

CADTH COMMON DRUG REVIEW

# Patient Input

**SOFOSBUVIR / VELPATASVIR / VOXILAPREVIR  
(VOSEVI)**

(Gilead Sciences Canada, Inc.)

Indication: Hepatitis C, chronic

**Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.**

The Centre Associatif Polyvalent d'Aide Hépatite C (CAPAHC) — no permission was given to post.

Canadian Liver Foundation — permission granted to post.

Canadian Treatment Action Council (CTAC) — permission granted to post.

HepCBC Hepatitis C Education and Prevention Society — permission granted to post.

Pacific Hepatitis C Network — permission granted to post.

### **CADTH received patient group input for this review on or before August 28, 2017**

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

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.

## 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 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 \$26 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 2.7 million Canadians through our public and professional education programs, patient support programs and other awareness, fundraising and outreach efforts. Over the past 45+ years, the CLF has invested more than \$50 million in health education and prevention programs.

## 2. Conflict of Interest Declarations

In the past, the Canadian Liver Foundation has received unrestricted educational grants from 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.

## 3. Information Gathering

To gather a broad range of input for numerous hepatitis C-related CADTH submissions, the CLF has repeatedly invited patients, caregivers and health care professionals from across Canada to fill out online surveys modelled on the CADTH questionnaire. The more than 400 responses to these various surveys have been used in compiling the feedback for this submission. Quotes from survey respondents are included in italics in various sections of this submission.

## 4. Impact of Condition on Patients

**Please note:** *As the CLF has completed multiple CADTH submissions over the last several years for different hepatitis C therapies, we have repeated some content below that was included in previous submissions.*

The physical, mental and emotional toll that hepatitis C can take on individuals is similar across all genotypes. The majority of people living with chronic hepatitis C in Canada are adults within the 1945-1975 birth cohort who may have contracted hepatitis C either here or before coming to Canada and lived with hepatitis C for decades without any obvious symptoms. Regardless of whether they have recently been diagnosed or have been aware of their diagnosis for several years, a large number are now developing advanced liver disease and without treatment will progress to liver failure, liver cancer or need liver transplants.

*"I have lived with hepatitis C for approximately 40 years. Symptoms such as insomnia, tiredness, itchiness, poor circulation, constipation and fear of accidentally infecting someone else makes day to day life difficult. I am also concerned that delaying treatment is causing more liver damage." – hepatitis C patient*

Individuals living with hepatitis C are often reluctant to talk about their disease for fear of the judgement of those closest to them. The stigma associated with hepatitis C can lead to misperceptions and fear amongst family, friends and co-workers and often personal relationships deteriorate or disappear completely. Without these support systems in place, individuals can spiral down into anger, depression and isolation.

*"...whenever I have told people about my condition it was always met with criticism, fear and rejection. People seem to "know all about it" when, in fact they do not." -- hepatitis C patient*

Psychological and emotional stress only adds to the physical strain which comes as individuals progress to more advanced disease. While some may be able to manage the associated conditions triggered by hepatitis C, others find their lives unbearable due to

debilitating symptoms which impact their ability to support themselves or even function on a daily basis. These symptoms can include nausea, headaches, sensitivities to light and food, memory loss, mood swings, itchy skin, abdominal pain, severe joint and muscle pain, portal hypertension, sleeplessness, slowed reflexes, psoriasis, peripheral neuropathy, osteopenia, diarrhea and muscle wasting.

*"I am 59 and my health is very seriously compromised. I failed treatment and have since been diagnosed with liver cancer. To treat the cancer, I've had chemo ablation, radio ablation, and surgery. I'm not working anymore due to my health problems. Once my cancer is under control, I will be placed on the liver transplant list.*

*– hepatitis C patient*

Not surprisingly, this litany of symptoms which can differ from individual to individual often means patients who once had full or part-time employment or even their own businesses must leave their jobs and rely on government support programs.

*"Since late 1980 I was always ill with flu symptoms, tiredness, nausea, sensitive to light and noise, depressed, aches and physical pains I had to quit my job and my relationship with my family went from up and down to critical." – hepatitis C patient*

## 5. Patients' Experiences With Current Therapy

**Please note:** As the CLF has completed multiple CADTH submissions over the last several years for different hepatitis C therapies, we have repeated some content below that was included in previous submissions.

Treatment rates in Canada continue to be very low meaning that many patients have yet to have undergone treatment. Conversely, there are patients who were diagnosed with hepatitis C many years ago who have undergone treatment multiple times unsuccessfully. Over the past four years, treatment options for genotype 1 patients have improved exponentially with the availability of interferon-free therapies sofosbuvir/ledipasvir (Harvoni), ombitasvir/paritaprevir/ritonavir + dasabuvur (Holkira Pak) and sofosbuvir/velpatasvir (Epclusa) offering patients a low pill burden, few side effects, shorter treatment length (12 weeks) and, above all, efficacy rates of 90% or higher. Patients who have taken these or other interferon-free direct-acting antivirals have had a radically different and far more tolerable treatment experience than with previous interferon-based regimens.

*"I underwent treatment three times: in 2002 (interferon + ribavirin), 2005 (pegylated interferon + ribavirin) and 2012 (triple therapy – pegylated interferon + ribavirin + Telaprevir). In 2015, I started on Harvoni and finished February 2016. It was so easy compared to what I went through with previous treatments. Living with the virus was like waiting for the other shoe to drop. After treatment this time, there was no sign of the virus. I've been given a new lease on life!" – hepatitis C patient*

*"The first time I underwent treatment it involved pegylated interferon and ribavirin. I was very ill with fatigue, nausea and lost a lot of hair. In the end the treatment was unsuccessful. The next time I only had to take 2 pills a day for 3 months and the only side effect I had was a slight headache. Today I'm cured!" – hepatitis C patient*

*"I was diagnosed with hepatitis C in 2009 and by 2012 I needed a liver transplant. After my transplant, I was treated with a new drug combination that didn't involve interferon. The only symptom I had was a sensitivity to the sun that lasted about two weeks. In September 2014, I received the wonderful news that I was cured." – hepatitis C patient*

Treatment options for patients with genotypes 2, 3, 4, 5 and 6 have begun to improve with the advent of a new pan-genotypic therapy sofosbuvir/velpatasvir (Epclusa) and targeted therapies for specific patient groups including grazoprevir/elbasvir (Zepatier) for genotypes 1 and 4 with advanced kidney disease and ombitasvir/paritaprevir/ritonavir (Technivie) for genotype 4. The numbers of patients treated with these therapies are still low however since they have only recently been added to provincial formularies. As the provinces begin to expand (or phase out) eligibility criteria, more patients should be able to gain access to the therapies that are best suited to their genotype and condition.

