to talk, or remember their family or their own names and reconsider this incredibly important and effective drug for this small population of patients that need it.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes No	☐ ☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes No	☐ ☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Megan Buchholz, RN*
Position	*Canadian Association of Apheresis Nurses, Secretary*
Date	*December 1, 2022*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Sanofi: Compensation for Educational Presentation	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

My name is Megan Buchholz and I am a Registered Nurse at St. Michael's Hospital who has worked in Apheresis for the past 14 years. I am writing to you today on behalf of myself and my fellow Apheresis Nurses across Canada. I am on the Board of Directors for the Canadian Apheresis Association of Nurses that is comprised of over 350 nurses that work in over 40 centers across Canada. We are the front line nurses that spend countless hours caring for our aTTP patients and providing life-saving treatments.

The CADTH's decision to reject funding for Caplacizumab has disappointed the Apheresis Nursing community. Statistics has shown that the demographics that is often afflicted with aTTP are primarily young women, most in their childbearing years. These women that are admitted to ICU are mothers that are separated from their small children for weeks at a time. The financial burden placed upon these families and the psychological trauma the children endure, displaced from their mothers, is devastating.

In my personal experience, and my 14 years in Apheresis, I have cared for nearly 200 patients with aTTP. Our hospital was one of the initial centers that participated in the Hercules trial and we recruited 5 aTTP patients, all of whom were women aged 33-60**.** All 5 women received the drug and all 5 were off the PLEX machine within 5-6 treatments, out of ICU faster in a shorter time period, and discharged from hospital sooner; moreover, reducing their length of stay. I have seen firsthand that the drug works and because of Caplacizumab, these women have their lives back without damage to their brains, kidneys or hearts.

In our clinical experience we do find most aTTP achieve remission with standard of care treatment, but not all. I recall a significant event of a 19-year-old patient to illustrate my point. They were a basketball star with a future so bright, diagnosed with aTTP after collapsing at home. After receiving all conventional treatments, they died in front of us from a massive heart attack. Another case was a mother of 3, a nurse and primary care giver at home to her severally autistic daughter. She died because Caplacizumab wasn't available to her. Recently I was called into work at 2 in the morning to treat an aTTP patient having her 5th relapse. She's a mother of 3 and again despite SOC and Rituximab remained refractory and was rapidly declining neurologically. Thankfully we managed to get Caplacizumab on a compassionate basis and she stabilized, and the access to this drug most definitely saved her life. Lastly, a 21-year-old who was receiving plasmapheresis for 15 days consecutively, got up to use the bathroom before treatment suffered with aphasia when she returned back to bed due to a stroke. These that I have highlighted are the patients that are in desperate need of this drug.

In my extensive clinical practice and experience, I have seen that this drug works and I have seen the worst that can happen from this disease. aTTP is a rare but catastrophic hematological emergency that, despite current standard of care in Canada, will take the lives of our patients.

We, the Apheresis Nurses of Canada, plead with CADTH to reconsider their decision and keep in mind about the patient's that I have highlighted above, that are no longer with us, or unable to

talk, or remember their family or their own names and reconsider this incredibly important and effective drug for this small population of patients that need it.

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0736
Name of the drug and Indication(s)	Caplacizumab (Cablivi) for the treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP)
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	☐
	No requested revisions	X

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
c) Implementation guidance

Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0736
Brand name (generic)	CABLIVI (CAPLACIZUMAB)
Indication(s)	Acquired Thrombotic Thrombocytopenic Purpura (aTTP)
Organization	Answering T.T.P. (Thrombotic Thrombocytopenic Purpura) Foundation
Contact information[a]	Name: Sydney Kodatsky

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Answering TTP, in consultation with its members, disagrees with the CADTH recommendation "not to fund" caplacizumab and with their rationale for the following reasons.

1. Caplacizumab works and has saved the lives of Canadians with aTTP when nothing else would work.
2. While CADTH recognizes that TTP is an (ultra-)rare disorder (p.5) affecting 1.7 – 2.2 persons per million, and serious (indeed life-threatening), they nevertheless contend it is possible to conduct "well-designed randomized trial (p. 4), ostensibly even to demonstrate impact on long-term outcomes, namely, relapse rates, organ dysfunction and other disabilities, and mortality/survival (p. 4). Such a trial would require international collaboration, coordination and recruitment across multiple centers to enroll sufficient numbers and, according to the CADTH recommendation, some patients retained in a blinded "no treatment/placebo control" over many years. This scenario is neither feasible nor ethical for many reasons, the most important of which is that other countries who already fund caplacizumab and have established it as standard of care could and would not support a trial with "placebo" group.
3. This reinforces a third point of disagreement with the CADTH recommendation, namely the rejection of Real-World Evidence (RWE) studies. CADTH opined that the "potential for biased patient selection and intergroup differences in measured and/or unmeasured confounding variables [meant that] no firm conclusions could be drawn on the results of these studies." In contrast, at this time, 22 other countries have agreed to fund caplacizumab for treatment of aTTP, drawing partially or wholly on the strength of submitted RWE.

