Common Drug Review
Patient Group Input Submissions

ticagrelor (Brilinta) for the prevention of atherothrombotic events with history of myocardial infarction

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
Heart and Stroke Foundation — permission granted to post.

CADTH received patient group input for this review on or before March 7, 2016
The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations.

While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Heart and Stroke Foundation

Section 1 – General Information

Name of the drug CADTH is reviewing and indication(s) of interest		Brilinta / ticagrelor
Name of the patient group		Heart and Stroke Foundation
Name of the primary contact for this submission:		[redacted]
Position or title with patient group		[redacted]
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Permission is granted to post this submission		Yes

1.1 Submitting Organization

The Heart and Stroke Foundation of Canada (HSF), a volunteer-based health charity, leads in eliminating heart disease and stroke and reducing their impact. Its mission is to prevent disease, save lives, and promote recovery.

The Heart and Stroke Foundation is one of Canada's largest and most effective health charities. Over the last 60 years we have invested more than $1.39 billion in heart and stroke research, making us the largest contributor in Canada after the federal government. In that time, the death rate from heart disease and stroke has declined by more than 75 per cent.

The Foundation's health promotion and advocacy programs across the country are saving lives every day. Working together, our employees, volunteers, donors and world-class researchers have made the Heart and Stroke Foundation what we are today: Canada's most widely recognized and trusted authority on cardiovascular health. Our vision is healthy lives free of heart disease and stroke. Together, we will make it happen.

The Heart and Stroke Foundation is a national organization led and supported by a force of about 125,000 volunteers.

1.2 Conflict of Interest Declarations

a) We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:

The Heart and Stroke Foundation of Canada (HSF) and the individuals involved in the preparation of this submission have no conflict of interests to declare. While the majority of HSF funding comes from individual donors, HSF has received unrestricted financial support from pharmaceutical companies to help us achieve our mission of preventing disease, saving lives and promoting recovery. This financial

support is used for the development of educational materials; education, awareness and community engagement activities; and funding of research awards across the country. Over the past five years, HSF has received unrestricted financial support from: Aegerion Pharmaceuticals, Amgen, Apotex, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb Canada, Eli Lily Canada, GlaxoSmithKline Inc., Janssen, McKesson Canada, Merck, Merz Pharma Canada, Novartis, NovoNordisk, Pfizer Canada Inc., Sanofi, Servier, Takeda, and Valeant

b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:

There is no conflict of interest to report.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The information on impact of myocardial infarction on patients and caregivers was gathered by HSF through an online survey using the online survey tool: 'Survey Monkey'. Access and links to the survey were advertised using targeted, promoted posts through Facebook and pop-ups on heart attack information pages of the English and French HSF public websites (www.heartandstroke.ca and www.fmcoeur.ca). The survey was made available to the public from February 9 to March 3, 2016. The survey, FB promoted posts and pop-ups were developed in English and French languages.

In total, 239 individuals started the online survey. Participants were not obligated to complete all questions in the survey. Participants were asked whether they have ever been told by a healthcare professional that they have had a heart attack. Of the 239 individuals who responded, 221 individuals indicated that they had been told by a healthcare professional that they have had a heart attack. Participants were also asked whether they were a caregiver for someone who is a heart attack survivor. Of the 208 individuals who responded to this question, twenty-six respondents that they were a caregiver for someone who has had a heart attack. Responses from participants that answered yes to having had a heart attack and/or yes to being a caregiver of a heart attack survivor were used to inform this submission.

Information to complete Section 2 was also generated through literature searches from peer reviewed publications, Statistics Canada, Public Health Agency of Canada, Heart and Stroke Foundation health information and guidelines and policies from credible organizations such as the Canadian Cardiovascular Society. The Heart and Stroke Foundation develops guidelines, policies and position statements that are based on scientific evidence. These guidelines, policies and position statements form the basis of the health information that is provided by HSF to the public, health professionals and the media in various formats (print, web, CPR training materials, media releases, etc.).

