

Section 1 — General Information	
Name of the therapeutic review	Drugs for Chronic Hepatitis C Virus Infection
Name of patient group	Pacific Hepatitis C Network (PHCN)
Patient group's contact information:	Pacific Hepatitis C Network (PHCN) Box 192 Roberts Creek, BC V0N 2W0 604.989.4969 <a href="http://www.pacifichepc.org">www.pacifichepc.org</a>
Date of submission:	January 13, 2014

## 1.1 Submitting Organization

Pacific Hepatitis C Network (PHCN) is a non-profit, provincial network of practitioners and peers focused on issues related to hepatitis C in British Columbia. PHCN exists to support a community-based response to hep C in BC, the core of which is the voice of people living with hep C. PHCN has an open membership, comprised of people living with hep C, medical practitioners, and social service providers.

## 1.2 Conflict of Interest Declarations

PHCN recently received a small one-time project grant from Janssen Pharmaceuticals for the PHCN "Treatment Information Project".

## Section 2 — Condition and Current Therapy Information

### 2.1 Information Gathering

Information was gathered through a combination of individual responses, PHCN survey results, and printed source materials.

### 2.2 Impact of Condition on Patients

Liver damage, extreme fatigue, "brain fog" (confusion of thoughts, unclear thinking processes) and ongoing depression are cited as the primary aspects of chronic hep C that are most important for patients to control. For many, these symptoms are lifelong. For others, poor hep C treatment options have meant a difficult journey of end stage liver disease and early death because of the lack of health system readiness to equitably engage all people living with hepatitis C. Having low barrier prevention programs, early screening/testing, ongoing monitoring and accessible treatment options for all people would significantly reduce the impact of hep C infection in Canada.

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

workplace. People describe having to take menial jobs requiring less cognitive function, although this can pose other challenges if that work requires physical labour of any kind. Very often, people cannot continue working, use up savings and must turn to income supports such as social assistance or disability benefits.

Our members also describe chronic and sometimes extreme fatigue not remedied by any amount of sleep. Insomnia can also be an ongoing and debilitating symptom for those suffering with chronic hepatitis C (CHC). Daytime resting and sleep can be necessary just to keep basic chores done (meals, cleaning, laundry). Many people must drastically reduce hours of work, or stop work altogether. For some, the impact is in family life - they have enough energy for work but none for family; some families experience great difficulty understanding and supporting their ill loved one because, as is often said, "This is an invisible disease". People don't always look sick - they look "normal". Even a milder form of hepatitis C fatigue can drain away the ability to engage in and enjoy daily work and family life, eroding and relationships and wider social networks and support systems.

Members describe other symptoms as well such as joint and muscle pain, stomach discomfort and problems with digestion, itchy skin, jaundice and depression.

These symptoms are often so severe people cannot get out of bed, have difficulty eating, and are unable to work because of these symptoms – often leading to financial hardship. All of these factors contribute to increased break down of a patients' social networks and relationships. As one respondent stated, "...it has been harder to start a relationship with women because I have to explain my hep C status..."

While many living with Chronic Hep C (CHC) experience depression, men especially spoke of depression and despondency that was tied to their inability to work and not be the family breadwinner. Decreased family income means no extra income for activities such as sports and school outings, which can, in turn, negatively impacts children's wellbeing and development. Partners feel the pressure to financially provide and take care of their sick spouse, which puts further strain on family relationships. Additionally, there is also a fear that a child or family member will contract HCV, despite daily precautions. This fear often adds to feelings of depression and can cause people to further isolate themselves from loved ones.

Single parents living with hepatitis C experience great financial stress if they experience hep C related symptoms that prevent them from working. Additionally, their children lose having a parent who can care for them. Childcare is expensive, but is often needed because of illness, attending medical appointments and sometimes because of parental hospital stays.

Single people become more vulnerable to financial and social hardships if they are not able to work. Additionally, with the loss of income, housing often become unstable – forcing people into temporary living situations (living with friends, shelters, the street) because rent/mortgages cannot be paid.