*"I am genotype 3 and was treated with Sovaldi + ribavirin for 24 weeks. My appetite was severely affected. I only ate because I knew it was important to keep body strong enough to fight. My hair became thin and brittle and I suffered from broken sleep patterns which*

*only contributed to the general feeling of exhaustion. Because of being so tired all the time, I was unable to do as much for my elderly mother. I didn't want to take part in any activities – all I wanted to do was stay home and rest. Unfortunately, in the end there was no major change in my viral count.” – hepatitis C patient*

## 6. Impact on Caregivers

**Please note:** As the CLF has completed multiple CADTH submissions over the last several years for different hepatitis C therapies, we have repeated some content below that was included in previous submissions.

The burden of care for patients with hepatitis C often falls to spouses, parents and adult children. While the symptoms of early stage hepatitis C may be mild or even non-existent, more advanced hepatitis C 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 and all household responsibilities. Those with advanced hepatitis C can experience episodes of hepatic encephalopathy or 'brain fog' which can lead to dementia-like symptoms. They can also develop ascites (fluid build-up in the legs and abdomen) which can require regular draining and esophageal varices which can lead to severe bleeding.

*“I was having to manage the household responsibilities with help from our daughter. My husband's mental changes were hugely apparent. At sundown, all he wanted to do was sleep and dealing with him was like talking to an eight year old child at times... He developed shaking hands that would cramp so badly at times that he couldn't hold a fork to eat. He also couldn't be left alone because his esophageal varices put him at high risk of severe bleeding. – caregiver of a hepatitis C patient*

*“I was put on the waiting list for transplant. During this time, it was my wife's responsibility to take care of my basic needs, manage my 25-30 daily pills, ensure I didn't drift into another hepatic coma and get me to the hospitals regularly. She was forced to leave her job and our routines all revolved around me.” – hepatitis C patient*

When a patient is unable to work, caregivers may 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.

Many caregivers have had to manage through multiple rounds of treatment that often resulted in failure. Interferon-based treatments came with severe side effects but treatment with direct-acting antivirals has not only improved the outcomes but also the treatment experience itself.

*“When he underwent his third attempt at a cure, all side-effects were manageable and so much less than any other regimen, despite his F4 cirrhosis and increasing MELD and symptoms. Anemia, fatigue, rash, leg cramps, and bowel disturbance were some of the side-effects, with the latter likely a result of the disease, not the medication. The dosing regimen was easy to administer and tolerate. Compared to the other two treatments he endured - first was 2006/7 with Ribavirin/Interferon and the second in 2012 with Telaprevir/Interferon/Ribavirin, this treatment was very manageable. The first was very difficult, the second try almost led to his death - became very very ill” – caregiver for hepatitis C patient.*

## 7. Expectations for the New Drug or Experiences Patients Have With the New Drug

We consulted with physicians who had treated hepatitis C patients with sofosbuvir/velpatasvir/voxilaprevir to gather their feedback on their patients' experience with the therapy but were unable to obtain feedback from patients who had taken the drug combination.

Hepatitis C treatment has improved dramatically over the last several years meaning that almost all patients can now look forward to a cure for their disease. Unfortunately however, the road to a cure can be more complicated for those who have undergone previous treatments unsuccessfully. Sofosbuvir/velpatasvir/voxilaprevir represents a viable re-treatment option for patients who have failed treatment with other direct-acting antivirals (DAAs) – specifically genotype 1-6 patients who have taken a NS5a inhibitor (found in Harvoni, Hologic Pak and Technivie) and genotype 1a and 3 patients who were treated with a non-NS5a regimen (Sovaldi with or without another drug). Sofosbuvir/velpatasvir/voxilaprevir is the first 'rescue' treatment available for these difficult-to-treat patients.

Patients who participated in clinical trials suffered minimal side effects. Diarrhea was the most commonly experienced side effect. Most physicians reported that the majority of patients they treated – regardless of what previous therapies they had been treated with before – managed to eliminate the virus. As a result, this therapy offers hope to those with multiple treatment failures that need an effective treatment alternative.

*“I have had treatment for hep C but due to the fact that I am genotype 3, the treatment did not work. Most of the antiviral medications have been mainly for genotype 1. It was upsetting after doing treatment for 24 weeks that it didn’t work. I am not able to try treatment at this time because I am not a good candidate – partly that is due to having been treated once already but also because I am genotype 3. After I receive my transplant, I’ll have to wait about a year and then do drug therapy that will hopefully eliminate the virus.” – hepatitis C patient*

*“This is the first salvage therapy approved and certainly should be made available to patients.” – physician treating hepatitis C patients*

*“This therapy represents a marked advance over existing therapies because it is the only therapy that has proven effective in patients who have failed prior treatments with direct-acting antivirals. Although we can piece together treatment regimens with existing approved therapies for those who have not responded to prior DAAs, we do not have data to guide our treatment decisions. This combination worked across all genotypes and across all resistance profiles regardless of treatment regimen, holding great promise for all those who have not responded to first-line therapy.” -- physician treating hepatitis C patients*

## 8. Additional Information

Each new drug therapy brings us a step closer to our goal of eliminating hepatitis C in Canada. Direct-acting antivirals have made it possible to treat a significant number of individuals with the most common genotype of hepatitis C (genotype 1). The advent of pan-genotypic therapies has broadened the pool of treatable patients to include those with genotypes 2-6. Unfortunately, there are still those who fail treatment and thereby fall through the cracks. Until now, doctors were left to try to cobble together a treatment regimen for these patients with the hope that they could find a combination that would work without reliable data to support their decisions. Sofosbuvir/velpatasvir/voxilaprevir offers the first viable alternative for patients of all genotypes with single or multiple treatment failures.

Every hepatitis C patient – regardless of their genotype, treatment history and complicating health conditions – deserves access to treatment that offers them the best possible chance for a cure. If they cannot eliminate the virus with existing first line therapies, it makes sense to have a second line therapy available to prevent these patients from progressing to liver cancer, liver failure or liver transplant surgery. Each of these outcomes would exact a much higher personal cost for the patients while at the same time driving up costs for the health care system. A ‘rescue’ treatment like sofosbuvir/velpatasvir/voxilaprevir would reduce the burden on patients and health care professionals while at the same time saving money for government and private payers alike

Each time the Canadian Liver Foundation has offered input on a new hepatitis C therapy, we have highlighted the fact that a therapy is only as good as the access to it. Sofosbuvir/velpatasvir/voxilaprevir would be a good addition to the arsenal treating physicians can use to care for their most difficult-to-treat patients. For this treatment to have maximum impact however, it must be available to all patients who need it. Physicians are the most equipped to decide what treatment option holds the greatest odds of a cure for their patients so there should be no restrictions on access.

