## Section 1 — General Information

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| **Name of the drug CADTH is reviewing and indication(s) of interest** | | **Asunaprevir** |
| **Name of the patient group** | | HepCBC Hepatitis C Education and Prevention Society |
| **Name of the primary contact for this submission:** | | REDACTED |
| Position or title with patient group | | Board Member and HCV+ Volunteer |
| Email | | REDACTED |
| Telephone number(s) | | REDACTED |
| **Name of author (if different)** | | |
| **Patient group's contact information:** | Email | info@hepcbc.ca |
| | Telephone | 250-595-3892 |
| | Address | #20-1139 Yates St. Victoria BC V8V 3N2 |
| | Website | www.hepcbc.ca |
| **Permission is granted to post this submission** | | X Yes ☐ No |

**CADTH will post this patient input submission on its website if permission is granted. See CDR Update — Issue 99 for details.**

### 1.1 Submitting Organization

HepCBC is a registered non-profit society run by and for people infected with, or affected by, hepatitis C. Our mission is to provide education, prevention and support to those living with HCV. We now have two offices, one each in Victoria and Vancouver, BC. Founded in 1996, and run primarily by volunteers living with HCV, we have activities and groups in Nanaimo, Vancouver, and Surrey, BC, and travel throughout the province doing outreach. Our representatives attend provincial and federal-level conferences and we give information and support world-wide through our website. We publish a monthly bulletin, the *hepc.bull*. We provide peer support, anti-stigma activities and prevention education to the general public, and general hepatitis information especially to baby-boomer, aboriginal and immigrant communities, and those living in rural/remote locations. We encourage testing among at-risk groups -- including those who are no longer at risk but may have contracted hepatitis C decades ago. We work alongside local HIV/AIDS organizations in support of co-infected people.

### 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:*

HepCBC Hepatitis C Education & Prevention Society has received funding for hepatitis C-oriented projects such as publishing educational materials, organizing educational forums, attending and presenting at educational conferences, advertising in newspapers (events and hepatitis C patient awareness), and holding awareness activities from the following pharmaceutical companies over the last four years: Merck Pharmaceuticals, Hoffman-LaRoche, Vertex Pharmaceuticals, Gilead Sciences,

Janssen Pharmaceuticals, Bristol Myers Squibb, Boerhinger-Ingelheim, and AbbVie, plus support from Rx&D pharmaceutical umbrella organization.

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

Three of those who contributed individual patient submissions have attended several educational conferences and meetings for which registration and travel expenses were funded by the pharmaceutical companies listed above.

## Section 2 — Condition and Current Therapy Information

### 2.1 Information Gathering

This report was developed using data from:

(1) A patient survey advertised through our website and our email list. In total there were submissions by four people living with hepatitis C (one male with genotype 1a and three females with genotype 1b, with mean age 65 years). All were from British Columbia, all four had advanced liver disease (two with cirrhosis) and all three females had successfully been cured using asunaprevir+daclatasvir on a clinical trial.

(2) In addition, three of the above are volunteers who have actively manned HCV+ phone and email support systems or several years, and have broad knowledge of patient concerns and experiences; one of these is a patient-researcher who has been reading and reviewing scholarly articles about hepatitis C for twenty years.

(3) We've included aggregate input from one of our monthly support groups as well.

### 2.2 Impact of Condition on Patients

In order of frequency, our members reported the condition-related symptoms below. No symptom was universally-reported; some people exhibit more symptoms than others.

Most frequently reported: Fatigue, digestive problems, muscle and joint pain, brain fog, irritability, depression, cognitive failure (concentration/attention span, speed of thought, fluency of speech, learning and memory), insomnia, slower motor reflexes, and general fear of social interaction (coupled with a fear of being stigmatized).

Also reported: Water-retention, acid reflux, gall bladder attack, lack of appetite, inability to digest many common foods, sensitivity to/avoidance of noise or light, sexual dysfunction, rapid eye deterioration, electrolyte imbalance, iron overload/imbalance, detecting chemical odours (in sweat, urine, stool, breath), anxiety, rage, hypothyroidism, Krohn's disease, seizure disorder, metabolic syndromes (fatty liver, pre-diabetes), toxic encephalopathy, ascites, and esophageal bleeds.

Day-to-day life is affected by all of the above, but in order of frequency and importance: Fatigue, muscle/joint pain, and slower motor reflexes limit both general activity and job productivity and/or

effectiveness. Cognitive failure, fear of stigma and fear of social interaction limits both job effectiveness and general social interaction. Pain during movement can lead to either overuse of painkillers (which can further damage liver) or to avoidance of movement (which can lead to weight gain and other degenerative problems) Digestive and iron-overload problems limit how one shops for and cooks food, one's diet vs. the family's diet, and when (how often) one cooks or eats, affecting this important part of family life and social interaction.

Financial difficulties ensue due to limited job possibilities coupled with the cost of controlling the disease: special food, supplements, and treatment drugs.

Feeling one must keep ones' HCV status secret, or to lie about it in order to preserve one's job or relationships is debilitating to one's spirit.

