Common Drug Review
Patient Group Input Submissions

Sacubitril (Entresto) for Heart failure, NYHA class II or III

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 September 23, 2015

Disclaimer: 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	Sacubitril
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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Name of co-author (if different)	[redacted]
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Address	1402-222 Queen Street, Ottawa, ON
Website	www.heartandstroke.ca
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

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 industry, including 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.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The information on condition impact to patients and caregivers was gathered by HSF through an online survey using the 'Survey Monkey' tool. Access and links to the survey were advertised using targeted, promoted posts through Facebook, pop-ups on heart failure information pages of the HSF public website (www.heartandstroke.ca), and through our Community of Survivors mailing list. The Community of Survivors mailing list is a group/list of survivors and/or caregivers who have consented to the Heart and Stroke Foundation sending directed e-mails related to recovery. The online survey was made available to the public from August 24, 2015 to September 13, 2015.

In total, 113 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 heart failure. Of the 113 individuals who responded, 42 individuals indicated that they have heart failure. Participants were also asked whether they are a caregiver for someone who has heart failure. Of the 113 respondents, 13 indicated that they were a caregiver for someone with this condition. Responses from participants that answered yes to a diagnosis of heart failure (n=42) and/or yes to being a caregiver for a person with the condition (n=13) were used to inform this submission.

Information was also generated through literature searches from peer reviewed publications, 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. Very few responses were obtained through the online survey which provides limited data to inform this submission. This submission reflects the views and/or experiences of a small number of survey respondents and is not representative of the views of all patients with heart failure or their caregivers living in Canada.

2.2 Impact of Condition on Patients

Heart failure is a very serious health problem in Canada with an estimated 500,000 Canadians living with heart failure (approximately 1 in 70 Canadians), although these numbers are likely an underestimate. A further 50,000 Canadians are newly diagnosed with this condition each year. Research in heart failure has improved outcomes for patients however the statistics tell us that up to 50% of heart failure patients die within five years of diagnosis. While research has improved the treatment and care for heart attacks and other heart diseases, the number of heart failure patients continues to rise.

Survey participants were asked if they had ever been told by a healthcare professional that they have heart failure. A total of 42 survey participants identified as having heart failure and their responses informed the following results. Respondents were not required to complete all questions in the survey.

When asked if they knew the classification of their heart failure, 9 patients of a possible 42 patients did: Class I (n=3), Class II (n=1), Class III (n=4), and Class IV (n=1). The remaining patients did not know and one stated “I’ve never been told”.

As a result of this condition, 22 patients said that it has affected their day-to-day life because they have to take medication at a specific time. Others were affected by having to take medication multiple times a day (n=20), having to visit their health care provider frequently (n=19), having to take time off work (n=10), and having to manage their condition with other forms of therapy (n=8). One patient commented “I’m unable to perform any chores” and another said “I can’t do the things I enjoy”. Another comment was that “I lost my leg due to heart failure”.

The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is an evaluation tool used to assess quality of life in heart failure (HF) patients and has been used in both research and clinical settings. The questionnaire has 21 questions that seek to understand the impact of heart failure on a patient's quality of life. Questions assess the impact of physical symptoms of heart failure such as shortness of breath, fatigue, swollen ankles and difficulty sleeping. Other questions assess the effects of heart failure on physical and social functions including walking and climbing stairs, household work, need to rest, working to earn a living, going places away from home, doing things with family or friends, recreational activities, sports or hobbies, sexual activities, eating foods one likes and mental and emotional functions of concentration and memory, worry, loss of self control, and being a burden to others (REF: MLHF User Guide, MAPI Research Institute). Responses to questions range from zero meaning the item in question had no effect on the person's life, to five meaning the item has affected the person's life very much during the past month (4 weeks). The total score for the 21 items ranges from 0 to 105, with lower scores indicating less effect of heart failure on quality of life and higher scores indicating greater effect. Scores for the physical elements of the questionnaire range from 0 to 40, while scores for the emotional elements range from 0 to 25. Cut-off values for patients with good, moderate and poor quality of life have been identified in published literature as less than 24 = good, 24-45=moderate and greater than 45=poor quality of life (Behlouli et al. Conf Proc IEEE Eng Med Biol Soc 2009:6242-6.).

Individuals with heart failure were asked to respond to the 21 questions of the Minnesota Living with Heart Failure Questionnaire to assess how much their heart failure has affected their life during the past month (4 weeks). Individuals were instructed to respond to questions on a scale of 0 to 5 with 0 indicating the factor had no impact on their life at all, 1 indicating very little impact and 5 indicating the factor had impacted their life very much.

Thirty-six individuals with heart failure answered the question. The mean score was 45 (range 0-91) and the median score was 44. Nine individuals scored less than 24 indicating a good quality of life, 10 scored between 24 and 45 indicating a moderate quality of life and 17 individuals scored greater than 45 indicating a poor quality of life. The mean physical score was 21 (range 0-40) and the mean emotional score was 10.2 (range 0-23). Fifteen of 36 patients reported that heart failure was making their sexual activities difficult (much or very much), 14 patients reported that their recreational pastimes, sports or hobbies had become difficult (much or very much), 12 patients reported that leaving home had become difficult (much or very much) and 11 patients reported that working to earn a living was difficult (much

or very much). As well 19 patients reported that side effects from their treatments had not affected them at all (n=11) or very little (n=8) from living as they wanted in the last month.

