

CADTH COMMON DRUG REVIEW

# Patient Group Input Submissions

**OBETICHOLIC ACID (Ocaliva)**

(Intercept Pharma Canada, Inc.)

Indication: For the treatment of primary biliary cholangitis

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

Canadian Liver Foundation — permission granted to post.

Canadian PBC Society— permission granted to post.

### **CADTH received patient group input for this review on or before January 20, 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.

## Canadian Liver Foundation

### General Information

<b>Name of the drug CADTH is reviewing and indication(s) of interest</b>	Obeticholic Acid
<b>Name of the patient group</b>	Canadian Liver Foundation
<b>Name of the primary contact for this submission:</b>	Melanie Kearns
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Website	<a href="http://www.liver.ca">www.liver.ca</a>
<b>Permission is granted to post this submission</b>	Yes

### 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 250,000 Canadians through our public and professional education programs, patient support programs and other fundraising and outreach efforts. Over the past 45+ years, the CLF has invested more than \$50 million in health education and prevention programs.

### Conflict of Interest Declarations

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

In the past, the Canadian Liver Foundation has received unrestricted educational grants and/or has worked on joint initiatives with AbbVie Corporation, Alexion Pharma Canada, Astellas Pharma Canada Inc., BD Biosciences, BTG Biocompatibles, Bristol-Myers Squibb Canada, Gilead Sciences Canada, Intercept Pharmaceuticals Inc., Lupin Pharma Canada, Merck Canada, Pendopharm, Qiagen and Sirtex Medical.

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

No conflicts to report.

## Condition and Current Therapy Information

### Information Gathering

To gather input for our submission, the CLF invited patients, caregivers and health care professionals from across Canada to fill out an online survey modelled on the CADTH questionnaire. The 50+ responses received have been used in compiling the feedback for this submission. Quotes from survey respondents are included in italics in various sections of this submission.

### Impact of Condition on Patients

Primary biliary cholangitis (formerly known as primary biliary cirrhosis) or PBC, is a disease that affects predominantly women aged 40-60 (an estimated 1 in 1,000 women over age 40). When a person has PBC, the immune system attacks the liver causing slow, progressive damage to the bile ducts (small tubes through which bile flows out of the liver). When the bile ducts are damaged, bile and other substances cannot be eliminated and accumulate in the liver. This build-up of toxic substances in the liver causes inflammation and eventually leads to scarring of the liver (cirrhosis) and liver failure.

There are approximately 9,000-11,000 people in Canada diagnosed with PBC. PBC cannot be cured and over time individuals with this disease get progressively sicker and their quality of life deteriorates. The most common and debilitating symptoms reported by PBC patients are extreme fatigue and constant itching (pruritus) but many also experience joint pain, insomnia, mood swings, depression, diarrhea, dry eyes, nausea, trouble concentrating, night sweats and osteoarthritis. More than half of PBC patients have at least one additional autoimmune disease such as thyroiditis, rheumatoid arthritis, Reynaud Syndrome, and IBD.

*“Severe fatigue is the worst symptom. I am no longer able to work due to the fatigue. I often have to cancel plans as I am not well enough to participate. I know if I take part in an activity such as shopping with friends, or going out for dinner, it will take about 48 hours to recover my energy.” – PBC patient*

*“Falling asleep while at my desk or fighting to stay awake was all encompassing. Reducing my work days to 4 days per week made no difference nor did sleeping for 8 to 10 hours per night. It definitely hampered my social life as well as my family’s social life. Outings became difficult to plan ahead due to fatigue. Itching was also a factor in daily life. Evenings were more difficult with itching as well at bedtime. Sharing a bed with my spouse became next to impossible as my constant scratching kept him awake. Skin sensitivity was a major factor in shopping and wearing of clothes. My skin was so sensitive to buttons, seams, tags, fabrics. Once I was prescribed cholestyramine it helped. The other factor is arthritis, painful joints, bones and muscles and dealing with osteoarthritis as well.” – PBC patient*

The constant fatigue makes it difficult, or even impossible, for those with PBC to work, care for children, participate in activities outside the home or even complete household chores. Some individuals have had to give up jobs or businesses as well as sports and hobbies leaving them depressed, isolated, and, in some cases, dependent upon government assistance programs.