Though the symptoms above can take several decades to become obvious, for many they become manifest much earlier and are often misdiagnosed as due to some other condition as doctors do not suspect hepatitis C in non-IVDU patients.

The patients in the baby-boomer age cohort have generally had hepatitis C for many decades. Some have been symptomatic for many years, while others are becoming symptomatic for the first time. In either case, hepatitis C is now affecting their careers and family life drastically; they think that without treatment, they will not be around much longer and must prepare themselves and their families for this. They hate the pain and the societal stigma, but especially the mental and physical changes which prevent them from working or playing as they used to. The ones that have been cured are generally celebrating the fact they are able to get their lives back, but wish they could have been cured much earlier.

What we are struck by at this particular time, both from the individual submissions we received and from what we are hearing on a daily basis from our clients, most of whom are in the "baby-boomer" cohort, is a growing sense of desperation and despair. They are like drowning men who can see the shore, but they're swimming against the tide, and the harder they swim, the further the shore seems to be receding into the distance. They know life-saving drugs are out there if they can just hold on long enough, to keep the liver cancer and end-stage-liver-disease at bay until the drugs are covered by their provincial drug plans. They know their time is almost over -- unless they can get treated in time. They are depressed, angry, and yet - sometimes - hopeful.

The debilitating stigma is still there, but it seems HCV+ baby-boomers are generally becoming more willing to be open about their status. The promise of the new drugs has meant hepatitis C has been covered more often in the media, and the public is starting to hear the voices and see photos of people fighting the disease who are clearly not IV drug users; stereotypes which fed the stigma are being questioned. This makes it easier for people to 'come out of the closet' and seek testing and treatment. Patients and their families are at the end of their ropes, ready to do whatever it takes to get onto treatment, even if that involves exposing themselves to possible stigma at work, or amongst friends and family.

At the same time a high percentage of HCV+ people are asymptomatic while the disease does its terrible damage to their bodies. Many of them do not even know they have the disease until they receive the terrible news that they have liver cancer, or need a transplant. These people need to be tested, found, and treated as soon as possible. They are in as much danger of morbidity and mortality as those who are symptomatic.

## 2.3 Patients' Experience with Current Therapy

Through the Internet and support groups, patients are very knowledgeable about the side-effects of interferon, ribavirin, telaprevir, and boceprevir (while simeprevir is now publicly funded in BC and patients know it has fewer side-effects than the other protease inhibitors, few patients are taking it simply because it is still paired with interferon and ribavirin.). While recognizing and appreciating their merits, they want to avoid all of these drugs (with the possible exception of simeprevir) as much as possible.

The concept "current therapy" has become far more diversified over the last year, with patients getting treated quite differently according to genotype, their stage of liver disease, and whether they have private insurance or not. A large percentage of patients we come in contact with are being "warehoused", either by doctors or by themselves, simply rejecting the idea of taking current therapies, knowing vastly superior drugs are so close to being approved.

Every patient agrees that interferon, though it has helped many be cured of hepatitis C over the years, is like a slow and long-lasting torture; the side effects (both short and long term) can be particularly debilitating, and the efficacy so low compared to current DAAs that it should no longer be given to any patient.

(F, 67): I am treatment-experienced, with interferon + ribavirin, 2010-2011. The treatment almost killed me and it didn't work. Later I was cured with an interferon-free, ribavirin-free BMS trial."

(M, 65): "My only experience with 'current therapy' was with a Merck interferon-free trial, but it did include ribavirin. I had a major episode of atrial fibrillation during the trial and I was taken off the trial. I am now hoping to get treated with a medication which does not interfere with my heart medications."

## 2.4 Impact on Caregivers

The main impacts we see on caregivers are poverty, a sense of isolation, and uncertainty about the future. Poverty is due to their untreated HCV+ partner's/parent's/child's inability to lend support to the family, followed by the increased medical expenses as their condition deteriorates. Often they experience a financial double-whammy if their CHC partner has been unable to have a normal working-life, and when the partner goes through treatment or serious phases of their illness, the caregiver may have to alter his/her working life as well. Caregivers often feel isolated due to stigma against those with hepatitis C and ignorance about how it is spread. They also spend much of their time looking after their HCV+ family member, or doing the chores the family member no longer can do, which cuts down on the time they used to have to socialize. There is little way to plan for a future when you don't know how long your partner will be able to live independently, or to live at all; uncertain if your partner will be able to benefit from the new HCV drugs, or if he or she will develop liver cancer or need a liver transplant before these new treatments are accessible.

Caregivers of aging CHC patients are particularly vulnerable health-wise, emotionally, and financially. They too are aging, and in addition to their partner's or loved one's illness, they are often weary and may be in need of care themselves. They suffer watching the mental and physical health of their CHC partner deteriorate, and may even be the victim of their partner's short temper. Caregivers share with the CHC patient the problems of societal stigma and insecurity about whether they will be able to live independently or comfortably in what they'd hoped would be their "golden" years.

