

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	ZAXINE for hepatic encephalopathy (HE)
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	HCV+ Volunteer, Board Member
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Permission is granted to post this submission	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> 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

HepCBC is a non-profit society run by and for people infected and affected by hepatitis C. Our mission is to provide education, prevention and support to those living with HCV. Our office with our only paid employee (an office mgr.) is in Victoria, BC. We also have activities and groups in Nanaimo, BC and Surrey, BC. 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 hepcbull. We focus on providing “clean and sober” peer support groups, anti-stigma activities, prevention education to young people, and 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 three years: Merck Pharmaceuticals, Hoffman-LaRoche, Vertex Pharmaceuticals, Gilead Sciences, Janssen Pharmaceuticals, Bristol-Myers Squibb, Boehringer-Ingelheim, and AbbVie.

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 of this report 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

This report was developed using data provided by ten (10) individuals:

(1) a patient survey advertised through our website and our email list. In total there were submissions by three (3) patients with hepatic encephalopathy, one of whom is a liver transplant survivor, and two of whom suffer from Primary Biliary Cirrhosis (PBC) and have been taking Zaxine due to for an extended period (***actually not Zaxine but Xifaxan, rifaximin's US tradename) through Salix Pharmaceutical's "Special Access Program" for Canadian patients. This program, in which Canadian hepatic encephalopathy patients received this drug free of charge, ran between 2010 and 2013. It stopped on Nov. 7, 2013 as Canadian law requires such a program to be terminated within 90 days of Health Canada's NOC (Aug. 13, 2013). Presently it is only available through direct purchase. This is a terrible burden for patients such as these who really need this critical drug benefit covered. One of the PBC patients also has Sjogren's Syndrome.*** (part in italics added by HepCBC on January 12, 2015 in response to a request for further clarification from a public member of the CADTH committee charged with reviewing this drug).

(2) Input from two (2) HCV+ volunteers who have actively manned HCV+ phone and email support systems for several years, and have extensive knowledge of patient concerns and experiences.

(3) Aggregate input from five (5) HCV+ participants at our August monthly support groups has also been added.

2.2 Impact of Condition on Patients

As a patient group for those affected by hepatitis C, we at HepCBC have had much experience with people suffering from both minor and major forms of hepatitis encephalopathy (HE). It is indeed a very debilitating condition, even when it manifests in its less severe form, and comes and goes. In the very end stages of liver disease, it is a nightmare for both patients and families. Some of us have watched HCV+ people and their families suffer for years, on and off as HE results in loss of confidence, a job, relationships, and ensuing financial hardship, further agitation, alienation, isolation, anger, and depression. We have also seen people in their last couple weeks of life, first in a state of total agitation and confused, irrational anger at their caregivers, later slipping into a coma. As patients with liver disease, we greatly fear this state, particularly any hurtful things we might say to dear friends, family, and caregivers, especially as this would be their final memory of us. We know that this drug is expensive, and that other less expensive will be – and should be – tried first. But we'd really like to know that ZAZINE is available in our doctors' toolkit if and when the need was there. Not only to prolong our lives, or to add quality time, getting us at least close to normal for however many months or years that this is possible, but also to help ease our final days with friends and family. We present below the actual stories of HE patients, either in their own words, or we give accounts of HCV+ patients we have known. Interestingly enough, only one HCV+ patient (with a liver transplant) sent written input to us through our website, but they are generally eager to share their stories of HE orally.

"I had a liver transplant in April 2002. I was psychotic by this time. I had 7 hemorrhagic bleeds over several years. MRI's demonstrated encephalopathy. For a long time before the transplant large portions of memory were missing. I was argumentative and belligerent. I had 2 car wrecks and don't remember those. I would get lost going home. And couldn't stay in my lane on the freeway... I have peripheral neuropathy and can not to this day hold my balance if I try to walk heel to toe. I have permanent brain damage affecting memory and sleep. I typically sleep 1.5 of 3.0 hours and wake up from REM sleep (a 90 min cycle). Rarely over the last decade have I been able to sleep 4 hours. I had an Extensive Neuropsychiatric Evaluation after the transplant and the diagnosis was cognitive impairment. due to slow processing speed. Because of multiple procedures and surgeries I have a very high tolerance to sedatives. I nap up to 4 times a day to catch up on sleep. I often fall asleep spontaneously (in recliner & movie theaters. If my mind is a little cloudy I do not drive...(example of how bad sleep patterns are):...I took 10 x 10mg Valium recently to no effect, after trying 2, then 4, then 5. .Then I mixed 20 mg Valium & 20 mg Ambien and slept for 6 hours. What a relief. The next night that dose had no effect and I doubled it after waking up at 3:00AM. Nothing works."

"I have Primary Biliary Cirrhosis and Sjogren's Syndrome. My more severe symptoms include shaking of hands or arms, agitation, excitement, disorientation. drowsiness and confusion, slowed or sluggish movement, and problems concentrating. In short I have problems functioning well in my day-to-day life. Every activity in my life is affected. Fatigue prevents many activities."

2.3 Patients' Experiences With Current Therapy

(liver transplant HE sufferer): "All I had was LACTULOSE which I absolutely hated the sweet syrupy taste. I had to stay near a toilet-because it would act 0-4 hours after taking. I eventually had to take it because I could not hold my balance or walk straight."