Limitations: This survey was not a population based survey. The responses obtained through the online survey provide limited data to inform this submission and reflects the views and/or experiences of the survey respondents. It is not representative of the views of all heart attack survivors or their caregivers living in Canada.

2.2 Impact of Condition on Patients

In 2012, almost 14,000 Canadians died as a result of a heart attack in Canada. Each year more than 305,000 Canadians are hospitalized for heart disease, and an estimated 1.3 million Canadians are living with effects of heart disease. The number of Canadians living with heart disease is self-reported (Canadian Community Health Survey) and is likely an underestimate. Over the last sixty years, remarkable progress has been made to increase survival from heart disease, with mortality rates declining more than 75 per cent. The decline in mortality is largely due to research advances in surgical procedures, drug therapies and prevention efforts. Yet, despite our progress to date heart disease remains one of the leading causes of death and hospitalization and the biggest driver of prescription drug use in Canada.

A total of 221 survey participants identified themselves as heart attack survivors, having 'ever been told by a healthcare professional that they have had a heart attack'. Responses from these individuals are reported below. Respondents were not required to complete all questions in the survey.

The majority of respondents (n=175) reported having had their most recent heart attack within the last 5 years (81 within the last year, 44 reported having had their heart attack 1-2 years ago, and 50 indicated it occurred 2-5 years ago). Fourteen per cent (n=31) reported having had their heart attack 5-10 years ago, while 6% (n=14) had their most recent heart attack more than ten years ago. One did not know how long ago their heart attack occurred.

One hundred and eighty seven survey participants responded to the question: "how has having a heart attack affected your day-to-day life?" Of the 187 responses:108 patients said they have to take medication at specific times.

- 86 patients said they have to take medication multiple times per day.
- 75 reported they have to visit a healthcare provider frequently.
- 50 reported they have to take time off work.
- 49 patients reported they have to manage their condition with other forms of therapy; and
- 38 patients reported that this condition does not affect their day to day life.

Other responses to the question "how has having a heart attack affected your day-to-day life?" included: fatigue (constant feeling of tiredness, tiring easily or often fatigued, n=6); fear (living with fear that it could happen again, fear of death or fear of returning to activities like running, n=4); anxiety (n=3); depression (much depression and sadness, n=3); and changes in mood (n=1). One patient commented that having a heart attack has 'changed my life dramatically'.

Sixteen patients stated they have made changes to diet and exercise including sodium restrictions, learning to cook, eating healthy, increased activity, regular exercise, daily activity, and ongoing participation in cardiac rehabilitation. One patient commented that they are 'unable to work out as vigorously', and another reported difficulty walking as a result of having had a heart attack.

Four patients are living with heart failure as a result of their heart attack, which as one reports: 'has completely changed my life'. One patient reported' statin induced myopathy' following their heart attack and another stated they 'tend to bleed at unexpected times' as a result of their condition.

Four patients reported their heart attack affected their vocation as they were unable to return to work or are in the process of losing their job due to: high stress, the job requiring lots of standing or the inability to perform duties related to the position.

Two patients commented on the impact their heart attack has had on travel, specifically stating: "no driving for a month, no flying for 2 months and no snowbird trip to Florida this winter..." and "I have had to curtail out of country travel due to insurance premiums."

When asked if there are activities that patients are unable to do as a result of having had a heart attack, 103 indicated that having a heart attack has not affected their ability to do activities, while 73 indicated their condition impacted their ability to do activities. Most patients reported that the impact their heart attack has had on their activity level was due to reduced energy, shortness of breath and fatigue following the event. The following table illustrates the activities and limitations to activities s as reported by survey respondents:

