

## Section 1 — General Information

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| <b>Name of the drug CADTH is reviewing and indication(s) of interest</b> | ledipasvir plus sofosbuvir – for chronic hepatitis C                |
| <b>Name of the patient group</b>   | HepCBC Hepatitis C Education & Prevention Society                   |
| <b>Name of the primary contact for this submission:</b>                  | REDACTED  |
| Position or title with patient group                                     | Board Member, and HCV+ Volunteer                                    |
| Email  | REDACTED  |
| Telephone number(s)  | REDACTED  |
| <b>Name of author (if different)</b>                                     | n/a   |
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| <b>Permission is granted to post this submission</b>                     | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> 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. Our only office is in Victoria, BC. Run primarily by volunteers living with HCV since 1996, 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 groups, anti-stigma activities and prevention education to the general public, and general hepatitis information especially to baby-boomer, aboriginal and immigrant communities. 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, Boehringer-Ingelheim, and AbbVie.

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

The author of this report and 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 fifteen people living with hepatitis C (6 male, 9 female, with mean age 60 yrs, range 35 – 70 yrs, average 59.1 yrs) Genotypes 1 through 4, and all ranges of liver damage (F0 through advanced cirrhosis) were represented. Thirteen were from British Columbia, one from Winnipeg, and one from Texas, USA. The Texan was the only respondent who had actual lived experience with this drug combo.

(2) In addition, three of the above are volunteers who have actively manned HCV+ phone and email support systems for several years, and have broad knowledge of patient concerns and experiences.

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

### 2.2 Impact of Condition on Patients

The patients in this 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. A few of their voices:

(F, healthcare worker): "I have progressive liver disease. The abdominal cramps and pain, the persistent physical and mental exhaustion mean that I cannot work in my profession and cannot even exercise to keep healthy. My husband does most of my personal care; he cooks and cleans the house."

(M, engineer and artist): "In 2008 I began to notice a dimming of my ability to focus on complex details. By 2011 I could no longer work, suffered sexual dysfunction, felt like the "walking brain dead", without energy or motivation, and discouraged."

(F, teacher): "I am currently not working due to extreme fatigue, inability to concentrate for a period of time, plus body and joint pain. I am not walking or exercising as I used to. I'm barely managing day to day chores and housework."

(F, housewife): “I have not experienced any physical symptoms that can be attributed to having Hep C. However, last October a liver biopsy indicated that I have progressed, in the previous year, from Stage 1 to Stage 3 fibrosis. My hepatologist has suggested that I seriously consider starting treatment. To this point I have not, because there has been nothing available that is tolerable with [consistently] positive results.”

(F, housewife and singer): “Not only do I feel the social shame at having the disease, but I am experiencing physical barriers such as exhaustion and lack of energy to do anything meaningful. I forget what it feels like to be ‘normal’ or feel healthy, and I am losing ambition to accomplish my goals. I suffer from ascites, and when I walk or try to do anything that takes muscle movement, such as walking, I feel that my legs will not hold me up. I have learned that the tiredness comes from toxins that cannot be cleaned out by the ailing liver, which then dumps the toxins for the kidneys to deal with. I have scarring on my kidneys as a result of the hepatitis C.

Eating, too, is a challenge. My main diet is peanut butter on toast, as it is one of the few things left which I can tolerate, and actually like. I have depression when I realize it takes me forever to accomplish anything, or when I feel sick, knowing that I may never feel good again. I have no life now. I have no way to pay for the expensive treatment. If Pharmacare does not cover the cost, I have no hope. ”

### **2.3 Patients’ Experiences With Current Therapy**

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) are particularly debilitating, and the efficacy so low compared to current DAAs that it should no longer be given to any patient. Their voices:

“Have done pegylated interferon with ribavirin. My treatment finished a year ago and I relapsed at SVR week 12. I’ve never done the sofosbuvir/ledipasvir treatment; I can only speak of the interferon course which caused me to feel worse than the condition [CHC] ever did.”