In fact, CADTH collaborator NICE reviewed even less data for caplacizumab (back in 2020) and recommended caplacizumab for reimbursement (https://www.nice.org.uk/guidance/ta667/chapter/1-Recommendations). NICE was able to effectively integrate RWE to supplement shortfalls in RCT in order to put patients' lives first. NICE engaged in a round-table discussion with the leading physicians and the patient group, before finalizing their decision. They noted within their recommendation there was some uncertainty, but the benefit to patients outweighed that. The NICE process was thoughtful and transparent, and should be the same in Canada, if we are truly willing to thoughtfully evaluate rare disease treatments.

TTP is a true outlying rare disease characterized by unpredictable acute episodes that are each considered a medical emergency. This uniqueness makes the evaluation by CADTH of caplacizumab even tougher. Caplacizumab does not target the underlying disease, rather it acts to eliminate the cause of life-altering/ending harm (small blood clots) during crisis (short-term use). Each TTP crisis carries a 30% risk of life-altering complications and/or death from these unpredictable small blood clots, but with access to

caplacizumab (designed to stop the dangerous clots until existing treatments can take effect) these risks are much reduced which aligns with our community's desire to survive and resume our lives.
The reality is, we the TTP patients know this drug works. Canadian patients are alive today because of compassionate access to caplacizumab. It has worked in Canada, and it has worked around the world. Since the first review of caplacizumab in 2019, a number of Canadian TTP patients have had access to the drug, and it has minimized devastating long-term and life-altering complications from the small blood clots that characterize a TTP crisis. It protects us, giving standard treatments the opportunity to "kick-in".

*19-year-old **Selena** was suddenly in the ICU stroking without an end in sight. Caplacizumab was added to her treatment and the strokes stopped. She was safe from the blood clots which gave standard therapies the time they needed to kick-in.*
In January 2021, [redacted] suffered a second relapse of TTP after contracting COVID-19 from her dying father who had tested negative days before. Despite receiving standard TTP treatment, Lorraine's case seriously worsened and she became very scared that maybe she would not dodge the bullet this time. Caplacizumab was added to her treatment regime and she was released from the hospital two weeks later, requiring half the time in hospital as her first two TTP episodes.
[redacted] a child and youth worker in Toronto, was rushed by ambulance to hospital with her 3rd TTP relapse in critical condition. She was intubated for a week in the ICU. Only after caplacizumab was added to her treatment regiment did her case turn around.

On Real-World Evidence (RWE):
• This submission included RWE in addition to the manufacturer's traditional data. While it isn't perfect (RWE never is – it's meant to capture real-world use, not structured trials), it is valuable additional information that proves that caplacizumab works in the real world. Patients like Selena, Lorraine and Yhulan are living proof of its efficacy.
• CADTH notes that RWE has a place in this process, and has communicated the need to include more RWE. We're fully on board with the need to do that. We even understand that CADTH undertook a study and has a current discussion paper out on RWE, and we're pleased to see the system finally moving in this direction. However, TTP patients cannot afford to wait. This time will cost TTP patients lives in Canada.
• Despite the ongoing discussion, this recommendation has shown us truly that RWE isn't being integrated into the evaluation process in a meaningful way.
CADTH notes repeatedly throughout the recommendation that "no firm conclusions" can be made. Indeed, this point is made over and over and feels like a dead end with no recommendation as to how to deal with the lack of conclusive evidence. There is the opportunity to provide "coverage with evidence developing", namely identifying the outcome measures to be collected as "real-world" evidence.
In summary, this recommendation is devastating for our community, and it is well known that a CADTH "no" is the end of the road for TTP patients. Patients like Selena, Lorraine and Yhulan will die waiting for standard treatments to "kick-in". We know from the negative recommendation of caplacizumab in 2019 that the rest of the system (pan-Canadian followed by provinces) won't even acknowledge the file without some sense of a path forward from a CADTH perspective. We urge CDEC to reconsider their stance.