Our members talk of the social isolation that comes from being chronically ill, but even more from the stigma that comes as a result of having hepatitis C, a communicable disease. We know that those who are socially isolated have poorer health outcomes, do not access care as quickly or as often as they should, and can have more hospitalizations due to acute illness.

Reduced income often means people living with CHC cannot afford the kind and quality of food, supplements and medications that help maintain good health. The stress of managing a chronic disease in these circumstances compounds compromised physical and mental health and increases potential for acute illnesses either directly or indirectly related to hepatitis C. Even with a stable lifestyle, people talk about having to visit the doctor often for monitoring, needing help with extra-hepatic symptoms and, for a few people, hospitalization when current treatments cannot be tolerated or have been unavailable (lack of care and monitoring of hepatitis C disease, not qualifying for treatment due to lack of 'objective liver disease', being turned down for 'lifestyle' reasons).

## 2.3 Patients' Experiences With Current Therapy

The current standard of care is pegylated interferon with ribavirin (PR), or PR combined with either telaprevir or boceprevir (for HCV G1). People's experiences with these treatment drugs range from being able to continue work while on treatment to experiencing such severe side effects that they virtually cannot function and need help with basic daily living. Having few or no side effects is a rare experience.

Side effects related to current hep C treatments include: daily nausea, vomiting, diarrhea; altered sense of taste; rectal itching, burning, or discomfort; moderate skin rash and persistent cough, as well as aching joints and severe debilitating fatigue and depression. For a few responders who had triple therapy involving telaprevir and PR, haemorrhoids, skin rash and anaemia were all drug side effects that were not life threatening, but certainly were "...difficult to live with...", especially when working and/or caring for children.

For many patients, skin rash, especially in triple therapy, can require close medical monitoring, prescription medication, or referral to a dermatologist. No responders we spoke with had experienced any extreme rash, however Anaemia is often reported as another reason people are medically advised to stop treatment. Triple therapy sofosbuvir and PR, has been reported to cause significant decreases in haemoglobin leading to Anaemia.

Some people opt to start taking anti-depressants to alleviate the debilitating depression that is a common side effect of current HCV treatments. In regard to mental health, also common during HCV treatment is "riba-rage"- burst of uncontrollable rage and anger that have been associated with ribavirin. Although more rare, a few people had to stop treatment because of severe mental health episodes, and one person described having a psychotic break requiring 6 weeks of hospitalization (interferon-induced).

Current treatment ranges from 40%-90% effective (i.e. sustained virological response) depending on the genotype of the patient. The current therapies rarely control the symptoms of hep C, and in fact, often increase the severity of the symptoms- especially fatigue. While treatment duration is getting shorter (averaging 6 months), people who do not have supportive social networks often do not complete treatment because of the severity of adverse effects. Taking multiple medications on a daily basis for an extended period of time is onerous and becomes more complicated if people do not have stable healthy living arrangements (i.e. stable housing, nutritious food, regular daily routine, supportive/safe personal relationships).

For patients who are not responsive to treatment, the prospect of subsequent treatments is often “unbearable”, because of the severity of adverse effects and length of treatment. Additionally, there are people who delay treatment because they fear the worst side effects.

There are reports that some patients’ experience with triple therapy includes the potential for numerous drug interactions with boceprevir and telaprevir. Patients must be vigilant in checking new prescriptions received from walk-in clinics, GP’s, or hospital emergency rooms. Some health care providers are unaware a person is taking HCV treatment medication, nor have much experience with HCV triple therapy and other potential drug interactions. People admitted to hospital while on HCV triple therapy, have been reportedly directed by a hospital doctor to skip doses of their HCV meds, or did not have access to the required food and 20 grams of fat (often told the “kitchen was already closed”). Patients may not be able to advocate for themselves in these situations if they are feeling quite sick, and don’t have the benefit of dealing with a health practitioner they are familiar with.