## 1. Submitting Organization

The Canadian Treatment Action Council (CTAC) is Canada's national non-governmental organization addressing access to treatment, care and support for people living with HIV and hepatitis C. CTAC's organizational goals are to meaningfully engage community members, service providers, policymakers and other relevant stakeholders to identify, develop, and implement policy and program solutions. CTAC understands that treatment access should be considered in its holistic form, encompassing the range of treatment, care and support needs required to reach the most successful treatment experience possible for people living with HIV and/or viral hepatitis co-infection.

Full CTAC membership is reserved for: a) individual people living with HIV (including HCV co-infection); b) organizations, groups or projects with a substantial HIV mandate (including HCV co-infection). Associate CTAC membership is open to any individual, organization, group or project that supports CTAC's mandate and objectives.

## 2. Conflict of Interest Declarations

CTAC received unrestricted organizational and educational grants from the following organizations in the 2017-2018 fiscal year: Gilead Sciences, and ViiV Healthcare.

## 3. Information Gathering

On Monday, August 14th, 2017, CTAC delivered a national consultation webinar that provided an overview of the Common Drug Review (CDR) patient input process, as well as key findings from the Sofosbuvir/Velpatasvir/Voxilaprevir clinical trials. This consultation webinar was presented by Amanda Fletcher, Policy Researcher at CTAC. CTAC members, organizational partners, and interested stakeholders were invited to participate. Four people attended the webinar. A link to both the consultation webinar video and online feedback survey were provided to webinar attendees. This link was made available through CTAC's social media outlets (ctac.ca, YouTube, Facebook, and Twitter) as well as a direct link in the webinar itself. The survey was live and online from August 14th to August 21st, 2017. Unfortunately, none of the attendees completed the survey.

Given the importance of including patient experiences in the consideration of new drugs, CTAC has compiled a patient input report based upon relevant past patient consultations. Data from CTAC's previous patient input consultations regarding the HCV medications sofosbuvir (Sovaldi), daclatasavir (Daklinza), ombitasvir/paritaprevir/ritonavir (Technivie), elbasvir/grazoprevir (Zepatier), dasabuvir/ombitasvir/ paritaprevir/ritonavir (Holkira Pak), sofosbuvir/ledipasvir (Harvoni) and sofosbuvir/velpatasvir (Epclusa) have informed this report.

## 4. Impact of Condition on Patients

Hepatitis C is a serious and life-threatening virus that can impair liver functions, lead to cirrhosis, and is considered the leading cause of hepatocellular carcinoma. Most recent data from Health Canada (2011) suggests that as many 245,000 Canadians are presently infected with HCV, with as many as 44% of those unaware that they are living with the virus. The Public Health Agency of Canada reported 10,890 new diagnoses in 2015.

HCV is transmitted through blood-to-blood contact. While approximately 20% of people infected will clear the virus naturally, approximately 80% will not and the presence of the virus will develop into a chronic HCV infection. Asymptomatic for much of its cycle, HCV infection slowly causes significant liver damage, contributing to fibrosis, cirrhosis, and even liver cancer. Public reimbursement for HCV treatment in Canada has been largely limited to those who have signs of liver damage progression (fibrosis), typically with a metavir score > F2. Although a recent agreement between the Pan-Canadian Pharmaceutical Alliance (pCPA) and several manufacturers has led some public drug plans to announce coverage for HCV treatment for patients regardless of fibrosis score in 2018/2019, barriers to public access have forced many Canadians to live longer than necessary with hepatitis C and its long-term health impacts.



Many people living with hepatitis C continue to wait for treatment and sustain fibrosis and incur liver damage that could be prevented through quick and effective treatment. Left untreated for long periods of time, chronic HCV can lead to decompensated liver cirrhosis or hepatocellular carcinoma, the leading causes of liver transplantation in Canada. Consider the impact of this strategy to vulnerable populations in Canada, as one caregiver respondent noted:

“As an example, an individual I am working with had taken great strides to achieve stability in her life with the hopes of getting on hepatitis C treatment. She is in supportive housing, and had stopped her substance use. After visiting the hepatitis C clinic and the pieces lined up, and would have been in a good spot to initiate treatment; however this news has sent her on a path that may indeed lead to liver damage, but also a more chaotic situation that would not be conducive to an easy treatment for her.”

HCV's often-asymptomatic nature is considered an important variable in its prevalence and spread. Many people live unknowingly with this infection and quietly suffer significant damage. As one respondent living with HCV reported, “I was unaware that I had hepatitis C until 2009, some 30 years after contracting it. It is my understanding that there are ongoing symptoms... but all would have been considered a normal part of my adult life as I was a teenager when I was infected.” Most people seek diagnosis and treatment when experiencing symptoms of fibrosis, cirrhosis, or severe liver damage, but these symptoms are the result of the infection already being possibly decades old. The respondent continued, “I was diagnosed with F3 liver damage, so it is reasonable to say that hepatitis C treatment saved my life.” People living with hepatitis C do sometimes report impact of their infection or liver damage early, however. Many respondents echoed the remarks of one 52 year-old female from British Columbia, who said her symptoms included “Chronic fatigue, some short-term memory concerns.” Both of these symptoms significantly impacted the respondent's ability to maintain employment or social activities

A significant number of people living with HIV infection are co-infected with HCV. A 2007 study from the Public Health Agency of Canada estimated that 20% of people living with HIV (roughly 13,000 people) are co-infected with Hepatitis C. Both viruses exacerbate the progression of the other, and many of their respective medications impact one another. For example, patients using HIV protease inhibitor tipranavir-ritonavir must be careful of possible drug interactions with sofosbuvir-based HCV treatments. People living with HIV-HCV co-infection have also been chronically underrepresented in clinical trials for new HIV and HCV treatments, delaying access to vital information on treatment efficacy and safety that effectively bars this population from new treatments.