Yes, as a result of this condition I am unable to do the following:	**N=73**
Most things, all activities, anything strenuous, all activities are impacted as a result of reduced energy, getting very tired and tiring easily, because I get winded, short of breath and I don't have the same endurance due to breathless bouts.	25
Lifting, lifting heavy items, lifting weights, carrying items	15
Walk long distances, walking in winter, walking up hills or in windy conditions.	13
Going on amusement park rides, scuba diving, waterslides, badminton, rock climbing, high intensity activities (hockey, crossfit, cycling, fitness classes, running, running marathons), hot tubs	12
Routine day to day activities, snow shovelling, outdoor activities during cold weather, heavy housework, making a bed, gardening, mow the lawn.	11
Work as long or as hard, go to work, do my job	8
Climb stairs, climb more than 3 stairs	5
Travel	2
Drive a commercial vehicle or race my motorcycle (until I'm done medications)	2
Sleeping is uncomfortable	1
Run and play with grandkids.	1

One hundred survey respondents identified symptoms they have experienced as a result of their heart attack. Patients most commonly reported the following symptoms: fatigue, lack of energy, weakness and tiredness (n=67); pain including angina/chest pain, leg pain and muscle pain (n=42); memory loss (n=33) and swelling/water retention (n=13). Other symptoms included shortness of breath (n=9), dizziness (n=6), irritability (n=4), anxiety (n=3), difficulty sleeping (n=3), anxiety (n=3), weight gain (n=2), depression (n=2), and sensitivities to temperature (n=2). The following table provides a fulsome description of symptoms reported by all survey respondents.

Yes, as a result of this condition I have experienced the following symptoms:	**N=96**
Fatigue, tiredness, no energy, weakness	67
Angina/pain, leg pain, chest pain, muscle pain, muscle ache, chest tenderness, leg vein tenderness, pressure on chest	42
Memory loss, unclear thinking, cognitive function, memory lapses, mild cognitive impairment, bad memory loss	33
Swelling, swelling in leg, swollen ankles, water retention, fluid retention surrounding my heart and lungs, edema	13
Shortness of breath, difficulty breathing	9
Dizziness, vertigo, feeling lightheaded, faintness	6
Irritability, temperament, mood	4
Have a hard time sleeping, don't sleep well.	3

Yes, as a result of this condition I have experienced the following symptoms:	N=96
Anxiety	3
Weight gain	2
Sensitive to temperature	2
Depression	2
Exercise intolerance	1
Congestive heart failure	1
Blood loss	1
Loss of 20 lbs weight in 6 weeks	1
Stomach acid/gas buildup	1
Bruising.	1
Sweating	1
Inability to palette and ingest all foods except fruits, simple vegetables, oatmeal and milk.	1

2.3 Patients' Experiences With Current Therapy

Two hundred and ten heart attack survivors indicated that they have been prescribed medication to prevent a second heart attack. Prescribed medications included drugs to control high blood pressure (n=166), drugs to control high blood cholesterol (n=181), drugs to manage diabetes (n=25) and antiplatelet or blood thinner medications (including but not limited to acetylsalicylic acid, clopidogrel, prasugrel, ticagrelor, and/or ticlopidine) (n=200).

Other medications patients reported being prescribed to reduce their risk of a second heart attack included anti-depressants, beta blockers, medications to lower heart rate, plavix and anti-seizure medications.

Patients did not report any hardships or difficulties in accessing their current therapy.

2.4 Impact on Caregivers

There were twenty-six respondents who identified themselves as a caregiver for a heart attack survivor. When asked about challenges faced in providing care for someone who has had a heart attack, the most common challenge was having to frequently transport the patient to their healthcare provider (n=10). Nine caregivers have had to take time off work, 8 reported having to provide additional care because of side effects from treatment, 6 have had to provide medication multiple times per day, and 5 have had to provide medication at specific times each day. Three caregivers indicated they have not faced any challenges in providing care for someone who has had a heart attack.

Other comments included providing transportation and support, 'being his voice during treatment, listening carefully to doctors, making sure everyone is aware of his history and ensuring he gets appropriate care', 'emotional support' and 'management of our stress'.

