Patient Group Input to CADTH

Section 1 – General Information

Name of the therapeutic review	Chronic Hepatitis C (CHC), second (2015) stage of review begun in 2014
Name of patient group	HepCBC Hepatitis C Education and Prevention Society
Patient group's contact information	#20 – 1139 Yates St. Victoria, BC V8V3N2 250-595-3892 info@hepcbc.ca www.hepcbc.ca
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1.1 Submitting Organization

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

1.2 Conflict of Interest Declarations

a) We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:

HepCBC Hepatitis C Education & Prevention Society has received funding for hepatitis C-oriented projects such as publishing educational materials, organizing educational forums, attending and presenting at educational conferences, advertising in newspapers (events and hepatitis C patient awareness), and holding awareness activities from the following pharmaceutical companies over the last four years: Merck Pharmaceuticals, Hoffman-LaRoche, Vertex Pharmaceuticals, Gilead Sciences, Janssen Pharmaceuticals, Bristol Myers Squibb, Boerhinger-Ingelheim, and AbbVie, plus support from Rx&D pharmaceutical umbrella organization.

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

The author has attended several educational conferences and meetings for which registration and travel expenses were funded by the pharmaceutical companies listed above.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The author developed this report using data from the significant writing (from several dozen patients) contributed following several of our calls for patient input about various hepatitis C direct-acting antiviral drugs (DAAs) over the last 7 months since CADTH's last CHC therapeutic review. In addition, the author is a volunteer who has actively manned HCV+ phone and email support systems or several years, and has broad knowledge of patient concerns and experiences. She has included aggregate input from one of our monthly support groups as well.

2.2 Impact of Condition on Patients

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

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

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

Day-to-day life is affected by all of the above, but in order of frequency and importance: Fatigue, muscle/joint pain, and slower motor reflexes limit both general activity and job productivity and/or effectiveness. Cognitive failure, fear of stigma and fear of social interaction limits both job effectiveness and general social interaction. Pain during movement can lead to either overuse of painkillers (which can further damage liver) or to avoidance of movement (which can lead to weight gain and other degenerative problems) Digestive and iron-overload problems limit how one shops for and cooks food, one's diet vs. the family's diet, and when (how often) one cooks or eats, affecting this important part of family life and social interaction.

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

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

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

The patients in the baby-boomer age cohort have generally had hepatitis C for many decades. Some have been symptomatic for many years, while others are becoming symptomatic for the first time. In either case, hepatitis C is now affecting their careers and family life drastically; they think that without

treatment, they will not be around much longer and must prepare themselves and their families for this. They hate the pain and the societal stigma, but especially the mental and physical changes which prevent them from working or playing as they used to. The ones that have been cured are generally celebrating the fact they are able to get their lives back, but wish they could have been cured much earlier.

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

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

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

2.3 Patients' Experiences With Current Therapy

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

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

Every patient agrees that interferon, though it has helped many be cured of hepatitis C over the years, is like a slow and long-lasting torture; the side effects (both short and long term) can be particularly

debilitating, and the efficacy so low compared to current DAAs that it should no longer be given to any patient.

2.4 Impact on Caregivers

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

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

Section 3 — Information about New Drugs

3.1 Information Gathering

Same as in Section 2.1

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

a) Based on no experience using new drug(s):

Patients tend not to differentiate the various new drugs from one another since they're all so much better than the existing ones, and share the characteristics of being mostly tested on genotype 1, far greater efficacy, a far shorter treatment time, no interferon or needles, very few side-effects, and an extremely high price-tag. However, ***HepCBC has a high anticipation that the new drugs will be tested and soon be approved for use (and coverage) for ALL genotypes, for co-infected folks, and for those who suffer from advanced cirrhosis. The comprehensive list of drugs and genotypes CADTH hopes to include in this review adds additional hope to these people.***

HepCBC is delighted to see the recent "stand-alone" submissions of two HCV drugs by Bristol-Myers Squibb. This should enable future combinations involving either or both of them to proceed through the approval process far more quickly than having to approve each combo one-by-one.