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

In our opinion, CADTH was able to generally summarize our patient input, especially around the quality of life issues faced by TTP patients and caregivers, but they failed to understand that we don't expect caplacizumab to reduce relapse rate, and we understand that this is not the purpose of caplacizumab. We believe that CADTH failed to recognize and consider the life-or-death nature of TTP, and the significant risks patients face

during a TTP episode, especially during plasma exchange and while waiting for medications to take effect. It must be strongly noted that our desire to survive a TTP crisis is paramount to a treatment that reduces relapses. We understand that the function of caplacizumab is to keep us safe while standard treatments have time to "kick-in". This caplacizumab "armour" makes every crisis safer. In addition to obvious damage from the small blood clots (stroke, heart attack etc.), research our Foundation supports out of London, ON is investigating the long term effects on the brain that may help understand why so many patients report long term memory and depressive symptoms.

We also believe that CADTH failed to recognize and consider detailed patient perspectives, notably from those who have received caplacizumab. These accounts were included in both the survey (via patient quotes) and via the patient account videos we submitted as part of the input process.

Some of the patients we featured are living proof that caplacizumab has worked within the Canadian medical system in a real-world setting, and yet the recommendation fails to reflect the importance of that.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒

Simply put, CADTH doesn't see the added value in the real-world evidence presented as part of the submission. We do appreciate the "Discussion Points" (Page 4) element of the recommendation and the associated commentary, despite disagreeing with the contents.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

The recommendation notes that they have considered implementation issues, but these have not been clearly articulated, nor adequately addressed. Specifically, we note the following:

- The recommendation simply states that CADTH received feedback from drug programs on implementation (p.7), with several different areas – but no details. What was the feedback? Was there discussion on how this therapy could be looked at from a criteria perspective? What was the discussion? As patients, we deserve to know, and be a part of, that discussion.
- CADTH questions the context of the evidence given the Canadian usage of rituximab in clinical practice for TTP patients. Our understanding is that rituximab is routinely provided to TTP patients receiving care in Canada; we would expect that this would continue during caplacizumab treatment as these treatments have different functions. A TTP crisis is a medical emergency. Caplacizumab buys patients time to survive until standard treatments (like rituximab) can "kick-in". Commentary about Canadian use of rituximab and potential benefits is unnecessary.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒

Input was obtained from the drug programs that participate in the CADTH reimbursement review process (p.7). The following were identified as key factors that could potentially impact the implementation of a CADTH recommendation for caplacizumab: *Considerations for initiation of therapy ,Considerations for continuation or renewal of therapy, Considerations for discontinuation of therapy, Considerations for prescribing of therapy, Generalizability of trial populations to the broader populations in the jurisdictions, Care provision issues, System and economic issues.* We request CADTH to address each of these issues, namely to propose a process by which patients could be identified as "in need" or "most appropriate" for treatment with capalacizumab, those indicator or outcomes to justify continuing or discontinuing the therapy, how the initial findings could lead to generalize use to the broader population, the necessary management and support, including data collection, from the health providers, and the societal and economic impact of reducing harm and mortality among this population.

The patient community firmly believes that caplacizumab would be effective and cost-effective if available to all aTTP patients that could benefit from it; however, failing this approval at least the subset of patients that can be identified as highest risk and likely to benefit must be provided access. As expressed in the opinion of the clinical experts consulted by CADTH (p.6), who noted that "caplacizumab may be a reasonable option to be reserved for patients with aTTP recurrence or refractory aTTP as these patients currently have limited treatment options." Not only will caplacizumab have the opportunity to save the lives of these patients (we estimate less than 40 per year across Canada), but treating these patients with caplacizumab is an opportunity to generate more RWE. It must be noted that reserving caplacizumab for the "sickest" patients is not the choice made by peer countries since identifying **each** patient that will suffer irreversible damage or death from unpredictable blood clots is impossible. Unselected patients will inevitably suffer life-altering complications, and some will die despite the existence of preventative treatment.

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Sydney Bryant Kodatsky*
Position	*Chair, Answering TTP Foundation*
Date	*06-12-2022*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Network of Rare Blood Disorder Organizations
Réseau des Associations Vouées aux Troubles Sanguins Rares

November 30, 2022

[redacted]

Re: Support for Answering TTP's stakeholder input regarding the reimbursement review for caplacizumab

To the Review Committee,

I am writing today in support of Answering TTP's response to CADTH's call for stakeholder input regarding the reimbursement review for caplacizumab, for the treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP) in combination with plasma exchange (PE) and immunosuppressive therapy.