When asked how caring for someone with this condition has impacted the caregivers routine, 7 reported their daily routine has not been impacted. Fifty eight percent (11/15) stated they are often more anxious or stressed, while 47% reported they are busier than they used to be (n=9), 42% stated they don't have much freedom (n=8), and another 42% reported they often feel overwhelmed (n=8). Seven report they have experienced significant financial costs and six report that their own health has suffered. Additional caregiver responses included "Unbelievable stress and worry for the first year", "little support was provided ... nothing offered for caregiver support", and "has taken a lot of time away from my children

and they probably have suffered as much as I... it not only impacts the caregiver but the rest of the family too".

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Information to complete Section 3 was gathered in the same way as Section 2. Please refer to section 2.1 for further information on this process.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

a) Based on no experience using the drug:

Ninety-nine patients responded to the question 'Other than being cured, what would be the best course of treatment look like for you?"

The two most common responses were to have no more medication, less or reduced medications and/or medications with few side effects (n=18); daily exercise or activity/physiotherapy/to strengthen a damaged heart (n=18); and nutrition related treatments. Patients expressed the need for accessibility to equipment, resources and/or professionals. Five patients felt they experienced the best possible treatment possible, while ten respondents did not know what else was possible and offered no suggestions as 'heart disease cannot be cured'. The following table provides a summary of responses received to this question:

Other than being cured, what would the best course of treatment look like for you...:	N=96
Exercise to strengthen my undamaged heart muscle, walking, daily activity, physiotherapy, feeling able to walk, "I would like to be able to be much more aggressive in the physical exercise. I feel like the rehabilitation is way too conservative to actually become stronger. "	18
Less or reduced medication, medications with few side effects, no more medication.	18
Nutrition awareness, diet, more support around diet, plant based diet, healthy eating, fat intake control	16
More accessibility to equipment and cardiologists, dietitians, exercise under controlled conditions, longer term rehabilitation, access to facilities for exercise and lifestyle change, access to cardiac and physical rehabilitation, visit with counselor in hospital, covered RN or PSW to visit once you are released, support, support groups, information.	13
I don't know/not sure/no idea. There is no cure for heart disease. I really don't know what else is possible.	10
A treatment that allowed me to return to activity level prior to heart attack, return to full function, feel strong, get my energy back, increase endurance, become totally active without limits, Recovery, with a full and vibrant life with no restrictions other than a good	10
diet and activity.	
Self and Doctor care, yearly/routine checks to make sure all is well, continue Meds as directed, being able to find a comparable drug that would return my appetite, a safe and effective anti-platelet, medication	12

I think I had the best course of treatment, Already have the best course of treatment. Nothing better could have been done. With today's technology, I am probably getting the best care available.	5
Manage symptoms, manage it with least amount of permanent intervention. More exercise, healthy diet, manage stress and work at keeping meds to minimum. Lifestyle support.	6
Weight loss	3
Losing my fear of another attack, never have to worry about another heart attack. Reassurance that every little twinge isn't another heart attack.	3
Be able to regenerate the death cells of my heart, regenerate heart muscle & unclog arteries	3
More proactive tests and not wait until after you've had a heart attack	2
I think medicine has come a long way just wish heart disease didn't exist.	1
More natural remedies	1
Quicker surgery	1
Minimal stress.	1
I don't see any choice at a better life	1
Not using a standard form of treatment. Every case is unique. Being able to customize after care or education to really benefit the patient.	1
A heart transplant	1
Time and patience to heal.	1
Anything that enhances quality of life	1
Anything.....please	1

b) *Based on patients' experiences with the new drug as part of a clinical trial or through a manufacturer's compassionate supply:*

Eighty seven respondents indicated they have ever taken or been prescribed BRILINTA (ticagrelor) as part of a study (clinical trial) or by their health care provider. Forty two were actively taking the medication, having last taken it today. Ninteen patients indicated they had last taken Brilinta more than one month ago and 21 indicated it was more than a year since they last took Brilinta.