## 5. Patients' Experience with Current Therapy

The original standard of care (daily doses of ribavirin, weekly injections of pegylated interferon for 48 weeks) had numerous side effects and limited efficacy, particularly for people living with genotype 1, the most common genotype in Canada. Respondents noted the challenges they experienced coping with adverse events caused by this treatment and with treatment failure. One respondent to our Sovaldi consultation said of their experience, “The depression was the most difficult, but fatigue was cumulative over time and after 24 weeks I found I was missing work quite often.” Another respondent described their side effects as “weakness, worse than flu... Could not function more than 30% of the day. I ended up in ICU with pneumonia. I felt I was going to die.” Several respondents noted their healthcare provider discouraged them from taking this treatment “...because of side effects of Ribavirin and Interferon poisons.”

Given the difficulties that Peg-Interferon and Ribavirin created for patients, the higher efficacy rates and reduced side effects of direct acting antiviral treatments (DAAs) were a welcome advancement. While clinical trials for peg-interferon and ribavirin had cure rates between 45-80%, DAAs have shown cure rates of 95% or greater. When asked about the potential of these medications as they were beginning to roll out in Canada, many patients expressed optimism about their potential. For example, when asked about their interest in taking a new DAA, one patient stated, “Yes! Minimal side effects, easier medication adherence, shorter treatment length.” Similarly, a respondent with experience of the old standard of care, felt new DAAs “...would have improved [my health] much more quickly with a lot less personal and family hardships.” One caretaker's experience highlighted the importance of these newer drugs for people living with Hepatitis C:

“While I work with individuals with hepatitis C in a professional capacity, it has also impacted my personal life. Two years ago I lost a friend who, like many others, could not tolerate interferon. We continued to hold on to the hope that an



interferon-free treatment would become available, as we'd been hearing talk of it for some time, but sadly he missed this opportunity and passed away due to complications caused by the hepatitis C.”

Despite improvements, DAAs still have their challenges. Many regimens require the use of older medications for patients with harder to treat infections, including those with past treatment experience or liver damage. Patients were adamant about the need to move on from older drugs, including one treatment experienced patient who said, “Interferon is a very taxing, difficult drug. We need to eliminate it as soon as possible... I suffered through virtually a whole year of treatment on the interferon regimen and it was brutal.” As one caregivers put it, “for those who do get the treatment, dealing with the side-effects can be extremely difficult, in particular, the depression. The injections associated with the interferon can also be a triggering factor for many people as well as a source of anxiety, given that many individuals being treated for hepatitis C have a history of injection drug use.”

## 6. Impact on Caregivers

Caregivers noted seeing a number of recurrent symptoms of both HCV and peg-interferon and ribavirin: fatigue, nausea, depression, anorexia/weight loss, possible treatment failure, and anxiety associated with side effects and the prospect of treatment failure. As new DAAs have become available, caregivers have noted that while side effects are not uncommon with newer treatments, they were generally considered milder and more tolerable than those associated with peg-interferon and ribavirin.

Where caregivers have been most challenged is in assisting patients to understand and, more importantly, be able to access emerging treatments. Merely connecting patients to treatment can be a challenge in Canada’s vast landscape, as one caregiver noted, “[people I work with] cannot access treatment. My region encompasses a very large area which is mostly rural. We have one liver clinic which only takes a handful of people every year.” Similarly, another provider described meeting, “people at the clinic who had to travel long distances for their treatment in Toronto, from Northern Ontario, and people who needed grants or other support to pay for their treatment. These hardships are much tougher for people who are experiencing the side effects of hepatitis C treatment.”

Once patients have been linked to care, caregivers have often been challenged by access requirements that public drug plans in Canada place on Hepatitis C Treatment, as one Nurse described: “Criteria calls for evidence of liver damage before treatment can be initiated, and it is frustrating for individuals, especially those who are experiencing multiple barriers, to be told that they are not sick enough to start treatment.” This places immense burden on caregivers to help navigate a complex and dynamic treatment landscape as well as call upon them a quick and coherent uptake of changing treatment requisites and standards. As one other service provider noted, both patients and caretakers can be frustrated by this, stating that patients were “not taken seriously until their health is seriously compromised.” While changes to access for many DAAs will begin to take effect over the next two years, it is unclear what that will mean for newer medications like Sofosbuvir/Velpatasvir/Voxilaprevir.

## 7. Expectations for the New Drug or Experiences Patients Have With the New Drug

The information in this section was gathered in the same means as described in section 2.1.

Although CTAC did not receive any patient input for Sofosbuvir/Velpatasvir/Voxilaprevir, patient concerns about existing treatment options, and data from the Sofosbuvir/Velpatasvir/Voxilaprevir clinical trials, can help us see some of the benefits patients might find in this regimen.

### One pill once a day, shorter regimens

Once-a-day single pill regimens have been developed for both HIV and Hepatitis C to help simplify treatment regimens and improve adherence. Caregivers in past consultation noted the need for simpler regimens, as “heavy pill burden” was a barrier to successful completing treatment. Sofosbuvir/Velpatasvir/Voxilaprevir has been formulated as a once-daily pill. A course of treatment can also be completed in 12 weeks and as little 8 weeks for some patients without compromising efficacy, improving the likelihood that patients will be able to complete treatment.

### Ribavirin free and pan-genotypic

Some DAA regimens also require the use of Ribavirin in patients with harder to treat infections. Given the well-known side effects of ribavirin and its potential to deter patients from treatment, effective regimens for harder-to-treat groups without the use of ribavirin are

needed. Sofosbuvir/Velpatasvir/Voxilaprevir was designed as a standalone regimen for all patient groups, including those often considered hardest to treat. Clinical trials of Sofosbuvir/Velpatasvir/Voxilaprevir have shown efficacy comparable to or better than other DAAs for people who have past treatment failure, those who are living with cirrhosis, and people who are NS5A-experienced. These results held across genotypes and when patients were affected by more than one of the above conditions.

### **Adverse events and drug-drug interactions**

The most common side effects for this medication in clinical trials included headache, fatigue, nausea and diarrhea. Adverse events were very rarely the cause for clinical trial participants to stop treatment.

There is some research linking more severe cardiovascular disease with hepatitis C. Likewise, people who are co-infected with HIV may be at higher risk for cardiovascular disease because of links between HIV and heart health.

## **8. Additional Information**

CTAC continues to acknowledge and appreciate CADTH suggestions as to how to improve patient input submissions.