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

Over the last few years, many of our members have been able to take hepatitis C "Direct-Acting Antivirals" as part of a clinical trial. Every one of their treatments have been successful (except for one who had to abandon the trial due to a possible drug interaction exacerbating his a-fib), they have had no side-effects. They love the shorter time period as well. Those who have gone through treatment with the current Standard of Care say there is not much to say except:

"NO MORE INTERFERON or RIBAVIRIN!" HepCBC sees there is at this time some need to retain their use for some patients with particularly hard-to-treat genotypes or advanced disease. However their use should be terminated in all but the most pressing cases. Of the two, interferon is generally the least tolerated by our members.

Section 4 — Additional Information

While HepCBC is pleased with the scope of this review, and commented that it was asking the right policy questions about reimbursement, treatment criteria, and re-treatment, we did make a few suggestions. We want CADTH to ask these additional questions:

TREATMENT CRITERIA: Upon what basis does CADTH make decisions regarding HCV treatment criteria: scientific evidence? Short-term fiscal expediency? Compare short-term cost of curing HCV and preventing CHC (and serious sequelae) versus long-term cost of treating patients with incurable chronic diseases such MS, diabetes, or HIV over a patient's lifetime.

HepCBC recommends treating those first who are in most danger of dying without the treatment. Treatment criteria has its place when trying to find and treat those most in need. However, except for this sort of triage, we do not see a purpose for criteria based on proof of liver damage. We recognize that treatment works better and results in the greater increase in QALYs the earlier it is given. We anticipate that at some point every patient will be cured. We hope that the % of patients treated will soon rise from the current 1.4% of the HCV+ population per year, to approach the 5% - 6% per year treatment of the French and German HCV+ populations.

REIMBURSEMENT and STAGING: What place does fibrosis staging have in determining the degree of physical damage? Are there other factors we should be looking at as well, such as autoimmune responses, mental health, or extrahepatic manifestations? And if fibrosis staging has a place, how accurate are the various means of determining fibrosis score and how cost-effective are they?

HepCBC recommends looking at extrahepatic manifestations of hepatitis C and considering these in any staging, triage, and compensation that occurs. Compensation for therapies for extrahepatic manifestations, and for non-invasive diagnostic procedures such as Fibroscan should be part of the therapeutic package.

ADVANCED DISEASE: (a) What recommendations, if any, do we want to make to limit the reimbursement of the DAAs for CHC in those with various degrees of liver de-compensation?
(b) Should we reimburse for drugs or treatments used to enable a patient approaching de-compensation to qualify for DAA treatment, or to enable any patient to remain on treatment?

HepCBC recommends that patients be reimbursed for drugs to control or reverse conditions such as hepatic encephalopathy, low platelets, anemia, or fluid retention which now preclude patients from going on to treatment, or which can result in patients having to stop treatment.

REVIEW PROTOCOL: (a) How can CADTH/CDR streamline future reviews of regimens for which all of its components are already approved in other regimens, rather than doing an entirely new review?
(b) Is CADTH/CDR doing all it can to ensure equitable pricing and access? In some cases it has called for lower prices, but there does not seem to be a clear pattern of when this call is made, and in those cases where it is, specific target pricing or pricing structures are not defined.

HepCBC notes that it would be helpful to all stakeholders if CADTH/CDR would take leadership on the issue of equitable pricing and access, possibly even mandating a particular equitable pricing structure or formula.

COSTS: ***HepCBC recommends amortizing the cost of treatment for this expensive but curable disease over time. The cost compared to treating a chronic disease will then become more easily justified.***

FINAL RECOMMENDATION FROM HepCBC: ***As a patient group whose members collectively possess broad, longtime and extensive experience in treatment with interferon, ribavirin, telaprevir, and boceprevir, we strongly protest any of these harsh and often debilitating drugs being prescribed instead of the next generation DAAs for short-term fiscal expedience. The very common side-effects of these drugs (experienced by most who take them) are within the realm of "cruel and unusual punishment", and unless their use is of proven scientific value in a particular case, they should be completely struck from provincial formularies.***

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