Of those who had ever used Brilinta (n=84), 29 responded that Brilinta is helping to control their condition, while five felt it did not control their condition and 50 respondents were unsure or did not know.
Seventy six patients were able to access the medication without difficulty. Of the eight who reported difficulties, the reasons provided for inability to access the medication easily included: "too expensive", "uninsured at the time", "caused very bad nosebleeds", "had to wait a couple of times for the drug store to get some in", "pharmacy never had enough in stock", "always had to go back later for the remainder" and "I needed special permission from MB Health but after that it was easy".

When asked about the side effects, if any, experienced using Brilinta, of the 83 respondants, 35 indicated they didn't experience any side effects; 24 stated they experiences shortness of breath, difficult or laboured breathing; 10 reported headaches; and 13 reported nose bleeds. Other side effects included bruising (n=8), bleeding (6), fatigue or tiredness (n=4), dizziness and loss of balance (n=2), angina (n=2) and another heart attack (n=1).

Of patients who had taken Brilinta (n=87), seventy patients indicated they had also taken acetylsalicylic acid (ASA or aspirin). Compared to ASA, 16 patients felt experiences of shortness of breath/difficulty breathing when taking Brilinta were worse or much worse (20 felt it was about the same, one felt it was much better and 29 were not sure or had no opinion); 8 felt that headaches were worse or much worse on Brilinta (24 felt it was about the same, four felt it was better or much better, and 27 were not sure or had no opinion); 9 felt that experience of nosebleeds were worse or much worse on Brilinta (18 felt they were about the same, one felt they were much better and 36 had no opinion or were not sure); 14 felt their experience of otherb bleeding was worse or much worse on Brilinta when compared to ASA (19 felt it was about the same, three felt it was much better or better) and 28 had no opinion or were not sure); 8 patients felt the experience of side effects on Brilinta when compared to ASA was worse or much worse (19 felt they were about the same, and 36 were not sure or had no opinion); one patient felt the ease of use of Brilinta compared to ASA was worse (43 felt it was about the same, 2 felt it was better or much better and 19 were not sure or had no comment); 23 felt Brilinta was worse or much worse compared to ASA in terms of affordability (24 felt it was about the same, three felt it was much better and 18 were not sure or had no opinion); and 7 felt that Brilinta was worse or much worse to access than ASA (38 felt it was about the same, 4 felt it was better or much better, and 14 were not sure or had no opinion).

Of patients who had taken Brilinta, 14 indicated they had also taken clopidogrel. When compared to clopidogrel, nine patients felt that their experience of shortness of breath/difficulty breathing was worse or much worse on Brilinta (3 thought it was about the same and one was not sure or had no opinion), four felt that headaches were worse or much worse (7 felt it was about the same and 2 were not sure or had no opinion), three felt that nosebleeds were worse (6 felt it was about the same and 4 were nor sure or had no opinion), 3 felt experiences of other bleeding were worse or much worse (7 felt it was about the same, one felt it was better and 2 were not sure or had no opinion); 1 felt that ease of use was worse (10 felt it was about the same and 2 were not sure or had no opinion); 3 felt affordability was worse or much worse (9 felt it was about the same and 1 was not sure or had no opinion); 2 felt accessibility was worse (10 felt it was about the same and 1 was not sure or had no opinion).

Of patients who had taken Brilinta, 1 indicated they had also taken prasugrel. When Brilinta was compared to prasugrel, the patient felt that their experiences of shortness of breath/difficulty breathing, nosebleeds, other bleeding, affordability and accessibility were about the same on both drugs. The patients' experience of headaches was better on Brilinta, yet their experience of other side effects was worse when compared to prasugrel.

Of patients who had taken Brilinta, 2 indicated they had also taken ticoldipine. When Brilinta was compared to ticlodipine, one patient reported worse difficulty breathing while another stated experiences with difficulty breathing was about the same on both drugs. Both patients reported their experiences of headaches, other bleeding, ease of use and accessibility were about the same on both drugs. One patient reported worse other side effects while on Brilinta and one patient reported much worse affordability of Brilinta when compared to ticlodipine.