## 1. Submitting Organization

Founded in 1996, HepCBC is a registered non-profit society run by and for people infected with, or affected by, hepatitis C. In 2017 we are adding hepatitis B to our mandate. Our mission is to provide education, prevention and support to those living with viral hepatitis. We have two small offices in Victoria, BC and downtown Vancouver, BC. Most of our staff are volunteers with lived experience (either past or present) with viral hepatitis. We also employ four contractors on part-time, short-term contracts. We run activities in many areas of the Lower Mainland and travel throughout the province doing outreach. Our representatives attend provincial, federal and international conferences and participate at health-related events. In addition, we provide support and information globally through our website. Other activities include: Online publication of a weekly bulletin (the *weekly.bull*), plus peer support, anti-stigma activities and prevention education to the general public, general hepatitis information, particularly to baby-boomer, aboriginal and immigrant communities and those living in rural/remote locations. We support and encourage HCV and HBV testing among at-risk groups, including those who no longer fall into this category but may have contracted viral hepatitis decades ago, most commonly through the medical system (whether in Canada or abroad), or through recreational drug use. We also work alongside other organizations, including local HIV/AIDS organizations to support those co-infected with viral hepatitis and HIV.

## 2. Conflict of Interest Declarations

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, Lupin Pharmaceuticals, Gilead Sciences, Janssen Pharmaceuticals, Bristol-Myers Squibb, and AbbVie, plus support from Rx&D, the pharmaceutical umbrella organization.

All three of the authors of this report have attended numerous educational conferences and meetings for which registration and travel expenses were funded by the pharmaceutical companies listed in (a).

## 3. Information Gathering

Data came from patient surveys which were advertised through our website, Facebook Page, and our weekly email bulletin. Note that with each new Direct-Acting Anti-viral (DAA) submission we have received fewer responses. We suspect patients are feeling overloaded with requests for such information from then and they no longer see a reason to keep telling us the same things.

Data came from volunteers and staff who have actively staffed HCV+ phone and email support lines over the course of several years, and therefore have an in-depth knowledge of patient concerns and experiences.

Two of the authors of this report are/have been patient-researchers who have been reading scholarly articles about HCV for many years (20+ in one case).

## 4. Impact of Condition on Patients

In the last several years HepCBC has completed over 16 hepatitis C drug submissions for both CADTH and BC PharmaCare, and has answered Questions 2.2, 2.3, and 2.4 as many times. While we do present some new patient impact information at this time, we refer those wishing more detailed answers to five of our previous CADTH DAA submissions from 2016/2017, below:

[http://hepcbc.ca/wp-content/uploads/2017/06/20170623\\_qlcaprevir\\_pibrentasvir\\_CADTH\\_redact.pdf](http://hepcbc.ca/wp-content/uploads/2017/06/20170623_qlcaprevir_pibrentasvir_CADTH_redact.pdf)

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[http://hepcbc.ca/wp-content/uploads/2016/04/20141221\\_ombitasvir\\_paritaprevir\\_ritonavir\\_dasabuvir\\_CADTH\\_redact.pdf](http://hepcbc.ca/wp-content/uploads/2016/04/20141221_ombitasvir_paritaprevir_ritonavir_dasabuvir_CADTH_redact.pdf)

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[http://hepcbc.ca/wp-content/uploads/2016/04/20140826\\_HCV\\_GT1\\_TherapeuticReview\\_CADTH.pdf](http://hepcbc.ca/wp-content/uploads/2016/04/20140826_HCV_GT1_TherapeuticReview_CADTH.pdf)

The first response is from a GT1 female from Ontario, age 68, now post-transplant:

*“Over the years, I experienced fatigue a great deal, but there was nothing else causing problems that I knew of. I thought the fatigue was due to everything that I was doing – teaching and being an organist as well as doing my job as a wife and mother. I looked around at many friends and wondered why they weren’t as tired as I was. No matter what, I couldn’t stay up as late or do as much without getting overly tired. I figured it was just me. (Eventually...), my doctor called me into his office to tell me that he had noticed my blood platelets were going down. (He referred her to an internist who told her...) that my spleen was enlarged and that my liver was hard. (But for over two years, no one followed up on this)...I was having trouble eating some food. Fish, especially, made me throw up, so I stopped eating fish. I started being very careful about what I ate when we went out, being careful to avoid things that I thought might make me ill...I continued doing the things I usually did, including administrative work at the local music festival, but still felt fatigued a great deal of the time. I began to notice some little things happening. I saw white spots on my tongue. My Dr. sent me to an ENT, as he was concerned it was cancer. He looked at my tongue on the first visit, and set up a second visit to do a biopsy. When I went the second time, he decided that he didn’t know what it was, but he didn’t think it was serious. (I found out later that this was a symptom of liver disease, as was the fatigue). This was 2½ years after my first specialist. I think another six months to a year went by before I plucked up the courage to ask my doctor if my gallbladder could be causing my symptoms. I knew that throwing up after eating certain foods could be caused by gallbladder trouble, and I knew I did have some stones. The only thing was, I didn’t have the pain that I thought was associated with gallbladder trouble. My right side was tender, though I thought it was from sleeping on my right side all the time. Fortunately for me, my doctor didn’t question anything, and instead, asked which surgeon I’d like to see...As I waited in (the surgeon’s) examining room, I knew the doctor was looking at things on the computer. When he came in to see me, almost the first thing he said to me was, “Have you ever had hepatitis?” My answer was, “Not that I know of.” Off I went for blood work (almost everything on the page had been checked off including Hepatitis A, B & C. He also sent me for a liver MRI...(She was told...) I had hepatitis C, and it had damaged my liver.”*

The second response was from a GT1b female from British Columbia, age 69:

*“I knew I had hepatitis C by 1992, but was advised by my doctor that the treatment (interferon and ribavirin) would be too harsh to justify it, given the lack of symptoms I had at that point. Over time, the main effect of hepatitis C on my body was on my brain. I had always been a very logical, methodical, intellectually-active person who loved to read, do research, write, and teach. However teaching became too stressful, so I developed my own home-based business but was eventually forced to close it down (retiring early) due to an inability to concentrate, or to remember what I had said or done. I would regularly fall asleep sitting at my desk during the day, then wake up in the same sitting position, hours later, confused and alone in a dark house. Hep C also slowly started limiting what I was able to digest, eventually forcing me to cut meat, nuts, milk, and cheese out of my diet. I finally sought treatment for the first time in 2007, once strange chemical smells started emanating from my body.”*

The third response was from a GT2b female from the USA, age 63:

