

## Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Caplacizumab

Indication: Acquired thrombotic thrombocytopenic purpura (aTTP)

Name of Patient Group: Answering T.T.P. (Thrombotic Thrombocytopenic Purpura) Foundation

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### 1. About Your Patient Group

Answering TTP Foundation ([www.AnsweringTTP.org](http://www.AnsweringTTP.org)) is a grassroots patient organization headquartered in Ontario and solely made up of volunteers across Canada who have been directly or indirectly affected by TTP. The organization was founded in 2009 by seven-time TTP survivor Sydney Kodatsky who recognized the need for a patient organization to support the TTP community, act as a unified voice for the patient community, fundraise for TTP research, and drive education and awareness about this rare disease. The foundation's Board is made of seven Directors with diverse skillsets and three of the seven Directors are also TTP patients.

The operations team is made up of two members of the Board: The Executive Director chairs the annual fundraiser and oversees the accounting with the help from a paid bookkeeper. The Chair runs the annual research competition, maintains the website, manages communications and educational materials, and runs the day-to-day operations of the Foundation. One of the organization's Board members is also the volunteer Director of Patient Relations. They hold a virtual peer support group meeting for the TTP community four times a year.

Over the years, the Foundation has also supported a research grant program, having understood the crucial need for biomedical, clinical, and population health for a rare disease. Since its inception, Answering TTP has committed over \$2 million to research grants through 2023.

In 2021, Answering TTP strengthened the level of support and education to Canadian TTP patients and helped drive greater awareness of TTP to the medical community by creating the Foundation's first national Canadian TTP Medical Advisory Panel comprised of six physicians from different areas of the country. This was also supplemented by the creation of an informal Patient Advisory Panel, comprised of five TTP patients and caregivers who volunteer their time to provide the patient perspective on Answering TTP's initiatives.

Answering TTP's work could not be accomplished without its passionate volunteers, who fundraise for the Foundation each year. While the TTP community is small, the experience of having TTP or taking care of someone with TTP propels patients, caregivers, friends, and loved ones to want to draw awareness of this disease and support Answering TTP's goals to act as a voice for this community.

### 2. Information Gathering

During the period of May 18, 2022 to June 8, 2022, Answering TTP Foundation conducted a patient survey through Google Forms. While based on our 2019 patient survey during the first review of caplacizumab, this survey was updated to reflect our group's growth, as well as changes to the environment since our first survey

in 2019. We also conducted two informal Patient Advisory Group meetings where participants were able to review and add survey questions to ensure that it reflected the experience of TTP patients and caregivers.

**Survey Recruitment:** All interview and survey questions were developed by Answering TTP Foundation with the help of a Patient Advisory Group made up of five Answering TTP volunteers, with outreach to all Answering TTP members through the organization’s website, social media pages (Facebook and Twitter), and direct email. We are also appreciative of the Canadian Apheresis Group and the Canadian Association of Apheresis Nurses, who generously agreed to share the opportunity to participate in the survey with their TTP patients. The summary of feedback was collated by Answering TTP.

**Survey Responses:** We received completed 49 survey responses.

**Demographic information:**

The survey was mainly completed by TTP patients (31 respondents). However, family members, caregivers, or friends of persons diagnosed with TTP were also invited to participate in the survey, of which made up 16 of the received responses. One healthcare professional that worked with TTP patients also responded, and one researcher provided their input.

- 29% of respondents were ages 50-59
- 20% of respondents were ages 30-39
- 18% of respondents were ages 60-69
- 14% of respondents were ages 40-49
- The age groups of 18-29 and 70 + made up of 8% of respondents respectively
- There was one respondent under the age of 18
- 80% of survey respondents identified as female and 20% identified as male

A significant majority of respondents lived in Canada. Half of the survey’s respondents lived in Ontario, 5 respondents lived in Alberta, 3 respondents lived in each British Columbia and Manitoba respectively and 2 respondents lived in each Quebec and Nova Scotia respectively. There was 1 respondent from the provinces of Saskatchewan, New Brunswick, PEI, and Newfoundland and Labrador each.

Outside of Canada, 3 respondents lived in the United States, and 2 lived in Europe (Germany and Switzerland, respectively).