The Network of Rare Blood Disorder Organizations (NRBDO) would like to reiterate the need for immediate access to life-saving caplacizumab for Canadian TTP patients who could benefit from it, including patients in crisis.

Each aTTP crisis is a medical emergency where every minute counts. The use of caplacizumab provides critical protection from devastating and unpredictable small blood clots while standard treatments have the opportunity to take hold. If reserved for refractory patients as a life-saving measure, it is estimated that only 38 patients a year would be treated, however all patients deserve to receive treatment that protects them from devastating disability.

Given the inadequacy of CADTH's current system of collecting input and measuring the value of novel therapies for rare diseases, the NRBDO was pleased to see that CADTH has undertaken a Real-World Evidence for Rare Diseases Learning Period. We participated in the public engagement on the report on a multistakeholder engagement strategy to integrate real world evidence (RWE) into decision-making about care for rare disease in June 2022, and look forward to next steps. While we understand that CADTH's learning period on RWE integration is ongoing, it is disappointing to see CADTH not consider the provided RWE in the review of caplacizumab.

From the review, we see that the RWE presented did not meet CADTH's expectations. This is the challenge with a rare blood disorder like TTP: data collection and trial design cannot be the same as a more prevalent disease or disorder. There is an extremely small patient population that has experienced the value of this treatment in a Canadian clinical setting - patients fortunate enough to receive

compassionate coverage or privileged enough to have private insurance coverage that has elected to reimburse. Evidence was also shared from other countries demonstrating the value in approving and reimbursing caplacizumab for TTP patients.

The NRBDO is committed to ensuring that the patient voice is heard. We strongly support the efforts of Answering TTP and the TTP patient community to seek reimbursement for caplacizumab and urge CADTH to consider all of the evidence presented, including RWE, when reconsidering this recommendation.

Sincerely,

[redacted]

Jennifer van Gennip
Executive Director, NRBDO

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0736-000
Brand name (generic)	caplacizumab
Indication(s)	aTTP
Organization	NRBDO, in support of Answering TTP
Contact information[a]	Name: Jennifer van Gennip

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

To the Review Committee,

I am writing today in support of Answering TTP's response to CADTH's call for stakeholder input regarding the reimbursement review for caplacizumab, for the treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP) in combination with plasma exchange (PE) and immunosuppressive therapy.

The Network of Rare Blood Disorder Organizations (NRBDO) would like to reiterate the need for immediate access to life-saving caplacizumab for Canadian TTP patients who could benefit from it, including patients in crisis.

Each aTTP crisis is a medical emergency where every minute counts. The use of caplacizumab provides critical protection from devastating and unpredictable small blood clots while standard treatments have the opportunity to take hold. If reserved for refractory patients as a life-saving measure, it is estimated that only 38 patients a year would be treated, however all patients deserve to receive treatment that protects them from devastating disability.

Given the inadequacy of CADTH's current system of collecting input and measuring the value of novel therapies for rare diseases, the NRBDO was pleased to see that CADTH has undertaken a Real-World Evidence for Rare Diseases Learning Period. We participated in the public engagement on the report on a multistakeholder engagement strategy to integrate real world evidence (RWE) into decision-making about care for rare disease in June 2022, and look forward to next steps. While we understand that CADTH's learning period on RWE integration is ongoing, it is disappointing to see CADTH not consider the provided RWE in the review of caplacizumab.

From the review, we see that the RWE presented did not meet CADTH's expectations. This is the challenge with a rare blood disorder like TTP: data collection and trial design cannot be the same as a more prevalent disease or disorder. There is an extremely small patient population that has experienced the value of this treatment in a Canadian clinical setting - patients fortunate enough to receive compassionate coverage or privileged enough to have private insurance coverage that has elected to reimburse. Evidence was also shared from other countries demonstrating the value in approving and reimbursing caplacizumab for TTP patients.

The NRBDO is committed to ensuring that the patient voice is heard. We strongly support the efforts of Answering TTP and the TTP patient community to seek reimbursement for caplacizumab and urge CADTH to consider all of the evidence presented, including RWE, when reconsidering this recommendation.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes No	☐ ☐
If not, what aspects are missing from the draft recommendation?		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes No	☐ ☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes No	☐ ☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes No	☐ ☐
If not, please provide details regarding the information that requires clarification.		

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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Jennifer van Gennip*
Position	*Executive Director*
Date	*01-12-2022*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below. N/A	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Sanofi	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