*“Hep C drastically affected my life. It took about 25-30 years for me to start showing intense symptoms. I believe it took that long because I was not a drinker. But when the symptoms started it came on strong. I had intense body pain and overwhelming fatigue. I kept going to my doctor trying to get help. They had no idea what was going on; at one point I was accused of drug seeking. After about 6 months, I was having trouble at work. I worked at a major grocery store and was required to work various shifts. I had trouble getting to work on time and (eventually) was fired. The funny thing is, I was initially glad because I could stay in bed and sleep. But within 2 months I was unable to pay rent and lost my apartment. I tried to get unemployment (compensation) but couldn't because I was too sick and was unable to look or accept any job. Because the doctors still hadn't diagnosed me I had no proof of my illness. I ended up sleeping in my car. After about 8 months my brother paid for a motel room for me but he felt I was faking it. So he quit helping after a few months. I was in my car for another year and went to a homeless clinic to get pain medication and help. My pain all throughout my body was intense. They ran a bunch of tests and found out I had HepC. It took another 2 months before I was able to see a liver doctor. He confirmed it and told me there were medications that could cure me. But I wasn't sick enough.”*

The final respondent is a 70 year old male, living in British Columbia, with GT3, who underwent a liver transplant at age 66. He has had three previous unsuccessful treatment attempts. He suffers from a lack of energy and stamina which forced retirement at age 59. He writes that he needs treatment “before his new liver is compromised.” He speaks for many GT3 sufferers when he writes that:

*“Having type 3 means there are limited options for treatment and [I] would welcome any new treatments.”*

and (particularly since he is a transplant recipient):

*“We don’t want to go through hell again with my new liver.”*

Like many other patients, this man was infected via blood transfusion (in 1957 at age 10). He also writes:

*“Treatment for GT3, post transplant has been hard to come by. [I] Hope it will relieve fatigue and other side effects”.*

## 5. Patients Experiences With Current Therapy

Several all-oral treatments for HCV have been approved, both federally and provincially. However, collectively, they do not work for all patients and some may be contraindicated depending on a patient’s characteristics. In our opinion, we need as many of the new DAAs approved as possible in order to increase prescribing flexibility, according to individual patient characteristics. In addition, although far less frequently than used to be the case, a few patients still fail the newer treatments. Cure rates are very high: 95+% generally speaking. But 95% is not 100%. The hard truth is: some patients still fail the newer treatments, despite the fact that those treatments are extremely effective. These patients need to have hope that there still remains an effective option for them to try.

Patients who are rather harder to cure should have options, preferably without having to use the now-infamous drugs, interferon or ribavirin, if possible. Having a selection of multiple DAAs available is particularly critical in combating antiviral-resistant varieties which inevitably develop and spread, particularly among the “incident” populations of IV and intranasal drug users and men who have sex with men. The long-term consequence of resistance to HCV medications remains unknown, and any way of preventing or slowing its development (and staying ahead in the development of new treatments) is going to be key to the global elimination of HCV.

While approval of multiple DAAs reduces the likelihood of treatment failure, especially as additional data becomes available and doctors become more knowledgeable as they gain “real world” experience as to what combinations to prescribe. Those with genotype 3, those with advanced liver disease, prior treatment failure or coinfection (either with HBV or HIV) are examples of some groups for whom at least one (and ideally more than one) effective treatment option is required.

Currently, the biggest barrier to treatment with the new DAA combinations is their high cost, which has led to both private and public insurers rationing HCV cures. (One of our respondents: *“I couldn’t believe that I was expected to get close to death before I would be worthy enough to get cured.”*) Moreover, as liver disease advances, the risks and subsequent costs to society are greatly increased, even following successful treatment (even following treatment, an elevated risk of liver cancer, hepatic encephalopathy, and other elements of end-stage-liver-disease remain, at least for several years following achievement of SVR). However, the treatment combination under review might enable costs savings because it can be utilized as a shorter first treatment in those who are DAA naïve and without cirrhosis. We are at last starting to see price reductions, and in parallel with these we have seen some provinces reducing (or even abandoning) treatment rationing by striking down “proof of F2 or greater [F2+] fibrosis” treatment criteria. However, in our opinion, treatment rates remain very low while prices of treatment remain very high, even though some of the newer treatment regimes (for example, AbbVie’s combo of glecaprevir and pibrentasvir) are significantly cheaper than others.

## 6. Impact on Caregivers

As noted in previous reviews, patients and their caregivers have repeatedly expressed to us that they want treatment options with greatly improved efficacy than in previous interferon-based regimes. In addition, they look forward to treatments which are shorter and require far less support, both mental and physical, than was previously required. Of course, they want their family members to regain their ability to support their families, or at least not be a burden to them, as soon as possible.

One of our respondents says, *“[My] wife is (my) caregiver. [It is] very hard on her to watch me go downhill and deal with numerous medical problems.”*

Another says, *“All of this was terribly hard on my adult children who were very worried about me but had no idea how to help.”*

Another says her husband, *“helped me get dressed and move around the house, made meals, did cleaning and laundry and everything else with very little complaint.”*

Yet another says: *“My son would come by and help wash my hair and bring me food. I could have gone to his apt to clean up but he shared it with 4 other people and I was ashamed and didn't want him to be embarrassed...”*

## 7. Expectations for the New Drug or Experiences Patients Have With the New Drug

The information was gathered in the same way as for previous submissions (section 2.1). HepCBC staff and volunteers carried out their own research from the data available and used this in combination with patient experience to formulate an informed opinion. We attended a webinar put on by staff of the Canadian Treatment Action Council (CTAC) about this combo. And while we are aware that CADTH has access to all published data, we have referred to some published information, in support of several of the points we make, particularly in the following sections.

### a) **Based on no experience using the drug:**

We studied Phase 3 clinical trial data which provide support for including SOF/VEL/VOX in provincial formularies. The success rates across the POLARIS 1 and 4 studies (those across all genotypes who were retreated for 12 weeks with the new combination following previous DAA failure) were 97%. POLARIS 2 evaluated 8 weeks of treatment across all genotypes in those who were DAA naïve. Cure rates were 95%, whether or not patients had cirrhosis. POLARIS 3 saw cure rates of 96% after 8 weeks and also 12 weeks of treatment for G3 patients with cirrhosis. Cure is defined as being virus free 12 weeks after cessation of treatment.

The unique factors about SOF/VEL/VOX would seem that it aims to provide a safe, effective, pan-genotypic, rapid cure primarily for those who require retreatment after failing a newer DAA treatment. Moreover, the additional good news is that SOF/VEL/VOX appears to provide an effective, shorter treatment option (8 weeks) for some patients who are DAA naïve and not yet cirrhotic.

