

Section 1 — General Information	
Name of the therapeutic review	Drugs for Chronic Hepatitis C Virus Infection
Name of patient group	Canadian Liver Foundation
Patient group's contact information:	3100 Steeles Avenue East, Suite 801 Markham, ON L3R 8T3 416-491-3353 clf@liver.ca www.liver.ca
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1.1 Submitting Organization

When it was founded in 1969, the Canadian Liver Foundation (CLF) was the first organization in the world dedicated to supporting education and research into all forms of liver disease. Today, the CLF continues to be the only national organization committed to reducing the incidence and impact of liver disease for Canadians of all ages living with or at risk of liver disease. The CLF is the sole lay organization in Canada directing funds specifically for liver disease research and has invested more than \$20 million in the scientific search for causes, preventative measures and potential treatments for liver disease, including viral hepatitis. As the largest community organization dedicated to liver disease, the CLF reaches over 250,000 Canadians through our public and professional education programs, patient support programs and other fundraising and outreach efforts. Over the past 40+ years, the CLF has invested more than \$50 million in health education and prevention programs.

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:*

In the past, the Canadian Liver Foundation has received unrestricted educational grants and/or has worked on joint initiatives with Abbvie Corporation, Astellas Pharma Canada Inc., Boehringer Ingelheim (Canada) Inc., Gilead Sciences Canada Inc., Janssen Inc., Merck Canada Inc., Novartis Pharmaceuticals Canada Inc. and Hoffmann-La Roche Limited.

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

The Chairman of the Canadian Liver Foundation, has received honoraria from Abbvie Corporation, Boehringer Ingelheim (Canada) Inc., Merck Canada Inc., Janssen Inc., Hoffmann-La Roche Limited and Bristol Myers Squibb.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The CLF has participated in four previous CADTH reviews of hepatitis C drug therapies currently approved for use in Canada. As part of our submissions, we invited patients, caregivers and healthcare professionals from across Canada to fill out online surveys modelled on the CADTH questionnaire. As the current therapeutic review includes boceprevir, telaprevir, simeprevir and sofosbuvir and the questionnaire includes the same questions, we have compiled our submission using input from the 296 survey responses previously received along with additional insights provided by our Chairman based on his extensive experience.

2.2 Impact of Condition on Patients

Please note: *Quotes in italic text are excerpts from patient survey responses.*

Hepatitis C affects individuals from all walks of life as a result of the different modes by which they contracted the virus. The largest age demographic is adults born between 1945 and 1975. The following are estimates of the demographic breakdown:

- **Ex-injection drug users** (experimented in the 1960s and 1970s) -- estimated 40% of all infected
- **Immigrants from high prevalence countries** (Vietnam, Pakistan, Somalia, Italy, Eastern Europe, China, Egypt, Japan, Korea) -- estimated 33% of all cases
- **Current injection drug users** -- accounts for ~10% of all cases
- **Post transfusion (prior to 1990)** -- < 5% of all cases

As hepatitis C can progress slowly and silently, many patients unknowingly live with the disease for years, even decades, without any obvious symptoms. Their diagnoses often come as a complete shock and they then fear for their future and worry about infecting others.

Hepatitis C exacts a high toll on patient's psychological and spiritual well-being as well as their sense of self-worth as a direct result of the stigma associated with hepatitis C and of the misperceptions and fears of those close to them. Patients report of being shunned by friends, family and co-workers which leaves them without social networks and support systems. Some have even reported negative reactions from health care professionals. The physical symptoms of the disease wreak havoc on their mental capacities and the burden of living with the disease leaves them isolated and depressed. Personal relationships disappear over time and many patients report that their marriages ended because their partners could not cope with their illness.

- *“My marriage ended directly due to this chronic condition.”*
- *“I do not have the energy to socialize so old friends have gone by the wayside. The stigmatization of the disease even among family members has been incredibly isolating.”*
- *“My life is filled with depression and I have been stigmatized by many doctors and health care professionals with some even refusing to treat me”*
- *“My marriage of 20 years broke up in part due to hepatitis C and my sister refused to see me anymore.”*

Once patients progress to more advanced disease they find their lives unbearable due to physical symptoms which impact their ability to support themselves or even function on a daily basis. Patients report struggling to maintain focus on work and even household tasks like cleaning, laundry, cooking or cutting the lawn are too much to handle due to the constant fatigue and pain.

- *“Lots of activities are out of reach – walking, lifting, riding a bike or simple things like cleaning the house, having a shower and making dinner all in a day can be exhausting.”*
- *“I am 35 and feel about 80.”*

Chronic fatigue, mental confusion (when the liver can no longer clear the body of toxins), memory loss and mood swings mean patients who once had gainful employment or even their own businesses now live at or below the poverty line.