“I’ve been through treatment 4 times unsuccessfully with interferon, and recently was on a Merck DAA trial. Though I was pulled from that trial after 10 days due to a pre-condition (atrial fibrillation episode), during that time my viral load dropped from over 10 million to just 84 copies. No side-effects. In fact, after a few days I felt better than I had in years!! The Merck DAA I was on is probably similar to the drugs being reviewed here.”

“I’ve been on 4 treatments, none of which was successful. The last treatment was in 2013 when I was on a 48-week regimen of interferon, ribavirin and Victrelis (boceprevir). This treatment was particularly grueling, and I was anaemic almost immediately. In addition to the lack of energy and extreme lethargy, I broke out in numerous rashes. I had little energy and my blood, platelet and hemoglobin counts were way out of normal range. I would not have been able to work when I was on this treatment, so it was fortunate I was on long term disability at the time. I was taking approximately 20 pills a day and an injection of interferon once a week. I was into remission at the 4th month and still in remission at the end of treatment in December, but unfortunately, I was not able to sustain my SVR and tested positive again in May of this year.”

“I am taking no therapy as I have had persistent clinical depression for 45 years. Interferon was not recommended for this reason”

A woman describes her unsuccessful 2009-2010 interferon and ribavirin treatment: "Treatment was brutal...it would have been worth it if I had cleared the virus, but unfortunately that is not the case. Side effects that were hard to deal with were weakness, loss of muscle tone (25lbs weight loss), anemia (required Epo injections) extreme emotional instability, dry cough, dry mouth, dry eyes, rash, and joint pain. Fortunately, I completed a 12-week clinical trial with Merck last week (still awaiting SVR news). This treatment was a little easier to manage. However, I still experienced fatigue, migraine, stomach upset, cramp, dizziness, and light-headedness. Being a much shorter treatment time made it tolerable."

Another woman describes her first treatment (52 weeks of interferon plus ribavirin) in 2007: "I suffered severe anemia during treatment and had to undergo a total of eight blood transfusions. HCV was non detectible at the end of treatment, however it returned one month later."

Note that these are not anomalies. Our files are full of reports such as these or worse. It is true there is a large undiagnosed baby-boomer population awaiting treatment. However there are two other large already-diagnosed populations hoping to get treated very soon: those who have never gone on treatment due to their fear of interferon (and, to a lesser extent, ribavirin), and those who have failed treatment with interferon. All of these patients are at risk of liver failure (or failure of kidney or some other organ[s] due to the HCV), liver cancer, or being put on the transplant list. The sooner all these people get treated, the more likely these expensive and debilitating HCV-related complications will be averted.

## 2.4 Impact on Caregivers

Caregivers of aging CHC patients are particularly vulnerable healthwise, 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. 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 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 to be their "golden" years. Some of their voices:

"If these new drugs are not covered by my provincial plan, we will have to take some actions to cover these costs – perhaps refinancing our house or selling our house and moving into an apartment. This is one reason I have decided to rejoin the work force although I may not be ready physically or psychologically to do so – only time will tell. Having said that, I would imagine we are far better off than most patients in this situation."

"My caregiver is tired, stressed out, and unable to attend to his own interests and hobbies because of his constant need to care for me."

"On first treatment in 2009-2010, my daughter took the year out to be with me. It was hard to cook, clean and take care of myself. My relationship with my husband was put through the test. We were getting counselling. They had it rough as well as me."

## 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:*

These two individuals' statements echo the community's consensus about the sofosbuvir and ledipasvir combo:

"I am waiting, as I know many others are, for a treatment that does not require interferon. I often feel a lot of stressful anxiety knowing that the damage to my liver is now advancing quicker than it has previously and that I do not yet have access to a tolerable, successful treatment (such as sofosbuvir plus ledipasvir)."

"Many good things have been said about sofosbuvir, however I do not know much about ledipasvir yet. I know that sofosbuvir is a cure and if it is mixed with something without bad side effects, it will be a good combination...If this new drug is safe to use for those with cirrhosis or liver transplant, then I am ready to try it out. As long as the side effects are not as bad as those with interferon use, I am willing."