### 3. Disease Experience

TTP is a rare episodic disorder that affects 2-6 people per million and the road to a TTP diagnosis can be fatal as TTP is characterized by the medical community as a true medical emergency requiring immediate treatment. The small blood clots that characterize this disease can have sudden and severe consequences, but because standard therapies are not targeted and take time to “kick-in”, patients are left in a life-threatening state for days and sometimes weeks. During this time up to 20% of patients die and others are left with life altering complications from stroke, heart attack etc.

In our survey, most patients (or the person they cared for) were first diagnosed with TTP between the ages of 20-30 (49% of respondents) and between the ages of 40 and 59 (31% of respondents). 16% were diagnosed when they were over the age of 60 and two (2) patients were under 20 years old at the age of diagnosis.

Between the time of initial symptom onset and treatment, many patients (35%) said it took within a week from their first symptoms to receive treatment, but for many patients, this took longer with 27% of respondents stating that it took more than a week, 9 respondents said it took more than a month.

During an Answering TTP Patient Advisory Group meeting, one patient said:

*“A lot of people who are diagnosed late have to deal with collapsed veins and there is no way to insert a central line for treatment... they had given up on me after 5 hours and 40 minutes of trying and I was told I was going. It was an apheresis nurse that begged someone on the floor to keep trying, saying to a resident doctor -this girl is dying, please give it another try- and that resident ended up being successful.”*

Persons diagnosed (or cared for) with TTP experience a variety of symptoms during their TTP episode or as a result of the treatment they have received. Survey respondents rated their symptoms on a scale of “no problem, minor, moderate, serious/frequent, and incapacitating/life-threatening” and these were some of the findings:

- Bruises, fever, fatigue, migraine, confusion, abdominal pain, and anxiety/depression or panic attacks were noted as “serious and frequent symptoms”. Half of the respondents noted bruising and fever/fatigue/migraine/confusion as “serious, frequent symptoms”.
- One-third of respondents listed anxiety/depression/panic attacks as a “serious, frequent” result.
- 18 respondents cited having abdominal pain and/or kidney problems as a serious frequent symptom.
- More alarmingly, 8 respondents had a stroke or acute myocardial infarction in an incapacitating/life-threatening manner, 9 respondents had fever/fatigue/migraine/confusion in a similar incapacitating manner, and 4 respondents noted kidney problems in an incapacitating/life-threatening manner.

Survey respondents added that bleeding from gums/nose, shortness of breath, vision loss from retinal detachment and jaundice were common symptoms/results during a TTP episode.

For TTP patients, a relapse can cause lengthy hospitalizations, disable, or even be fatal. TTP patients live in a state of uncertainty, not knowing if a relapse will occur. Our survey asked how many relapses the person diagnosed with TTP (or the person they care for) has had since the initial episode and diagnosis.

- 48% at least one relapse, with 22.4% having 3-4 relapses, 12% having 1-2 relapses, 10% having 5-6 relapses, and scarily, 2 respondents said they suffered 7-10 relapses.
- 47% of respondents said they did not have a relapse.

Due to the unpredictability of this disease, many TTP patients stay an average of 9.7 days in the intensive care unit and an average of 14.4 days in hospital. Our survey respondents echoed this in their responses. In a question asking about the longest amount of time that a TTP patient stayed in hospital during a TTP crisis:

- 83% of respondents noted that their hospital stay was more than 7 days, with 37% having stayed in hospital for 28 days and more, 31% in hospital for 14-28 days, and 16% for 7-14 days.
- One respondent said their hospital stay was for 120 days.
- Only 3 respondents said their hospital stay was less than one week.

#### 4. Experiences With Currently Available Treatments

A TTP episode is **always** a matter of life or death, especially with the current standard of care. As new treatments like caplacizumab have been released, there is an increasing recognition that TTP patients do not have to face the life-threatening consequences that come with each TTP episode.