- *“I have been on disability for six years”*
- *“I went from living a comfortable life to living far below the poverty line.”*
- *“I have a limited budget and constantly go hungry.”*

Patients also report a range of other debilitating symptoms including nausea, headaches, sensitivities to light and food, itchy skin, abdominal pain, sleeplessness, slowed reflexes, psoriasis, peripheral neuropathy, osteopenia, diarrhea and muscle wasting.

2.3 Patients' Experiences With Current Therapy

Please note: *Quotes in italic text are excerpts from patient and health care professional survey responses.*

Many hepatitis C patients have undergone treatment several times with different generations of drug therapies – often unsuccessfully. Currently, eligible patients in most provinces can access triple therapy which combines pegylated interferon, ribavirin and one of two direct-acting antivirals -- boceprevir or telaprevir -- for 12 -48 weeks. At this time, neither simeprevir nor sofosbuvir are widely available as they have only recently been approved for use in Canada. Simeprevir is another triple therapy option for genotype 1 patients while sofosbuvir is used as a triple therapy for genotypes 1, 4, 5 and 6 but without interferon for genotypes 2 and 3.

Triple therapy with boceprevir or telaprevir still necessitates the use of interferon and ribavirin which means patients experience many of the same symptoms when undergoing treatment as they did with previous dual therapy. Patients report suffering from everything from moderate fatigue and muscle aches to anemia, sleep loss, depression, mood swings, joint pain, rashes, hearing loss, skin sores, hair loss, headaches, chills, nausea, severe fatigue and excessive weight loss. With telaprevir in particular, a special warning was issued about a life-threatening rash.

(dual therapy) *“Treatment was difficult physically, mentally and put a strain on my marriage and family. I had many side effects including overwhelming fatigue, weakness, shortness of breath, nausea, headaches, mouth sores, hair loss. I developed anemia, hyperthyroidism then hypothyroidism. I had bouts of mania, anxiety and panic attacks and was somewhat agoraphobic.”*

(triple therapy) *“Telaprevir was terrible...really made me sick. I experienced weakness in my extremities especially legs, nausea, headache, severe itchiness, diarrhea, sore throat, cough...general feeling of unwellness.”*

Hepatitis C treatment with dual therapy involved weekly injections of interferon and 6-8 ribavirin pills per day. Triple therapy added even more pills – 9-12 per day for boceprevir or telaprevir – making the treatment regime complicated for both patients and caregivers to manage especially when also coping with side effects and the additional medication required to treat them.

“Triple therapy has increased our cure rate a little, however for patients with more advanced liver disease current treatment options are a struggle to deal with side effects of interferon therapy as well as anemia factors. We have had increased use of blood transfusions which also does not come without risk.”

Triple therapy with boceprevir and telaprevir has significantly improved the cure rate for genotype 1 patients who can withstand the interferon-related side effects. Unfortunately, many of the sickest patients cannot tolerate this therapy leaving them with no other options until the newest drugs, simeprevir and sofosbuvir, become widely available.

2.4 Impact on Caregivers

Please note: *Quotes in italic text are excerpts from caregiver survey responses.*

The burden of care for patients with hepatitis C often falls to spouses, parents and adult children. The symptoms of hepatitis C and the side effects of current therapy can leave patients completely dependent and unable to contribute financially, physically, psychologically or emotionally to the household or the relationship. Caregivers report having to endure their loved one’s mood swings, dietary problems, lack of energy and concentration while shouldering the responsibility for managing doctor’s appointments, drug regimens and all household responsibilities. Due to a patient’s inability to work, caregivers often become the sole income earner which adds even more stress. As the patient’s symptoms and behaviour become more difficult to manage, families and marriages can break apart due to stress, financial difficulties and social isolation.

“My spouse has hepatitis C and he becomes regularly fatigued and depressed. I can’t rely on him being able to complete tasks at home. We have had to spend a lot of money on nutritional supplements, medications and food supplements. The financial pressures on our household are overwhelming.”

“Loss of income, changes to social interactions/relationships with family and friends, social isolation. Stress, depression and living with someone who was like a Dr. Jekyll and Mr. Hyde. It was very hard to know from one moment to the next how he would behave or respond to any given situation. He struggled with dietary changes and meal planning was impossible. He lost 50lbs, all of his hair, and was very anemic especially with the first treatment. 48 weeks seemed like endless torture with no certainty as to whether or not it would work.”