(PBC HE sufferer): "In 2007 I was diagnosed with Primary Biliary Cirrhosis. My hepatologist prescribed URSODIOL. At that time I was virtually symptom free and remained that way until 2011 when my first attack of HE occurred. It was characterised by disorientation, loss of coordination, slurred speech, stumbling gait, and inability to focus mentally. Because of this [NOTE: unusual for PBC] presentation, it

was felt by my doctor that I had had a slight stroke. However, in consultation with the stroke clinic it became clear that that was not the case. The symptoms lessened but never really disappeared but nobody really knew what to do with me. I went to Emergency three or four times but there was never a conclusive diagnosis. One doctor prescribed LACTULOSE but, since I didn't really understand its purpose I was inconsistent about taking it. I continued in this foggy state for over a year. The attacks occurred several times. I was prescribed CIPROFLOXACIN; it was somewhat helpful for a short time but soon had no effect in the long term. Fifteen months after my first HE attack, I had an extremely serious attack. Not only did I demonstrate the earlier mentioned symptoms but in addition I was delirious and behaving in a totally uncontrolled manner. To this day, I have absolutely no recollection of those two days.”

“When I was released from the hospital, I went to see my hepatologist. As it happened, he was able to get access to RIFAXIMIN through a special access program.”

(Patient with PBC and Sjorgren’s Syndrome): “For several years, I have taken both ZAXINE (through Compassionate Study program of Salix) and LACTULOSE. LACTULOSE causes loose stools and for that reason I use it seldom.”

(HCV+ patient who works as a volunteer at HepCBC): “I have known six patients with severe HE, and all lost their jobs and became alienated from their families during their periods of HE. Two eventually got liver transplants and are doing great now. One is still awaiting a transplant and though he is out of a hepatic coma at present, he is dealing with HE and related depression daily. Two almost died and are still quite ill, but have overcome most of their HE, enough to do volunteer work but not to hold down a paying job. The last died a terrible death over a very short time. All of these six patients took LACTULOSE alone for their HE and other symptoms of ESLD; no other drugs were used.”

“LACTULOSE helped keep the first three alive while awaiting a liver, though they were slipping in and out of coma. The two who now volunteer are still taking LACTULOSE regularly, and it helps them maintain their mental strength. Perhaps if ZAXINE were available to them, they would be able to hold down a paying job and support their families. Doctors could at least try ZAXINE with patients such as those if it were covered by Pharmacare. The patient who died did not respond at all to LACTULOSE, and died of an intestinal obstruction. If she had been able to take ZAXINE, she might be alive today.”

2.4 Impact on Caregivers

(PBC patient): “...Although I am the one with the disease, my husband was extremely effected also. I needed careful watching, I was never left alone for any extended time, and all my actions were monitored. Since a lot of my bizarre behaviour occurred at night, he always slept lightly so that he could hear me if I was out of bed.”

(Partner of patient with PBC and Sjorgren’s Syndrome): “Since patient began taking ZAXINE the impact of her condition on my life has been considerably less. Less worry because patient is more energetic, mood is more optimistic. Concentration and focus is better. Fatigue improved. Able to eat foods containing protein again. Able to gain some weight , now back to normal. Looks good too. Definitely less fatigue. Better daily function. ZAXINE works beyond our expectations to help clear up HE symptoms.”

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Same as in Section 2.1.

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:*

- Lives of patients would be greater in both length and quality.
- This drug is great for those people who cannot take LACTULOSE, or who experience a better result when it is added to their LACTULOSE regimen.
- While we have not heard specifically that patients would put up with side-effects of this drug in return for its benefits, we have heard no reports of side-effects from it.
- This drug would likely result in fewer deaths, fewer coma patients, more successful transplants, fewer hospital visits, less time off work, greater financial stability, greater mental stability, and fewer family breakdowns.
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b) *Based on patients' experiences with the new drug as part of a clinical trial or through a manufacturer's compassionate supply:*

(PBC patient) "...When I was released from the hospital, I went to see my hepatologist. As it happened, he was able to get access to RIFAMIXIN through a special access program [SAP through US manufacturer, Salix] .This drug gave me a new life! I could actually feel the fogginess dissipate. I can focus, multi-task and problem solve, all the cognitive abilities one expects to have. My coordination has returned. I still have some trouble remembering events and physically I have very limited stamina but I have come such a long way all as a result of RIFAXIMIN."

(Patient with PBC and Sjorgren's Syndrome): "Good. Can function better. Improved Feeling of well being. I have been on the study for ZAXINE and I have been on the drug for a few years. Made my Life livable. Have been using ZAXINE for a few years. Improves my wellbeing and health. No side effects! I can live again."

"Positive effects on my symptoms (shaking of hands or arms, agitation, excitement, disorientation, drowsiness or confusion, slowed or sluggish movement, and problems concentrating. The best result is it allows me better concentration. I am able to focus better with less Confusion and improvement in Calmness."

"There are no adverse events or Negative Effects. And it sure is easier to use than the other drugs. More convenient. Less unpleasant."

"Now with taking ZAXINE, I can live a good life with dignity."

"When the Study concluded; there was no access to ZAXINE in Canada.

I contacted [representatives' names] from Salix, USA. They have been wonderful and have been providing me with ZAXINE on a compassionate level. I am grateful to [representatives' names] from Salix USA for allowing me to have a better quality of life!"

"Unfortunately ZAXINE is Out of Reach expensive, \$1400 to \$1600 a month so (without reimbursement by Pharmacare) is not accessible as of yet to the public."

Section 4 — Additional Information

(PBC patient): "I hope this account is helpful to you. I can't imagine what state I would be in without this medication."

(Patient with PBC and Sjogren's Syndrome): "I know that ZAXINE could help a lot of people with this condition to have a better quality of life. I believe many people have this condition, but they have not been diagnosed yet. ZAXINE must become readily available and affordable to All Canadians."

(HepCBC): We fully support listing ZAXINE in Canada for use with any patient with HE, either added to other drugs such as LACTULOSE, or as a stand-alone, depending on the patient's needs. We recognize the cost factor would likely not make it the first drug to try, but to have it available (and financially accessible) to deal with this terrible condition would be a real blessing to these patients and their loved ones.