Our survey asked which treatments the person diagnosed with TTP has received in the past or present and almost all respondents (44 of 49) noted that they or their loved one had received plasma exchange (plasmapheresis). Other treatments were also used:

- 45 of 49 respondents were treated with steroids (prednisone), and 32 were treated with Rituximab (Rituxin).
- Cyclosporin was used for 12 patients and 9 patients had their spleens removed.
- 34% (or 16 respondents) to the survey had been treated with Cablivi (caplacizumab).
- Other patients were also treated with Cyclophosphamide, Vincristine, CellCept, and Velcade.

When asked what the worst part(s) of treatment was for a TTP patient, many described the hardship of a long hospital stay, the side effects of receiving steroids, and the impact during and after plasma exchange. Many stated that the effects of the steroids resulted in weight gain, hair loss, sore bones, being unable to sleep, retina issues, depression, and Cushing's disease.

*“The plasma exchange treatment for 3 months was very draining and I was scared that I was going to get an infection in my line that was inserted in my neck. Also, getting blood products scared me. After my treatment, I did not feel like talking to anyone. I went into depression for a long time. Mental fog was another symptom.”*

*“I cannot overemphasize the impact of daily plasmapheresis treatments... After so many relapses and scarring each line insertion gets more delicate. The risk is real with critically low platelets.... it takes more time for your bruised neck and chest to heal with low platelets. I'll never forget my best friend pressing bandages against my chest at the direction of my plasmapheresis nurse as they attempted to stop the bleeding from the line early on in my second relapse during a treatment.”*

**Current standard of care:** The current standard of care for TTP is plasma exchange (plasmapheresis), combined with immunosuppressant drugs. Both are administered to deal with the urgent drop in platelets and small blood clots that form throughout the body that characterizes an episode. Some patients may require additional use of immunosuppressants during remission, but until recently, there has been no targeted or indicated treatment for TTP.

Our survey asked respondents that received plasma exchange to note the longest period they received this treatment for.

- 35% of respondents received plasma exchange for less than 5 days to 3 weeks, with 7 of those respondents receiving plasma for 1-2 weeks and 5 respondents for 2-3 weeks.

- 56% of respondents received plasma exchange from 3 weeks to more than 12 weeks. 20% of those respondents undergone plasma exchange for 3-4 weeks, and 16% undergone plasma exchange for more than 12 weeks.
- Of all patients that received plasma exchange, 68% said they had hives from the treatment, 37% were anaphylaxis (as diagnosed by their doctor), and two respondents developed TRALI (Transfusion-related acute lung injury), a serious complication during transfusion causing rapid lung injury.

Beyond the physical symptoms of plasma exchange, the emotional effects loom larger and are more long-lasting. Plasma exchange is a frightening, risky, and an unpredictable treatment to patients. During a TTP episode, this untargeted treatment can be repeated sometimes multiple times per day, and then tapered-off as tolerated. Sudden life-threatening flares during tapering, or soon after, are not uncommon and requires the process to be started again with daily apheresis treatments. Plasma exchange can only be administered to hospital in-patients and may require weeks and sometimes months of hospital stays. For the duration of this time, the patient remains at risk of severe complications and death.

*“It is very difficult with plasma exchange through your arms or through a line in your neck. You may have to stay in the Apheresis clinic for 3-6 hours. You receive other peoples’ plasma which may cause other reactions and so more drugs are required to treat the patient.”*

*“I cannot underscore enough that plasma exchange is a huge deal to me. Being hospitalized for weeks away from your young family, and having your entire blood volume passed through a machine and fed back to you combined with strangers’ blood is mind boggling. To date I’ve required over 700 units of blood plasma for plasmapheresis - an extraordinary amount of blood from strangers. I still can't believe that with all the advances in medical care there isn't a safer, more targeted treatment available to me. Instead with every relapse I need to cross my fingers that plasma exchange can "rebalance" my body with blood from strangers.”*

*“It is a HUGE deal! Even with solvent-detergent plasma, the chance of reaction is still high, and one worries what might happen with each treatment. In our case, there were many side effects and rarely was there a 'straight-forward' session.”*

*“I had an allergic reaction each time. Hives all over my body and was given steroids and another medication to resolve. It caused confusion, retina issues and swelling. Gained weight and had to use a wheelchair to get around. With my last relapse, I was given plasma exchange for 3 months. Risk of infection was high for my line insertion (neck area) and because I received high number of blood products.”*

Our survey wanted to know more about any difficulties with accessing the treatment they or their loved one received (i.e. cost, travel, time off work) during their TTP episode. Many respondents said that the cost of

medication was unaffordable, and they had been unable to work during their TTP episode(s). Caregivers of TTP patients also have to take time off work to care for their loved one.