When asked about symptoms related to this condition, 38 of a possible 42 patients reported experiencing symptoms. The most common symptoms experienced were increased shortness of breath (n=30) as well as fatigue, loss of energy, extreme tiredness or weakness (n=30). This was followed by increased swelling of the ankles, feet, legs or abdomen (stomach area) (n=20), increased heart rate or irregular heart beat (n=15), bloating or feeling full all the time (n=14), increased urination at night (n=14), sudden gain of more than 3 lbs over 1 to 2 days, or 5 lbs in a single week (n=13), decreased alertness or difficulty concentrating (n=13), cough or cold symptoms that last for longer than a week (n=11) and loss of or change in appetite or nausea (n=7).

2.3 Patients' Experiences With Current Therapy

Thirty-three patients of a possible 42 reported that they have been prescribed medication for management of heart failure. When asked about medications other than Sacubitril being taken for their condition, 13 patients reported the following medications:

- Ramipril (n=3), Cozaar (n=1)
- cozaar bisoprolol lasi (n=1)
- metoprolol (n=2), Carvedilol (n=2)
- Ramipril Bisoprolol (n=1)
- spironlactone (n=2)
- Digoxin/toloxin (n=2)
- Norvo-semide (n=1), fuorosemide/Lasix (n=3
- teva-spirotin (n=1)
- Xerolto (n=1), Warfin(n=3), Aspirin (n=3), ASA (n=1)
- Statin (n=1)
- Zoplicone (n=1)
- Effient/prasugrel (n=1)

One patient stated that there are simply "Too many to list". When asked "when was the last time that you used or took this/these medication(s)?" All respondents answered "today" (n=19). Fifteen of a possible 19 patients reported that their medication helped to control their condition, 2 patients reported that it did not and 2 were unsure. No patients had difficulty accessing their medication. All patients were able to access their medications without difficulty (n=19). When asked "Have you experienced any side effects as a result of taking this medication?" Fourteen of a possible 20 patients reported not having any side effects. Six patients reported experiencing side effects which included fatigue, tiredness, weakness or lack of energy (n=6), dizziness (n=4), low blood pressure (n=3), diarrhea (n=2), back pain (n=2), headache (n=1) and high potassium levels (n=1).

2.4 Impact on Caregivers

Thirteen people identified themselves as a caregiver for someone with heart failure. One of those thirteen reported not facing any challenges related to being a caregiver. Those who did experience challenges reported having to provide medication multiple times per day (n=6), having to provide medication at specific times (n=4), having to provide additional care because of side effects from treatment (n=4), having to frequently transport him or her to their healthcare provider (n=4), having to take time off work (n=4), and one caregiver responded that "dealing with their angry moods" was challenging.

When asked how caring for someone with this condition has impacted their daily routine, 3 caregivers reported that it has not affected their daily routine. Seven caregivers reported often being more anxious or stressed, 6 caregivers reported not having much freedom, 5 often felt more overwhelmed, 4 caregivers reported being busier than before and having experienced financial costs respectively. Three caregivers felt that their own health had suffered and one respondent wrote "I can't leave and go to work". When asked if there were any additional comments the caregivers would like to convey regarding their experience, one stated "Need support for caregivers. Seems no one cares about us."

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:*
Through the survey, patients were not asked to compare existing therapies with Sacubitril. When asked "Other than being cured, what would the best course of treatment look like for you?" Responses included "keeping the condition stable with no further issues", "exercise program at little or no cost", "the current medication", "no major side effects", and "being able to return to my previous active life."

b) *Based on patients' experiences with the new drug as part of a clinical trial or through a manufacturers compassionate supply:*
Thirteen patients reported having been prescribed Sacubitril by their healthcare provider or as part of a clinical trial. Ten of these patients are actively taking Sacubitril (having last taken this medication 'today'). Six of the 13 patients reported that taking Sacubtril has helped to control their condition, 1 patient reported that it did not and 6 patients were unsure. Twelve of these patients must take at least one additional medication, other than Sacubitril, to control their condition. No Sacubitril users had any issues obtaining their medication.

When asked "Have you experienced side effects as a result of taking Sacubitril?" Five patients reported they had and 8 patients reported no side effects. Of the 5 patients who experienced side effects, 4 reported experiencing fatigue, tiredness, weakness or lack of energy and 3 reported experiencing cough, respiratory issues or infection. Other side effects reported were dizziness (n=2), low blood pressure (n=2), headache (n=1), back pain (n=1), and one patient stated having "muscle aches and cramps confusion difficulty breathing nervousness pins and needles in my hands, feet and lips occasionally swelling of fingers, hands and feet dry throat and mouth occasional blurred vision thinning of hair vertigo anxiety (nervousness)" and another patient reported having an allergic reaction to Sacubitril that caused hives.