Approval of the combination will offer hope by providing an effective salvage treatment to those patients, whatever their genotype, with or without compensated cirrhosis, who have previously failed one of the newer treatments, including NS5A and non-NS5A failures. Even those with baseline resistance associated substitutions (RASs) had SVR rates of 94 – 100%. In addition, the combination is effective in curing DAA treatment naïve patients without cirrhosis, of all genotypes, in as little as 8 weeks. However, our analysis of the data from the trials, together with other emerging data from patients who have been treated with the new DAAs, requires us to note some issues that need to be carefully considered along with any approval.

All-oral regimens are generally easier to tolerate than those containing interferon. Nevertheless, there are some side effects with every HCV treatment, albeit that the side effects are much milder and less likely to interfere with a person's normal daily activities than those in interferon-based therapies. Data from the trials indicate not only high cure rates but relatively mild (and to be expected) side effects amongst patients on strong medication. The side effects cannot be compared in severity to those that used to be routinely seen in patients taking interferon-based therapies. Data from the trials indicate not only high cure rates but relatively mild (and to be expected) side effects amongst patients on strong medication. The side effects cannot be compared in severity to those that used to be routinely seen in patients taking interferon-based therapy. The side effects appear to be quite similar to those experienced by patients on other all-oral HCV DAA treatments: minor cases of headache, fatigue, diarrhea and nausea.

We note a small number of Serious Adverse Events (SAEs) but these were seemingly not related to the treatment medication. In POLARIS 3, there was one death approximately 11 weeks following treatment but this is reported as being due to raised blood pressure (there was a history) and was unrelated to the medication received on treatment. A further patient died two days after 12 weeks treatment but this from a heroin/fentanyl overdose and therefore unassociated with treatment.

Thus, we anticipate fewer adverse events and less disruption to daily activities. Theoretically, there should be a reduction in hospital visits compared with the older, 1st or 2nd generation treatments. However, and as always, we support continued close monitoring of all patients undergoing any kind of HCV treatment regime. Although the new DAAs appear to have fewer side effects, as their use becomes more frequent, we expect more side effects and contraindications to emerge. This is inevitable as trials are generally conducted according to stringent eligibility criteria and may exclude or not capture certain populations. They also do not, due to their nature, capture long-term data and thus do not show any long-term effects which might show up over time.



Furthermore, we have noted the recent and ongoing investigations into the possibility of HBV reactivation among HCV patients taking the new interferon-free DAA treatments. Thus we believe that until more information is available, patients who could be susceptible (i.e., those who have been previously infected with HBV, whether resolved or not) should be monitored closely and treatment modified appropriately. We believe that all HCV patients, considering HCV treatment with DAAs on an all-oral regime (i.e., no interferon), should have their HBV status confirmed prior to starting treatment. In this way, steps can be taken (e.g. the inclusion of anti HBV therapy) to minimize the risk of a potentially fatal HBV flare. We note that SOF/VEL/VOX will be dispensed with a boxed warning regarding HBV reactivation and contraindications such as treatment with rifampin.

We also note that research has indicated a possible resurgence of liver cancer for a short period following (3rd generation) DAA treatment. While this is worrying, it also emphasizes the point that treatment of HCV patients before they present with advanced liver disease is essential to minimize the risk of eventual HCC. HCC is a factor that must be considered carefully before a treatment regime is prescribed, at least until more data becomes available.

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

We do not have any patients within our group who have tried this combination.

## 8. Additional Information

The points we have made in Section 3.2 above support:

Approval of SOF/VEL/VOX (Vosevi™), as it is a very versatile and effective treatment with high cure rates across all genotypes, even among those who are traditionally more difficult to treat. Critically, it provides a retreatment option of 1 pill a day for those who have already failed a DAA treatment. We recommend:

- Close monitoring of all patients on HCV treatment is required, whatever the regime.
- That doctors and specialists should be mindful of contraindications and the importance of keeping abreast of emerging data reflecting "real world" use.
- That HBV status and HCC history (if applicable) of an HCV patient needs to be factored in to a decision on whether to treat, choice of treatment, and the monitoring regime to be applied both during and after treatment.
- That emerging data (especially in relation to treatment of HCV in those at high risk of HCC) continues to make a case for treating HCV patients before their liver disease is advanced.
- That greater access to treatments such as this one be assured to all patients who would benefit from them - through the continued lowering of prices and lowering of barriers to universal access such as requirements to prove significant pre-treatment liver-damage (F2+)
- The combination should be as easy to administer and to use as all the other approved 3rd generation DAAs, as it forms a single pill.
- In the overwhelming majority of cases, being cured of HCV will clearly benefit a patient in terms of their overall health.



## References

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## 1. About Your Patient Group

Pacific Hepatitis C Network's vision is 'BC free from all new infections with the best possible care, treatment and support for those living with the virus'. Our mission is to provide a means for sharing information and coordinating mutual support and action that will strengthen the capacity of individuals and organizations throughout British Columbia to prevent new HCV infections and to improve the health and treatment outcomes of people already living with HCV. Our members include people living with chronic hepatitis C, people who are HCV antibody positive, people at-risk for hepatitis C infection, and anyone concerned about hepatitis C (service providers, health care providers, family, friends). Our websites are: [pacifichepc.org](http://pacifichepc.org) [hepctip.ca](http://hepctip.ca) and [help4hepbc.ca](http://help4hepbc.ca)

## 2. Information Gathering

Patient and caregiver perspectives and experience in relation to living with hepatitis C, their experiences with hepatitis C treatment and with sofosbuvir/velpatasvir/voxilaprevir specifically. Information was gathered informally through discussion with members and others (many) in July and August 2017. As with our past information-gathering, people we talked with had varying experiences with treatment; none had treated with sofosbuvir velpatasvir voxilaprevir. We sought opinion on the value of having sofosbuvir velpatasvir voxilaprevir approved for use in Canada. As a hepatitis C treatment specific to treating those who have treated in the past and either didn't respond or relapsed and that is a single-pill, once daily and pan-genotypic option, those we asked spoke strongly about the need for such a treatment.

## 3. Disease Experience

Our members have described hep C as a disease that kills slowly, by degrees, a disease that can and does affect all aspects of a person's life and that of their family and friends and their colleagues and community. The disease itself can keep a person housebound but so can stigma. One person said, "If I cared what people thought, I'd crawl into a hole and never poke my head out again. That would be it. It's that bad sometimes".