*From a caregiver's perspective: "The cost of Cablivi was not covered. He had to stay in the hospital for over a month, was discharged for a weekend then re-admitted due to nothing else working. The stress around the cost and nothing working was crazy."*

*"The insurance I had at the time wouldn't pay for the two treatments - the Rituximab and the caplacizumab. Since I've not been able to return to work, I'm presently trying to get ODSP, I'm having a hard time paying for transportation and parking for my bi-weekly appointments. I was laid off work because of Covid one month before I was diagnosed."*

*"I missed 6 months of work and my husband had to miss work as well. He had to be there to communicate with the doctor and nurses. I was not alert on my treatment days and needed him for emotional support."*

## 5. Improved Outcomes

The reality is that for TTP patients, there has been no alternative to the current treatment regimen until Health Canada approved caplacizumab on March 2, 2020. Caplacizumab was given a priority review by Health Canada, which signified the need for a therapy of this kind. Which is why when CADTH declined it for reimbursement, the TTP community was extremely disappointed despite the significant unmet need here in Canada.

On a day-to-day basis, during a TTP episode, survey respondents have general anxiety over their treatments not working, having to put their life on hold, and the general depression that ensues with not being able to move forward when life is put on hold due to TTP.

*"When having an episode, the biggest fear is that perhaps the treatment won't work and that I am facing a life-threatening disease if not treated and there are no guarantees that it will always work - the risk of heart attack, stroke or death is very real."*

*"Rest of life is put on hold; patients need to face risk of serious or fatal outcomes each time, which left me with PTSD."*

*"It's like my entire life is put on pause ... in addition to all the physical symptoms, the level of anxiety knowing I have 2 young kids is sometimes unbearable."*

*"My daughter was to graduate from her policing course that year she fell ill and had to drop out of school, take medical leave from work for a year. She felt socially isolated from her family and friends."*

As a result, TTP patients and their families have their lives uprooted and the impacts are beyond physical - extending socially, financially, and psychologically. If advancement in treatments reduce the risk of

death/irreversible consequences from each TTP crisis, patient's mental health during remission will improve. It is the uncertainty of the life-threatening timing of the next relapse that brings about real mental stress. A high prevalence of PTSD and depression in TTP survivors has been reported and a study found that 80.8% of individuals with TTP have mild depressive symptoms, compared to 10.5% found in the general population. Survey respondents have noted financial difficulties, an impact on their mental health, continuous fears of relapses, and impacts to their social life and career goals due to TTP. Simply put, TTP patients deserve a treatment that can ease the burden and significantly reduce their risk of death or disability.

*"I've lost friends who don't understand and can't cope with the illness. I'm unable to return to work, my savings is gone, I've maxed out credit cards and I'm having huge issues keeping up with bills. Psychologically, I've been super depressed. This is the first time in my life that I've had serious thoughts about suicide (I got help), that my future doesn't have an outcome."*

*"You never feel safe from this disease as you never know what or when something will trigger a relapse."*

*"The threat and anxiety of it returning and whether or not we can access the life saving medication Cablivi which was generously funded through an organization"*

*"TTP has left me in fear and worrying about having a relapse. It caused me to worry about anything I ate, drank or activities that I did. Most importantly, my husband and I were going to be starting fertility treatments in January however I was diagnosed with TTP in October which put those plans on hold. TTP has potentially caused us not to be able to have another child and if we decide to take the risk, my pregnancy will be high risk."*

*"Ultimately, I had to adjust my career goals and how I was going to build my family... Instead of working my way up the corporate ladder, I had to sidestep."*

*"We were a dual-income, one-child family before, with plans to have a second. TTP meant that we would not risk having another child. TTP meant that one working parent became a completely disabled dependant for roughly a year, and after that was somewhat disabled, only able to work a small number of hours for pay and not contribute to household chores. The other parent had to pick up the slack and do all the wage-earning, all the child-rearing, all the cooking and cleaning. It is an understatement to say it has been hard. That has social implications: we don't have the energy to socialize."*

