



Platelet
Disorder
Support
Association

Empowering ITP Patients

January 26, 2022

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Dear CADTH team,

We want to thank you for taking the time to review whether fostamatinib (Tavalisse) should be recommended for reimbursement for adults with ITP. Although the outcome is not what we were expecting or hoping for, it's clear a lot of aspects were considered in this analysis, and we appreciate the time you spent on this.

Our Ask:

The ITP patient community hopes that this draft decision could be revised to a 'reimburse with condition(s)' recommendation. Our suggested conditions could be 1) to demonstrate previous failure to at least one other second line; and 2) mandatory enrolment of all treated patients into a registry to capture efficacy and safety (see below), until there is greater comparative evidence. This would be in line with Health Canada's indication for use. The ITP community does not want to see any more lives lost to ITP in this day and age when there are so many therapies available, and many more in development too.

We would also like CADTH to consider a one- or two-year pilot where reimbursement for Tavalisse would be granted, with a commitment from us and from our physician partners to collect registry data to inform the rates of bleeding, hospital visits (including visits to hospital for critical bleeds and long-term health outcomes) and adverse events. This information will inform efficacy and safety using real world data and provide information on resource utilization.

Supporting Evidence:

Responsiveness

ITP is an extremely heterogeneous disease. Not only in terms of the clinical presentation and disease course, but also in response to different therapies. It is not possible at this time to predict which ITP patient will respond to a particular treatment, or which ITP patient will only partially respond to a particular treatment or have no clinically significant response at all. **We feel that CADTH should recommend reimbursement for Tavalisse so that treatment can be**

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individualized and if a patient does not respond to other second line therapies, they are not 'out of luck' for something they have no control over.

There will always be ITP patients who do not respond to Tavalisse. With regards to the FIT trial, based only on 150 participants, the number of individuals who responded to Tavalisse is favorable and supports approving Tavalisse for reimbursement. And if you couple that data with what PDSA provided CADTH from our closed Facebook support group, you will see that most of the patients actually using this drug have not responded well (or at all) to other therapies - so Tavalisse may be the only option for them.

ITP Expert Opinions

In Canada, we are very lucky to have several hematologists who specialize in ITP and have even been involved in the development of professional medical ITP guidelines. In regard to the comment *"There is very little evidence to guide the selection of second line or third line therapy ... "*, while we agree that the evidence is limited, there are professional guidelines that were updated in 2019 both [American Society of Hematology guidelines](#) , [International Consensus guidelines](#) from globally recognized ITP experts, as well as [Choosing Wisely Canada](#) and [International guides](#).

Professional guidelines do not support splenectomy as a go-to second line therapy. Rituximab is not preferred over TPO-RAs in the guidelines. Rituximab is not new, but it's used off-label for ITP. While reimbursement of Rituximab would be a step forward, it still would not give Canadian hematologists the flexibility to provide a high standard of care to their patients who cannot afford to access drugs privately and would not support professional guidelines built on evidence. And patients are looking for therapies that not only work, but that do not disrupt their life. For instance, *patients have expressed they would rather take an oral medication with no dietary restrictions rather have to take time off work or away from their family to receive an infusion for hours.* However, if that is the only option available, many would be chose treatment over risk.

The CADTH review stated *"The clinical experts consulted stated that contemporary ITP guidelines suggest that, in general, splenectomy and Rituximab can be considered second line therapy. There are third line options available; however, the comparative efficacy of these agents are unclear"* is based on limited and outdated knowledge and appears to cherry pick therapies leaving out TPO RAs, leaving out professional medical ITP guidelines, and does not leave room for newer innovative therapies that are not considered third line, that target different mechanisms to treat ITP to increase the chance for response among those with ITP that fail to respond to first line and other second line options. Third line options are more 'supporting' options to support second line therapies. For instance, some patients have reported success adding dapsone to their TPO-RA regime when they noticed the drug started to no longer work for them. This knowledge is not widely known among all hematologists and clinical providers which is why it is crucial for CADTH to listen to respected hematologists working/researching/publishing in the area of ITP specifically.

In a study involving many of PDSA's medical advisors who are Internationally recognized ITP specialists, [Boccia et al \(2020\)](#) used data from post hoc analysis of the phase 3 FIT open-label extension study vs patient subgroups by line of therapy (second line versus third-or-later-line) and stage of disease (persistent versus early or late chronic ITP) and reported: *In this post hoc analysis, fostamatinib was more effective as second-line than third-or-later-line therapy for ITP.* While Tavalisse may not be ready to be used right now as an upfront second line therapy considering the Health Canada indication which limits its use, this data suggest that this is a therapy of great value to ITP patients and at the very least should be considered if other treatments cannot work well for a particular ITP patient.