The symptoms described in our information gathering were most often along the lines of 'just unwellness'. This can be, 'I have to rest more now and can't look after my business the way I used to,' (this same person went on to describe the constant worry and anxiety about losing their business because they can't keep up or 'do anything that needs doing when it needs doing') to 'I'm disabled'. Not being able to think clearly or properly, extreme fatigue ('I could lie down on the side walk in January and just go to sleep right there'), joint and generalised body pain, feeling ill or nauseous. While not reported this time, we know some people can experience extreme nausea, lasting 12 hours or longer, numerous times a week.

The other point people made about fatigue and 'brain fog' is that it is unrelenting – nothing helps, no amount of sleep or coffee or walks or rest makes it better. These symptoms are non-specific and 'extra-hepatic' so very often physicians don't make the link between the symptoms and their hep C or, unfortunately, make light of the symptoms – minimize them. For some people, this experience makes them stay away from their doctor or not discuss how they are doing and people often talk about feeling embarrassed or ashamed and angry but powerless to do anything. And sometimes they question their own experiences, "I don't know? Maybe it's not that bad, maybe I'm hypo? But what's that saying – just because you're paranoid doesn't mean someone isn't following you?"

The experience of brain fog includes difficulty thinking, remembering, understanding, and focusing. Brain fog can be disabling and impact negatively on a person's ability to function at home and in the workplace.

People with brain fog describe having to take manual jobs requiring less cognitive function, even though this can pose other challenges if that work requires physical labour of any kind as fatigue is sometimes also a symptom of hepatitis C.

Again, HCV doesn't only take a physical toll on patients, but takes psychological and emotional tolls on them and their support networks as well. This is due, in part, to that fact that hepatitis C is a disease that one still often requires a degree of illness before treatment will be considered.

These physical and psychological tolls are often worsened by the social isolation, which comes from suffering fatigue, other HCV symptoms, and from the stigma that comes as a result of having hepatitis C, a communicable disease. “I live in fear of people finding out.”

## 4. Experience with Currently Available Treatments

Many of those we spoke with had either direct experience with new DAAs or had close family or friends who had. A smaller number had treated previously with interferon-based drugs; all spoke to the night and day differences between their previous treatment experiences (non-responders and relapsers; many side effects, some ongoing, more ill during and after treatment than before), all had cured using new, interferon-free DAAs. One person who hadn't treated previously but as a GT3 had to overcome a number of barriers in order to qualify for interferon-free DAA regime. Two people who finally had cured with new DAAs reported improved liver function and fibroscan scores; others were looking forward to seeing their results in follow-up appointments.

Treatments and subsequent experience included:

- Pegylated interferon and ribavirin: dry mouth, fatigue, flu symptoms, lowered platelet counts, lowered red blood cell counts, nausea, rash or itchy skin, changed tastes. One person very ill, couldn't function at all for full length of treatment.
- Harvoni: headache, nausea, no side effects, treatment success, relapse after completing treatment.
- Sovaldi with ribavirin: depression, fatigue, headache, loss of appetite, skin issue

New DAAs are much easier to take: fewer pills, no injections, shorter treatment times, fewer side effects and much better cure rates. So many people talked about getting their lives back with these treatments and the life-changing reality of being cured. Of course, some people still have increased risk of liver cancer and some feel they will be managing non-specific symptoms for the rest of their lives. And some people are left without options if they relapse or don't respond to the current available treatments.

## 5. Improved Outcomes

Those who have tried and failed currently available treatments are sidelined from the excitement and promise of new DAAs, for the most part. The very difficult aspect of that reality is that someone who failed treatment is already sick enough to qualify for treatment so the need for effective re-treatment regimes carries some urgency.

People in this situation feel that they are in the same situation as most living with hep C were in prior to DAAs – without options, managing symptoms, hoping for a cure before liver disease gets too bad for treatment. Some feel they will die of liver disease or liver cancer. One person said, “I might still get liver cancer but at least I'll have done everything that could possibly be done”, meaning that an effective treatment for re-treating gives them the chance to live a regular lifespan but even if they do end up with liver cancer, they would be able to accept that better than if they knew there was a treatment available but they couldn't afford to take it or they couldn't get it covered.

Some people who are waiting to treat also want to know what their options are if treatment fails. They understand that treatments are excellent and have near 100% cure rates but still, some do fail. Some felt that the stress of having a virus that could kill you and that you can't get treatment for actually means you get sicker sooner (than if you know there is a treatment available) They also felt that having an option to address treatment failure would help keep stress levels down.

The community often expresses that no one should be left behind and that means reasonable access to the best and widest application of treatments as possible.

## 6. Experience with Drug Under Review

None of those we had discussion with had direct experience with the drug under review. When shown the clinical information about sofosbuvir/velpatasvir/voxilaprevir, the response was very favourable – everyone knows someone that failed treatment and needs another option. People who have failed treatment know that they will get sicker without any real hope for a cure. That puts them right back to where we were before the new DAAs. That is frightening and depressing and for those needing this treatment, it feels like – and for some, it is - a death sentence.

## 7. Anything Else?

From our previous submissions, accurately reflecting our recent discussions too:

The pleas for access to better treatments that have “shorter treatment times, less side effects, higher SVR rates, the ability to continue working while being treated”, “the ability to cure those who have already been treated without success and the ability to cure without pegylated interferon and ribavirin”, or access to treatments that may be able to bring “an end of worrying over the health of my liver”, “healthier livers”, “being cured faster and will not have to go thru multiple treatments”, and “quick treatments that cure all GTs” are still strong, even after new hep C treatments have recently been included onto formularies for a limited group of patients.

There is a want to get better, to improve health, and to fully participate in all that they can dream of being involved in or that they haven't allowed themselves to dream of because of concerns around their hep C. There is hope that the treatments will become available to them without them first having to get sicker.

“To be rid of something that has the potential to *destroy one's body* would have profound physical and psychological benefits.”

Thank you for this chance to have our say!

## Appendix: Patient Group Conflict of Interest Declaration

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

We received an education session in July 6 2017 from the drug maker (Gilead) providing information about the sofosbuvir/velpatasvir/voxilaprevir clinical trial data.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

N/A

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Gilead Science Canada				✓
AbbVie				✓
Bristol Myers Squibb	✓			

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Deb Schmitz  
 Position: Operations Manager  
 Patient Group: Pacific Hepatitis C Network  
 Date: August 28 2017