In addition, several patients have had to change their medication to a different class of drug, which is not contraindicated with triple therapy. This can be especially onerous for patients co infected with HIV and HCV, as it can mean switching from a stable HIV drug regime to new one, where the patient may have to cope with new and different side effects. The triple therapies have also resulted in greater financial expenditures for clients. Direct acting antivirals (DAAs), which require close monitoring, mean more frequent blood work and therefore higher travel expenses with more trips to the doctor or lab. Telaprevir, requiring 20 grams of fat with each dose, also increases the food costs for most patients (items like butter, cheese, oil, and nuts are often expensive). Patients also incur further expenses because certain supplements are recommended for people on treatment, such as folic acid, or meal replacement drinks for patients’ experiencing weight loss or nausea.

People also described difficulty accessing current therapy. Lack of informed doctors and nurses, long wait times and geographic distance to specialists are frequently listed as barriers, especially for people living in rural areas of British Columbia. Additionally, criteria to qualify for financial coverage of treatment are often at a higher threshold than people’s current physical disease progression. For example, people have experienced debilitating fatigue, jaundice, flu-like symptoms and depression, however their liver enzymes are not elevated ‘enough’ or their liver fibrosis marker is too low to qualify for Pharmacare assisted treatment. Without financial assistance, many people are unable to afford treatment, thus treatment remains inaccessible for the many people who do not fit the existing advanced disease criteria.

## **2.4 Impact on Caregivers**

All caregivers express concern about how hep C is impacting their loved ones health and if they hadn’t yet had treatment, are concerned about what treatment would be like. One of the most difficult situations, aside from End Stage Liver Disease (ESLD), was when treatment had failed and their loved one was still ill, or if treatment wasn’t an option for their ill loved one. During treatment, caregivers talked about needing to stay both alert to possible very severe adverse reactions while not interfering or being ‘in the face’ of their loved one on treatment. The length of treatment was described as challenging, because the caregiver became responsible for managing more (or all) of the household chores, child care and income earning, as well as caring for their loved one. This increased load could be very difficult and sometimes caregivers ended up feeling resentful of their partner and then guilty because they were mad at a sick person. After treatment some caregivers said their lives returned to normal, especially after a successful treatment with fewer

adverse effects, but not always. Sometimes their loved ones continued to experience fatigue and other post-treatment conditions that continue to impact their lives and their families.

## Section 3 — Information about New Drugs

### 3.1 Information Gathering

Information was gathered through a combination of individual responses, PHCN survey results, and printed source materials. Staff at the Vancouver Infectious Disease Clinic at St. Paul's Hospital also gathered information from interested participants attending their regular hep C support group.

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

a) Single and even double therapy treatment would address large gaps and unmet patient needs in regard to HCV therapy. There is currently no HCV treatment available in Canada for null responders or people who do not complete a course of treatment. Furthermore, due to its low toxicity and lack of significant drug interactions, new single therapy options opens up treatment to patients who cannot tolerate previous therapies (due to HIV co-infection, autoimmune conditions or other co morbidities). For example, sofosbuvir has also greatly improved treatment outcomes (80%) for one of the most at risk patient groups, those with cirrhosis. Sofosbuvir would also address a large gap and unmet patient need because it is pan genotypic, interferon free, and is a single dose/pill. The importance of having multiple treatments available for people cannot be understated, since there are many people with co-morbidities and genotypes not responsive to current treatments.

Many people are very excited about simeprevir, sofosbuvir and faldeprevir coming to market because there is anticipation that these drugs will eventually eliminate the need for pegylated interferon and ribavirin. The potential to have either a single or double therapy -eliminating the need for triple therapy- would increase the number of people able to benefit from HCV treatment. People expect their lives to improve because of clinical reports of increased cure rates, shorter treatment duration, and fewer drug interactions/toxicity issues. Shorter treatment times and more manageable side effects mean individuals can continue working, and taking care of their families. Continuing to engage in everyday activities, as well as having financial and emotional stability results in a lower financial and emotional burden on individuals and families. The promise of a therapy that would eliminate a chronic communicable disease is the light at the end of the tunnel for people living with the health and social impacts of hep C.