Other internationally recognized ITP specialists, Dr(s) Newland and MacDonald revealed in their 2020 [study](#) the following: *"Fostamatinib as a prodrug, and R406 as its active moiety, represent a novel treatment approach which can be orally administered and requires minimal titration; reducing both clinical time and the need for professional healthcare support. It was shown to produce a rapid, durable response among patients with long-standing ITP who were considered difficult to treat having previously received rituximab, and/or TPO-RAs or had undergone splenectomy. Subgroup analyses illustrate good overall responses independent of duration of ITP, baseline platelet count, previous TPO-RA or rituximab therapy, and prior splenectomy. These results demonstrate that fostamatinib is able to improve platelet numbers among diverse types of patients, including those with and without multiple exposures to prior ITP treatments, and those with longer and shorter durations of ITP. The findings from the FIT (1,2,3) clinical trials programme resulted in the approval of fostamatinib by the US FDA in April 2018 and the EMA in Europe in January 2020. Patients who responded to fostamatinib demonstrated good control of hemostasis."* The findings from the above are also supported in another professional publication ([Duliege AM et al, 2019](#)) which was also authored by several of PDSA's medical advisors specializing in ITP.

CADTH's statement: *"Patients identified a need for treatments that would reduce symptoms and rates of bleeding events and improve QoL compared with currently available therapies... not demonstrated with fostamatinib (Tavalisse)"* **does not reflect the individual patient experience.** PDSA did provide CADTH with direct patient accounts demonstrating how compared to other things tried, Tavalisse was working for them. In terms of the EQ-5D for QoL, those five domains are what we use within our patient registry launched in 2017. The issue with using the EQ-5D is that these aspects of measuring QoL don't all apply to patients with ITP. There are NO mobility issues with ITP. There are NO self-care issues with ITP unless relating to excessive fatigue and depression. There generally is NO pain and discomfort with ITP. Within our ITP Natural History Study patient registry (close to 2000 participants) we have only 5 adult ITP participants (mainly from the USA) who have disclosed they have used (or are currently using) Tavalisse. We do not have the data to provide you, and likely won't in the near future, because patients in Canada cannot access this drug due to affordability issues. This is why we are suggesting our registry proposal to capture this data if it's needed for reimbursement purposes.

ITP is a rare disorder. Only a small number of all those with ITP will require treatment, an even smaller number will require access to second line therapies. Of those that require access to second line therapies only a small number of that group will not respond to traditional second line therapies (such as TPOs and Rituximab) so you are left with a pretty small number needing to use Tavalisse as a later second line therapy choice. You cannot expect the same level of evidence for a small, rare disease group.

Summary Point: ITP experts feel Tavalisse is a good therapy for some patients with ITP who may not respond well to other therapies.

Real-life cost savings

We understand there is a standard way to predict overall cost, but has CADTH considered the real-life costs?

Imagine this patient scenario: No access to Tavalisse. Patient can only access steroids and IVIG. Both only work for about a week, then the platelet count decreases again, and bleeding symptoms return. Long term use of steroids has caused diabetes, mental health consequences, and fatigue and weight gain/blood pressure issues. Breakthrough bleeding can occur on steroids (but yet it's reimbursed and continues to be). A critical bleed happens at a low platelet count (can be any location) requiring hospital admission for more than one day, tests to determine the extent of the bleed, and then emergency management that likely consists of platelet transfusions, expensive and in short supply IVIG, and other therapies that increase the cost not to mention bed cost, provider cost, and cost to the patient's family (emotionally, and financially with missed work etc.) What are those relevant costs PER patient?

The cap for what is considered appropriate to fund based on QALY's may not be appropriate because the QALY calculation cannot be accurately assessed when you simply compare the benefits of treatment approach A to treatment approach B. For reasons already explained, it's not possible to compare treatment approaches in that way because not all ITP patients respond to the same therapy, not all therapies are used long-term, and many ITP patients are using more than one therapy at a time, and thus this entire calculation maybe based on questionable data. Not to mention, QALY calculations have their limitations, and often require further mathematical solutions to address such limitations. Can CADTH provide the breakdown of how the prices per QALY was made? Does CADTH's economic analysis of projected costs capture that not everyone who is eligible to use the drug (if reimbursement was approved) would actually respond to the drug?

When considering costs, CADTH has an obligation to the Canadian people to also make ethical decisions. One could argue that it is unethical to reimburse steroids for long-term use but not better second line therapies that may increase the chance for long term remission when you know you are doing more harm than good? In Ontario and many other provinces, a splenectomy is needed before access to more robust therapies can even be applied for. Splenectomy success is only 60% at best and the overall cost and burden and risk are significant. IVIG is very expensive. Immunoglobulins are in limited supply. PDSA is part of the

Canadian Blood Services Working group designed to explore strategies to ensure Canadian patients sustain an adequate supply. Much of Canada's supply is from other countries, such as the US, where the shortage is already a reality.

We understand some literature has been published that supports earlier upfront use of Tavalisse, but at this time, PDSA would support reimbursement with conditions if that means access to this drug can occur for individuals who do not respond (or do not respond well) to other second line options. It is unknown how many ITP patients will (and will not) respond to Tavalisse, the later may be significant.

Summary Point: While CADTH has looked at the economic reality in a standard way, we are concerned about the costs associated with not reimbursing Tavalisse on our overall health care system.

Summary of PDSA's Response to CADTH:

We respectfully request that CADTH consider changing the recommendation for Tavalisse to 'reimbursement with condition(s)'. These conditions might include mandatory enrolment in a patient registry to capture real world data on efficacy and safety.

Sincerely,

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