Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest		ombitasvir/paritaprevir/ritonavir
Name of the patient group		HepCBC Hepatitis C Education and Prevention Society
Name of the primary contact for this submission:		REDACTED
Position or title with patient group		REDACTED
Email		REDACTED
Telephone number(s)		REDACTED
Name of author (if different)		REDACTED
Patient group's contact information:	Email	info@hepcbc.ca
	Telephone	250-595-3892
	Address	#20-1139 Yates St. Victoria BC V8V 3N2
	Website	www.hepcbc.ca
Permission is granted to post this submission		☐X Yes ☐ No

CADTH will post this patient input submission on its website if permission is granted. See CDR Update — Issue 99 for details.

1.1 Submitting Organization

Founded in 1996, HepCBC is a registered non-profit society run by and for people infected with, or affected by, hepatitis C. Our mission is to provide education, prevention and support to those living with HCV. We have an office in Victoria and have recently opened another in downtown Vancouver, BC. Most of our staff are volunteers with experience (either past or present) of hepatitis C. We also employ 4 contractors on part-time, short-term contracts. We run activities and groups 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: publication of a monthly bulletin (the *hepc.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 testing among at-risk groups, including those who no longer fall into this category but may have contracted hepatitis C decades ago either through the blood 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 (for example with hepatitis B and/or HIV).

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 and on buses (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&, the 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:*

2 of us who have completed patient submissions and both of the authors of this report have attended several educational conferences and meetings for which registration and travel expenses were funded by the pharmaceutical companies listed in (a) above.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The information was generated using data from:
(1) patient surveys advertised through our website and our email list. There were only 5 submissions from people either living with hepatitis C or affected by hepatitis C. All were from British Columbia.
(2) one of us is a volunteer, who has actively staffed HCV+ phone and email support lines over the course of several years and therefore has an in-depth knowledge of patient concerns and experiences; both authors of this report are patient-researchers who have been reading scholarly articles about HCV for many years (20+ in one case).
(3) input from our monthly support meetings has also been included.

2.2 Impact of Condition on Patients

In the last few years HepCBC has done 14 hepatitis C drug submissions for both CADTH and BC PharmaCare, and have answered Questions 2.2, 2.3, and 2.4 as many times. Our respondents are, understandably, feeling rather jaded because they are being asked to answer the same questions so many times. However, we acknowledge that, with so many new DAAs "in the pipeline", requests for input are becoming more frequent. To avoid re-inventing the wheel we suggest you review our more detailed answers in our five most recent hepatitis C drug submissions, made in July, August, October and December of 2014 and in March of 2015 (in which 2 separate submissions were made for 2 drugs from the same company).
http://hepcbc.ca/wp-content/uploads/2015/03/20150310_daclatasvir_DAKLINZA_CADTH_redact.pdf

http://hepcbc.ca/wp-content/uploads/2015/03/20150310_asunaprevir_SUNPREVA_CADTH_redact.pdf

http://hepcbc.ca/wp-content/uploads/2015/01/20141221_ombitasvir_paritaprevir_ritonavir_dasabuvir_CADTH_redact.pdf

http://hepcbc.ca/wp-content/uploads/2014/10/20141008_ledipasvir_sofosbuvir_HARVONI_CADTH_redact.pdf

http://hepcbc.ca/wp-content/uploads/2014/10/20140711_sofosbuvir_SOVALDI_Pharmacare_redact.pdf

2.3 Patients' Experiences With Current Therapy

See Section 2.2 above.

2.4 Impact on Caregivers

See Section 2.2 above. In addition to the many previous "Impact on Caregivers" sections already written, we'd like to review this statement made for Holkira Pak:

(M, 65): "The new therapies are so gentle compared to interferon-containing regimes. I do not see AbbVie's 3D as having any impact on caregivers at all (during the patient's time of treatment)."

This last comment is extremely important in relation to this particular drug combination review: it is fair to suggest that the AbbVie combination currently under review for G4 infection is likely to be perceived by patients and caregivers in a similar way to the perception of Holkira Pak, as it is an identical combination minus dasabuvir.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

The information was gathered in the same way as for previous submissions **(See Section 2.1)**. An online patient survey; personal experiences of volunteers and staff; and input from our monthly support meetings. In addition, although we are aware that CADTH has access to all published data, we have referred to academic literature in support the some of the points we make, particularly in the following section.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

a) Based on no experience using the drug:

HepCBC believes that there is certainly a gap in treatment options for the less common genotypes in Canada. The percentage of sufferers infected with genotype 4 (GT4) globally has been estimated from 8.3%[(1)] to as high as 20%, depending on various researcher assumptions and data collection methods.

The estimated number of sufferers in North America with GT4 approximates 55,000, accounting for only 1.2% of infections in this region[(1)]. These numbers are not small, even if they appear to be in terms of overall percentages of HCV infection in North America.

However, GT4 is the overwhelmingly predominant GT in North Africa and the Middle East; in fact, other GTs are quite rare there. Moreover, increased global mobility means that the less common genotypes that we see in Canada (such as GT4) can and will travel. We already know that European countries are starting to see an increase in numbers of those infected with GT4. Regarding Canada specifically, in addition to economic migration, we are currently witnessing "compassionate migration" in the form of the movement of Syrian refugees to many countries including ours. The infection rate in Syria is estimated to be between 1%-2% of the population[(2)], of which most will be GT4. Therefore, it is fair to suggest that there is the possibility that the countries with significant Syrian refugee intake may well see a rise in numbers of those affected with hepatitis C, GT4. These countries could include Canada as it meets its obligations to the current crisis. While we are in no way suggesting that these groups are likely to transmit the virus to Canadian citizens or Permanent Residents (as Syrians are likely to have been infected via the blood system in Syria rather than to be PWIDs), we are raising the possibility of a potential rise in numbers of GT4 sufferers in Canada over the coming years.