Double and single therapy HCV treatment represents lower barrier options for people in contrast to the current triple therapy. Low barrier treatments, with fewer adverse effects lead to greater treatment adherence rates, and therefore improved health outcomes. This is especially true for people who require additional support to complete a course of treatment. For example, people living with hep C who are also intravenous drug users, have difficulty receiving HCV treatment because they are often deemed 'unreliable' or unable to complete treatment because of the current medication and dosing regime. From a medical position, street drug use is not contra-indicated with HCV treatment medication. Since research shows Canadian rates of HCV transmission and infection are higher among intravenous drug users, having a single treatment that is tolerable and easy to adhere to, could dramatically lower HCV transmission and infection rates among this population. This would work to decrease the long term burden on the Canadian healthcare system, as well as providing accessible treatment options for all Canadians.

Responders report an increased willingness to experience some adverse side effects – even with single therapy - if evidence shows an outcome of increased hep C cure rates (i.e. sustained virological response).

b) Double therapy did not seem to have a significant impact on side effects from hep C, when compared to triple therapy. However, side effects from double therapy were reported to be somewhat less severe and more tolerable than triple therapy. Anaemia and diarrhoea were cited most often as side effects for people taking telaprevir and sofosbuvir (with interferon).

Telaprevir was given a 'black box' warning in February 2013 because of the link between telaprevir PR combination therapy and cases of severe rashes leading to fatal skin conditions (i.e. Toxic Epidermal Necrolysis (TEN), Stevens Johnson Syndrome (SJS), and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). While a few responders reported telaprevir related rashes- there were no reports among PHCN members of severe rash or fatal skin conditions. However, potentially fatal side effects causes great concern, especially when other treatment options are very limited.

The decreased pill burden makes treatment much easier to adhere to because of fewer missed doses, as well as timing and food requirements.

We did not have any responders that had experienced single therapy, however people who had taken double therapy reported that the shorter treatment duration time and the less severe side effects made their course of treatment 'successful'. Additionally, all responders in double therapy reported an SVR after treatment. This was cause for great excitement and relief. Even with the side effects still present with double therapy – an increased possibility achieving SVR with one course of treatment is a major breakthrough for HCV treatment.

#### Section 4 — Additional Information

While currently outside the scope of this CADTH review, the new treatment drug daclatasvir (in combination with Lambda interferon) is showing positive outcomes for patients currently in clinical trials. A number of respondents are currently taking daclatasvir (with Lambda interferon) and reporting few adverse side effects. Because of these positive initial responses, PHCN is encouraging CADTH to review daclatasvir in the near future.

Currently, there is a gap between Health Canada 'approved' drugs (for example, Sovaldi/sofosbuvir) and drugs available to patients in British Columbia. Our concern is that people who need it the most (those who are quite sick and unable to work, who are receiving financial assistance or disability benefits) will not have access to these drugs because without employment, they do not qualify for private insurance drug plans and these drugs are not covered by provincial Pharmacare. This was the case when telaprevir and boceprevir first came on the market in Canada. It is our hope that BC Fair Pharmacare will approve and cover the cost of the medication quickly for people receiving financial assistance or disability benefits.

We are also concerned about the cost of treatment once these drugs are approved in Canada. Many insurance plans will only cover a portion of the new treatment costs, or a person is not 'eligible' to have new treatment covered because they have not first attempted current treatment. For example, one respondent who works full-time and has extended health benefits cannot afford sofosbuvir treatment because of the \$16,000 cost still associated with the treatment. Because of their genotype and other serious health conditions, current treatment is not available to them, and they are not eligible for current clinical trials.

It is our hope HCV treatment criteria will be changed so new drugs will be available to all patients, regardless of previous attempts with current treatments. Not being able to take current treatment because of co morbidities, or failing to complete conventional therapy because of adverse side effects should not prevent a patient from receiving current effective treatment.

Additionally, it is our hope all treatment drugs being reviewed would be available to people with fibrosis markers of less than F2, since there is growing evidence to show increased health outcomes for people who receive earlier treatment for hep C. Earlier treatment can also help control the transmission of hep C. Overall, early eligibility for double (and eventually single therapy) will result in financial savings for the Canadian healthcare system because of lowered transmission rates, fewer hospital visits, lowered rates of liver cancer, liver transplants and liver failure linked to hep C. We hope that best practice will be considered in the approval process for new hep C treatments.