As already noted, hepatitis C treatment is complex and comes with many side effects which often require additional medication. For physicians and nurses, the challenges of caring and achieving a cure for hepatitis C patients are enormous. Patients require a great deal of education and counselling about treatment options and if they decide to undergo treatment it can require additional tests, lab results, forms and appeal letters before patients can actually access the therapies they need. For patients that do undertake treatment, it will take weeks to determine if the treatment will work and many patients have to discontinue before the course of treatment is complete due to their lack of response or severe side effects.

“Current triple therapies are moderately effective in early disease. However, side effects are significant. Efficacy is not good when the patients have advanced fibrosis.”

“Current treatments are much more effective than the previous dual therapy but also come with additional side-effects. We see increased and more severe anemia which warrants more use of Eprex, more blood transfusions, anorectal symptoms, rash, dysgeusia, depression, irritability, mood swings, fatigue, shortness of breath, loss of appetite and many more symptoms which need to be managed and often result in prescribing of medications to manage side-effects.”

Section 3 — Information about New Drugs

3.1 Information Gathering

As noted in Section 2.1, the CLF has gathered patient input for previous CADTH reviews of all the hepatitis C drugs involved in the current therapeutic review. Our responses below are based on the feedback from patients, caregivers and health care professionals who participated in those surveys. While we were not able to collect feedback from specific patients who had participated clinical trials for simeprevir and sofosbuvir, our submission includes insights from healthcare providers who have treated patients with these therapies as part of clinical trials.

3.2 What Are the Expectations for New Drugs or What Experiences Have Patients Had to Date With New Drugs?

The first DAAs, boceprevir and telaprevir, represented a huge leap forward in efficacy for patients with genotype 1. Unfortunately, the addition of a third drug made the treatment regime more complicated for patients, caregivers and health care professionals and all the interferon-related side-effects remained the same. Many patients have undergone treatment multiple times and are desperate to find a drug therapy that they can endure and that will ultimately cure them. When asked about the factors that would affect their decisions regarding future treatment, patients rated ‘possible side effects’ and ‘odds of a cure’ as being the most important amongst the variables listed below:

- Total length of treatment
- Predictability of the length of treatment
- Medication schedule
- Possible side effects
- Odds of a cure for their genotype
- Interferon-free

Simeprevir and sofosbuvir both offer improvements in efficacy and side-effects – the two key factors that rated highest with patients. In addition, they provide shorter and more predictable treatment lengths – simeprevir is 12-24 weeks while sofosbuvir is 12 weeks for almost all genotypes (12-16 weeks for genotype 3) -- and a reduced pill burden (1 pill per day vs. 4-6 for boceprevir and telaprevir). These improvements will make a substantial difference in patient's willingness to undergo treatment and their subsequent compliance.

Section 4 — Additional Information

In 2013, new statistics were released showing that liver cancer is one of deadliest cancers and is one of the few cancers in Canada that is on the rise. The rise is attributed primarily to undiagnosed and untreated hepatitis B and C. Treating hepatitis C patients at a point at which they are most likely to respond (long before cirrhosis has developed) will make a significant impact on liver cancer rates in the future. And yet, the benefits of treatment extend beyond the benefits of preventing progressive liver disease and liver cancer. Successful treatment of patients with hepatitis C means that they are no longer infectious to others. Thus by decreasing the size of the infected pool, an additional benefit will be a reduction in the risk of transmission, and ultimately a reduction in the new infection rate.

The most conservative estimates are that there are 180,000 people living with chronic hepatitis C in Canada. A more realistic number is closer to 350,000 to 400,000. At present, approximately 5,000 patients are treated annually in Canada which means that with the aging of the predominantly baby boomer infected population, mortality will increase substantially in the years to come.

Decisions as to which patients to treat and when to treat them should not be determined solely by the severity of their liver disease. As hepatitis C progresses, it can also impact other organ systems causing, for example, progressive renal failure. In addition, the psychological state of patients should be taken into consideration. Patients with hepatitis C live under a perpetual cloud – they know they have a stigmatized disease and understand that over time it is only getting worse. They worry that they may not survive long enough to get treated or that they may need a liver transplant or that they may develop cancer. All hepatitis C patients suffer under this mental stress, including those with mild disease who have not been deemed to be eligible for treatment in many provinces. It is unacceptable to continue to allow patients to live with this psychological burden when effective treatment is available.

We recognize that the newest agents – simeprevir and sofosbuvir – are expensive (an estimated \$80,000-\$100,000 for a course of treatment) and that the interferon-free agents coming in the next 2-3 years will be even more so. We cannot therefore afford to treat everyone all at once. We must however determine a way to incorporate the newer and more effective drugs and to increase the numbers of patients being treated. We therefore request that CDR initiate a dialogue with the hepatology community and with the CLF to establish models of reimbursement whereby all patients are able to access treatment before developing significant liver disease.