Treatment with peg-interferon and ribavirin, which is currently approved for GT4, yields success rates of between only 43% to 70% for a 48 week course of treatment[(3)]. Some GT4s are now being treated with sofosbuvir+peg-interferon+ribavirin with a much higher rate of SVR. A drug combo like ombitasvir, paritaprevir and ritonavir (both with or without ribavirin) would be much easier for GT4 patients to tolerate as it does not contain interferon, and has equally high or higher rates of SVR.

We would, however, much prefer ribavirin-free regimens due to their minimal if any side-effects. The shorter treatment time of the new DAAs definitely diminish ribavirin's negative impact somewhat.

Adverse events reported for this combo are extremely mild, primarily consisting of known ribavirin-related issues such as fatigue, nausea, rash, insomnia, and asthenia.

We are looking with interest at the Agate 1 trial which showed that success rates for treatment either with or without ribavirin can be almost the same if the treatment period is prolonged (i.e. to 24 weeks). It has even been shown to cure people with compensated cirrhosis, and those who have failed treatment with Harvoni and Sovaldi. This is pretty amazing.

OUR RECOMMENDATION: The approval of the ombitasvir, paritaprevir and ritonavir combo (both with or without ribavirin), with its great SVR rates of between 91%-100% [(4)], would provide better treatment options for GT4s. All drugs in the AbbVie combination under review have already been approved by Health Canada for GT1, except that one ingredient (dasabuvir) is left out of the combo as it does not demonstrate activity against GT4, while the other DAAs do[(3)]. The FDA approved this GT4 triple combination (brand name: Technivie), with and without ribavirin on July 24, 2015 [(5)]. HepCBC believes Health Canada should follow the FDA's lead so that all GT4 patients in North America have the option of an effective all-oral option. Cutting treatment time down to some 25% of what it has been thus far while increasing cure rates to between 91%-100% provides a clear rationale for approval. Finally, Technivie has been demonstrated to be safe and effective with few adverse effects or even side effects[(5)]. Therefore, it seems likely that in the absence of any complicating factors, this would be an excellent all-oral GT4 HCV treatment regime. Taking this new drug combo for such a short period of time will require less clinical management expertise and time, fewer hospital visits, and less time off work.

b) *Based on patients' experiences with the new drug as part of a clinical trial or through a manufacturer's compassionate supply:*
   - We never were able to interrogate anyone who has had experience with this new drug combo.

Section 4 — Additional Information

HepCBC warmly welcomes this new treatment, the first interferon-free treatment for genotype 4. However we are still very worried that the current high cost of DAAs for HCV will result in higher demands that patients meet stringent treatment criteria, not for any medical reasons but to limit the quantity of treatments paid for by the provincial/territorial drug plans. We know that the sooner treatment is started, the more likely it is to work, and the more likely it is to prevent cancer, heart disease, and other hepatic and non-hepatic manifestations of hepatitis C. Earlier treatment also results in a greater quantity of quality-adjusted years of life added to patients' lives.

SUGGESTED SOLUTION 1 (Temporary Triage): We do understand the glaring urgency of treating those who are in most danger of progressing to de-compensation or liver cancer, or needing a liver transplant. We believe that in return for treating these patients, most patients remaining might accept waiting an extra year or two for treatment. After those most critically in danger are treated, treatment should simply be offered to "anyone with active chronic hepatitis C" (regardless of the state of liver damage).

SUGGESTED SOLUTION 2 (Economies of Scale): We urge those negotiating drug prices at all levels of government to offer to increase the number of patients treated in return for a lower price. One way of increasing the number of patients treated is to screen and identify more of them through initiatives such as age-cohort testing, which we recommend. Another way is to lower or abolish medically-unsound

treatment criteria. HepCBC strongly opposes the use of such criteria as proof of liver damage such as "high or higher than Fibrosis-score 2".

References:

(1) Messina, J. P., Humphreys, I., Flaxman, A., Brown, A., Cooke, G. S., Pybus, O. G. and Barnes, E. (2015), Global distribution and prevalence of hepatitis C virus genotypes. Hepatology, 61: 77–87. doi: 10.1002/hep.27259

(2) Mohamed A. Daw and Aghnaya A. Dau, "Hepatitis C Virus in Arab World: A State of Concern," The Scientific World Journal, vol. 2012, Article ID 719494, 12 pages, 2012. doi:10.1100/2012/719494

(3) University of Washington (2015) Hepatitis C Online: Treatment of HCV Genotype 4: http://www.hepatitisc.uw.edu/go/treatment-infection/treatment-genotype-4/core-concept/all [accessed on 15/09/2015]

(4) Abbvie (24/07/2015) TECHNIVIE™ (ombitasvir, paritaprevir, and ritonavir tablets) Receives FDA Approval as the First and Only All-Oral, Interferon-Free Treatment for Genotype 4 Chronic Hepatitis C in the U.S. http://abbvie.mediaroom.com/index.php?s=20295&item=122629 [accessed on 15/09/2015]

(5) FDA US Food and Drug Administration (24/07/2015) FDA approves Technivie for treatment of chronic hepatitis C genotype 4: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm455857.htm [accessed on 15/09/2015]