## Section 3 — Information about the Drug Being Reviewed

### 3.1 Information Gathering

***Same as previous Section 2.1***

### 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:*

HepCBC is generally enthusiastic about asunaprevir, though its use is fairly limited compared to daclatasvir. It is especially successful with genotype 1B patients. We are only aware of its being used in combination with daclatasvir (or daclatasvir+beclabuvir) plus or minus ribavirin, plus or minus interferon. A small % of patients report common side-effects such as headache, fatigue, nausea, and diarrhea (plus pruritis or insomnia if ribavirin is added), but these very rarely lead to withdrawal from treatment. Asunaprevir (with daclatasvir or daclatasvir+beclabuvir) is particularly well-tolerated and safe, has extremely high efficacy even for patients with cirrhosis, has a short treatment time, has minimal drug-drug interactions and presents the opportunity to further individualize treatment combinations.

Patients tend not to differentiate the various new drugs from one another since they're all so much better than the existing ones, and share the characteristics of being mostly tested on genotype 1, far greater efficacy, a far shorter treatment time, no interferon or needles, very few side-effects, and an extremely high price-tag. They really like the fact BMS' asunaprevir, in combination with daclatasvir (and possibly other drugs in the future), will give some competition to Gilead's Harvoni and AbbVie's Holkira Pak, anticipating that the price of a cure will go down and Pharmacare will be more likely to cover their treatment and to get rid of the criterion of proving significant liver damage. They also are pleased that it is being reviewed on a stand-alone basis and that the manufacturer appears open to research and use of its HCV drugs with products from other companies. They are excited about asunaprevir's diverse uses and that it has successfully been through trials paired with not only with daclatasvir, but with daclatasvir+beclabuvir (with/without ribavirin) and with daclatasvir+pegylated interferon+ribavirin. They are also very pleased to see that some of the most successful trials involve its use with cirrhotics (Unity2 trial). The lack of food requirements is a plus, and the number of pills per day is of little consequence to patients; the addition of ribavirin and/or interferon is more problematic though the shorter treatment time means that the side-effects will not be as serious over time. The addition of asunaprevir to Canada's hepatitis C "medicine chest" will be very exciting. Patient advocates are keenly aware of the prospect of actually being able to eradicate the disease entirely from the world, though the price will have to be greatly reduced if we are to truly eliminate it from every person in every country. Patient voice:

(M, 65): "Although I have not had 'direct experience' with daclatasvir and asunaprevir, 2 of my very dear friends were cured with it. THANK YOU. They were both GT1b. I personally could not get on a trial with daclatasvir/asunaprevir. I have 1a and failed treatment 4 times. The first 3 were with INF/RBV and the last on inhibitors. My experience on inhibitors was fantastic in terms of quality of life but a pre-existing cardiac condition acted up and I had to be pulled off. I have only hear GREAT THINGS about daclatasvir and asunaprevir both personally and from my exposure to the clinical trial reviews. I would really like to

see the daclatasvir+asunaprevir combo approved as soon as possible and hopefully covered very quickly by provincial Pharmacare plans."

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

Three respondents had direct experience with asunaprevir, as genotype 1b patients in a daclatasvir+asunaprevir trial. Patient voices:

(F, 67): "After being cured, a person could lead a relatively "normal" life again. The positive side would be freedom from the damage the virus does to the liver and a possibility of the liver regenerating itself in 8 years or so. I had already failed one treatment INF plus ribavirin which had totally debilitating side-effects. Before the daclatasvir/asunaprevir trial I was F4 cirrhotic, Fibroscan 49.6 kPa. The treatment had no side-effects and I was even able to walk the half-marathon in the middle of treatment without any difficulties. One year following treatment I tested at 18 kPa so my cirrhosis is almost gone. I look forward to reversing it entirely over time."

(F, 68): "I had the IL28b TT allele, and it was no problem with the daclatasavir/asunaprevir combo. I had already gone through several other treatments unsuccessfully: INF alone for 1 year with difficult side-effects; INF+ribavirin for 1 year with even more difficult side effects but increased weight loss; low-dose "maintenance" INF for 1 year with few side-effects; and Pegasus+ribavirin for one year with very difficult side effects. Before treatment I was F2. A year later I was F1. It was great not to have to use a needle, and amazingly the treatment had no side effects. In fact, I don't believe people should expect any side effects from the new DAAs. I have slowly and steadily been getting back to what I now realize is normal. I am not in constant fear of infecting anyone. I have my energy back, and am physically able to visit my family in Australia. I am able to take on more volunteer work. If I had not retired, I would be working! Many, even most of my aches and pains are gone. I still suffer eye problems that started soon after my interferon treatments that have necessitated eye surgeries. Since being cured I have had two other surgeries that I had been postponing, since I was worried about infecting my surgeon. I have a life partner now. It really makes me happy to be able to share this!"

## Section 4 — Additional Information

(F, 67): "Patients are really concerned that the prices of these drugs will be so high that CADTH (and/or provincial Pharmacare plans) will either not approve the treatment at all, or will make treatment qualification criteria very high, or will decide that treatment-naïve people should first take and subsequently fail the current standard of care (with both interferon and ribavirin) before they're allowed to take any new DAA therapy. There are no other diseases in which a patient has to prove significant damage to his/her bodily organs in order to get treated. And there are no others in which a patient has to take such clearly inferior - even harmful – treatments simply because of price."