Another worry of patients is that their choice of drugs and when to take them may have long term negative consequences if they do not choose wisely: "The dilemma I am facing is that I have heard that sofosbuvir may soon be approved in Manitoba. If I should take this drug and I relapse, my specialist has advised me that there is a possibility I may not be eligible for the sofosbuvir/ledipasvir combination in the future."

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

Only one respondent had experience with this drug combo. His report:

"At the beginning of the clinical trial my HCV RNA was 10,870,000 IU/ML. Week 2 was 7,7400,00. Week 3 was 78. Week 4 was 'undetectable'. I had no side effects. I've been SVR for 16 months now."

"When I entered the clinical trial in April, 2012 I was very sick. I could not work, reason or think very well. My color was grey. I have seen dead people that looked better than I did. My overall state was miserable. I was diagnosed with stage 3-4 cirrhosis by needle biopsy. My doctor said that in all likelihood I would die from liver failure within 2 years. Toward the end of the 12 week treatment, I realized my brain was returning to me. I was overjoyed to feel the wheels begin to turn again. As weeks passed, I started to see things around me. My world, that I now realize had been reduced to the size of a postage stamp, started to expand. I began to feel happy, and hopeful - feelings I had not had in years. My social life was nearly dead. My wonderful, supportive wife and I began to have dinner with friends again. I chased my lovely wife around the bedroom, and she let me catch her! I got my life back because of this new drug. I have been a successful artist for 30+ years, and am back to working nearly all day again - a far cry from sitting in a chair all day and staring out the window in a stupor."

I went to see my hepatologist in Dallas recently. Using a high resolution scan made for non-invasive observation of the liver, he was completely surprised to see no cirrhosis in my liver. There was fibrosis, but no cirrhosis.”

## Section 4 — Additional Information

“There are many patients with my condition – Hep C with compensated cirrhosis. Our time is running out... The rules dictated by the drug companies regarding trials are very stringent and, for the most part, seem to eliminate the patients such as myself that require the drugs as urgently as possible. Hospitals, drug companies, and governments must all work hand-in-hand very closely in their efforts to combat and eradicate this virus.”

“If you have Hep C you will eventually start to feel bad, and everything about you will start to turn down, like a dimmer switch on a light. Hep C attacks your liver, and will eventually do terrible damage to it, as well as to the rest of you. However, getting rid of Hepatitis C. is not for everyone.”

There is a great concern among our community that the all-but-certain approval of this drug combo is going to contain such stringent treatment criteria that many if not most of our members will be unable to access this treatment they have been waiting so long for, and which they truly see as a life or death matter. They have also been hearing recommendations to treat first those people most in risk of dying of the disease (those with F2-4 fibrosis) and those most in risk of transmitting it (IVDU). While we certainly agree that these two populations should be treated as soon as possible, two ironies stand out in this proposed triage solution:

For one, the earlier one’s HCV is treated, the more likely it is that treatment will succeed, and the more quality years of life will be attained. So the idea of denying treatment until one can demonstrate significant organ damage seems not only cruel but unpractical.

The second irony is that providing treatment to IVDU while denying it to non-IVDU will only encourage those who are in recovery, or have never used drugs, to consider using drugs simply to qualify for treatment. While this may sound ridiculous, we know that others have attempted binge-drinking to raise their ALT levels to the point they are eligible for treatment. CHC patients are getting desperate, and it’s really critical that ALL patients be given access to these life-saving treatments. These three patients will have the last word:

“Patients with Hep C need to be given a chance to get treatment as early as possible ...The shorter period of time this is [between diagnosis and treatment], the more society will benefit from these individuals contributing to society rather than draining it over a long term.”

“Please provide all of us with a treatment that is going to make us disease free. This, in the long run, will save the health care system a lot of time and money by stopping the disease before it progresses to the transplant stage...If you or your loved one had this disease, what treatment would you want?”

“Please make this available before my time runs out. Thank you.”