The anxiety over treatments and having to delay planning for the future also extends to caregivers. 32% of respondents to the survey were caregivers, family members, or friends of those with TTP and in response to a question about the caregivers' quality of life during their loved one's TTP episode, this is what some caregivers had to say:

*"Quality of life changed completely. I would say the fear of never know what may happen next."*

*"The worry and anxiety. Huge impact on work"*

*“As a caregiver, I had to be with my spouse every day to make sure he got to each department within the hospital and listened to the different doctors. Regular life activities go on hold and I did miss time from my own job. My mental health was fragile but had to be strong for my spouse.”*

*“I was with her minimum 15hrs daily and away from my other children then when strokes began slept at the hospital with her. She was in hospital for 5 weeks therefore had to quit my job.”*

TTP patients and caregivers expect that access to caplacizumab will provide:

- The ability to survive the next TTP crisis which carries a 20% mortality rate;
- A treatment that provides them with less uncertainty in the early stages of their TTP episode and peace of mind during remission;
- A reduction in the number of plasmapheresis treatments, of which respondents have said is an arduous process with risks; and
- **The ability to plan for the future – something that current TTP patients cannot do.**

## 6. Experience With Drug Under Review

Of patients and caregivers, 16 respondents (34%) had received access to caplacizumab. This access was varied – 7 patients had participated in a Canadian clinical trial, 6 had received it via the manufacturer’s compassionate access program, and one respondent had received it repeatedly via their private insurance coverage.

Patients and caregivers with experience with caplacizumab were clear about the benefits provided by this therapy, with one respondent saying it is a “total game-changer” for TTP treatment. Respondents with experience on caplacizumab noted shorter hospital stays, faster healing, and prevention of further disease as key benefits, while two respondents emphasized the reduced mental health burden – specifically, the anxiety surrounding relapses.

*“My anxiety about relapse during remission has been drastically reduced. I now stress about not only when the next relapse will happen, but if I will survive it. Access to caplacizumab reduces the 20% risk of death with every relapse. Access to caplacizumab has changed everything about my outlook for the future with this disease.”*

*“My expectations would be that the drug would allow my body to heal quicker and my platelet count would increase and remain at a stable level”*

*“Cablivi probably would have prevented stroke, DVT and retinal detachment as these items all happened after diagnosis and treatment for TTP had started.”*

*“Caplacizumab will keep me safe and reduce the number of risky and unpredictable plasmapheresis treatments I need. It will get me home to my young children and will get me there faster.”*



*“Cabliivi would save my life if I were to get another relapse. In my last relapse, standard therapy did not work. My stay was 3 months in the hospital. I could have lost my life. The drug would shorten my stay in the hospital.”*

*“We fully believe that being part of that (Capla) clinical trial saved her life. Yes, TTP has been hard, and she has had life-long disability as a result. But it could have been so much worse without Cabliivi. We fully expect that if her TTP recurs, that she will be at risk of further organ damage, which might lead to more cognitive impairments, or further affect her kidneys, or add to the muscle weakness.”*

On the disadvantages for caplacizumab, patients noted the cost of treatment (for those without private coverage) and overall availability for patients. However, more respondents stated the advantages being:

- Shorter treatment time
- Less stress on the hospital system, due to duration of hospital stays and plasma resources
- Reduced risk of TTP side effects

*“In crisis I would recover from TTP episodes quicker (less immune suppression and cancer risk) to get back to my life so much faster. And with a lower risk of damage to organs and other long-term disabilities associated with TTP from the clots that could potentially change my life tomorrow.”*

*“A shorter treatment duration will also reduce the amount of immunosuppressant medication that I will need going forward. As a metastatic cancer survivor, this is amazing news as the use of immunosuppressant medications invite the deadly cancer back.”*

Our survey respondents truly believe that their quality of life could change if Cabliivi was accessible. Respondents said that the simple fact of knowing it is available would be lifechanging as it would take away the stress of TTP episodes, lower anxiety knowing they can resume life again earlier, and create less mental stress about the disease and cost of medication.

*“Knowing it is available and its another tool to treat TTP takes a lot of stress away when you know you could potentially relapse at any time and maybe the next time conventional treatments won't work.”*

*“Less worry about if we would have access to this treatment in future, or if we would have to pay high prices to save the family members life”*

*“My anxiety over the next relapse would be greatly reduced because the fear of death would be significantly diminished. The relief would be freeing.”*

*“PTSD and anxiety related to relapses is one part of the reduced quality-of-life that TTP has caused our family. Having ready access to Cabliivi would mean that recurrences would be less terrifying, with a greater hope that she could make it through one without picking up more disabilities and cognitive impairments.”*

We believe that this should be available **immediately** for all TTP patients upon the order of their physician – there is a real and specific value for patients of which the standard of care is ineffective. They die otherwise.

## 7. Companion Diagnostic Test

N/A

## 8. Anything Else?

### Commentary

The Canadian TTP community was devastated to learn of CADTH’s 2020 recommendation – even as the rest of the world (including the United Kingdom’s NICE, the United States, Denmark, Belgium, Netherlands, Finland, Italy) saw the clinical value and recommended its use for patients. This has been incredibly frustrating for Canadian TTP patients, as we watch members of our international community receive access to treatment that, for some reason, our system does not deem beneficial.

The effects of COVID-19 has created surgical backlogs, a need for health human resources, and we understand there is a current blood donation shortage with major concerns about future plasma capacity in Canada. Caplacizumab not only saves TTP patients’ lives but has the capability to ease the burden on the health system by freeing up hospital beds due to shorter stays and reducing plasma resources needed to save a patient during a TTP episode.

### CADTH Review Framework: Significant Unmet Need

As discussed above, TTP is a rare disease with significant unmet need with respect to treatments. We are encouraged by CADTH’s inclusion of Considerations for Significant Unmet Need within the Procedures for CADTH Reimbursement Reviews, and hope that CADTH applies those considerations during the review of caplacizumab.

### Survey Responses: “Anything Else?”

The vast majority of our survey respondents provided responses to the open-ended question of **“Is there anything else you’d like decision-makers to know as they consider recommending caplacizumab for reimbursement?”**.

Selected responses include:

*“Please please fund this as if you can minimize hospital stays and reduce the need for life saving plasma, I believe it is a win win situation, hopefully costing the health care system less in the long run.”*

*“One of my friends lost her battle with TTP days after delivering (early) her second baby girl. She was a kind, thoughtful and lovely person who was taken too young. Her daughters will grow up without their mom because she did not have access to caplacizumab. She'd relapsed more than once, she'd survived before. In the end, she lost the race to tame the TTP with untargeted treatment. Don't let this happen again. It doesn't need to be a race anymore. Caplacizumab can give us the time we need to survive and emerge without life altering disability.”*

*“Peer countries to Canada support the use of Cablivi. I assume that Canada can benefit from their knowledge and make the right decision to support Canadian TTP patients.”*

*“Cablivi kept my daughter 19 years old safe from further damage that TTP had already caused her during her 5 week stay in hospital. She fought for 11 days without caplacizumab, sustained 3 strokes and was moved to ICU hearing all the negative information from doctors that she wasn't responding to the typical treatment plan for TTP. 2 weeks into fighting for her life she was given caplacizumab and within only 13 hours of receiving the drug and not changing any other treatment she was receiving she started seeing improvements with her blood labs. 3 days later she says "I am feeling better" and her labs are out of the critical range. Caplacizumab is the drug that kept her safe from further damage TTP had planned for her. Caplacizumab bought her the time she needed for her typical treatment plan to work. Caplacizumab was a key factor that saved my daughters life please keep her and other ttp patients safe and grant access to this life saving drug. My daughter is here today to continue her life's journey because of it.”*

**As noted via the experiences above, our patient community is passionate about access to a proven treatment that can protect their lives during a TTP episode. TTP is a true medical emergency and having immediate access to a life-saving treatment such as caplacizumab could mean the difference between life and death to patients. We firmly urge CADTH to recommend caplacizumab (Cablivi) for TTP in Canada.**