*“Unable to work and am currently on disability. Was having a lot of problems but due to my stubborn nature I just kept pushing myself until my body basically said no more. I'm unable to do the basic of things such as housecleaning or washing dishes... All I want to do is sleep.” -- PBC patient*

*“Am 39 and feel like I am 90. Have 3 children and work full time so exhausted all the time. Memory problems and cannot focus. Developed depression and anxiety as well.” – PBC patient*

*“I experience fatigue, nausea, mild itching and fevers, with fatigue being the worst by far. I operate a commercial greenhouse so my work is seasonal. By the time I'm finished in June I'm sacked and sick all summer and into fall. 2016 is probably the last year I will be open to public as it's just too much for me. I have no social life as I'm just too fatigued to have any desire to do things at the end of*

*the day. I used to be extremely active, I rode horses, went sledding, fishing worked at very physical jobs. I do none of that now. I'm an artist and have no energy or desire for my art anymore.” – PBC patient*

*“The severe fatigue is very debilitating. Since I was diagnosed with this disease it has greatly impacted my quality of life. I am no longer able to make plans, as I really don't know from one day to the next how I will feel. I've really found out who will stand by me on my bad days and be a support when I need someone. As it is an invisible disease so many people haven't a clue how it affects one's life. I would say the fatigue is the worst, along with making sure all your medications are managed. PBC is an autoimmune disease and with that most of us have other autoimmune diseases. I feel I've become a burden and I was always someone who was of service to others.” – PBC patient*

## Patients' Experiences With Current Therapy

There is currently only one drug therapy available to treat PBC – ursodeoxycholic acid (UDCA or brand name Ursodiol) – which can help slow down the progression of the disease. There are an estimated 7,000 PBC patients in Canada being treated with UDCA. However, as many as 40-50 per cent of PBC patients do not adequately respond to UDCA while an estimated 5 per cent cannot tolerate it at all leaving them with no treatment options.

Among those patients who are able to take UDCA, some experience relatively few side effects while others suffer from many of the same symptoms as those who are not being treated -- ongoing fatigue, nausea, diarrhea, itching – which require additional medications.

*“I find that Urso makes me even more fatigued. If I know I have an event coming up, I will stop taking it three days in advance so I can participate. Urso does not help with the itching. It is very expensive to take Urso, and I went through my \$2,500 workplace insurance cap before the year was out.” – PBC patient*

*“I am taking Ursodiol which causes frequent belly pain, diarrhea and heart burn. I am now taking pantoprazole to counteract those issues.” – PBC patient*

*“The only treatment I have been given is Urso...which I do not tolerate well. My doctor would like me to be on at least 1000 mg /day which my stomach does not tolerate - increased nausea and gastro upset. I currently take 500 mg day regularly and when my stomach is ok I try to add another 250 mg. I have tried dosing at different times/amounts to try to alleviate side effects....Urso also caused me to gain weight (30 pounds within 4 months after starting)...I have been unable to lose weight being on URSO & have gained more since - some of which is due to reduced ability to exercise due to other symptoms worsening.” – PBC patient*

*“Taking 1000mg Urso daily. It has caused diarrhea and severe nausea, many days I am not able to leave the house. And my LFT's are still not normal.” – PBC patient*

Over time, those who do not respond to UDCA, cannot take UDCA and even some who have been taking UDCA for years, will progress to advanced liver disease and suffer jaundice, variceal bleeding, portal hypertension and may develop liver cancer. 1 in 40 PBC patients will require a liver transplant. Up to 30 per cent of PBC patients who receive a transplant will have a recurrence of PBC.

*“I am on Ursodiol currently. My liver blood levels have not come down completely into the normal range therefore slowly, my liver will get worse. I sometimes have pain in my liver, my hands and feet swell and I have night sweats sometimes. My disease was caught early and I was diagnosed 4 years ago. I don't have too many symptoms so far but I know that this will get worse as I continue to live with this disease.” – PBC patient*

*“I was on Urso. It did not lower the enzyme levels and I was nauseated most of the time. Randomly during the day I would all of sudden start retching for no apparent reason.” – PBC patient*

UDCA is covered in whole or in part by many drug plans but those without coverage face financial hardship in trying to afford the medication as well as other required medications to treat symptoms and other associated health issues. Those on the verge of retirement live in fear of not being able to pay for their medication once their workplace insurance coverage expires.

*“The financial burden of this disease is terrible. I can no longer work and have so many appointments and tests to manage. People get tired of it after awhile and no longer offer any assistance. I was diagnosed at Stage 3, so I'm pretty advanced. I have portal hypertension, along with varices. I have to have regular endoscopies to monitor these. Regular ultrasounds and CT scans are another two tests that are repeated frequently.” – PBC patient*

*“I have chronic diarrhea now. Also terribly bloated, I look about 8 months pregnant. Since I am on CPP disability and my husband works for the federal government we do have 80% coverage. I am a cardiac patient and have meds for that. I suffer from depression/anxiety and have meds for that. I have reflux and on meds for that. I am on sleeping meds and pain meds. My husband is a cardiac patient, meds for that, has Type 2 diabetes so meds for that. It adds up to more than half of my disability cheque. I have not been on Urso or Zaxine for three weeks as I can't afford them.” – PBC patient*

*“Most definitely difficult financially since retiring as I no longer have drug coverage and ursodeoxycholic acid is very expensive. At present time I am 64 and will no be covered by government drug plan until I turn 65. I also require various other medications such as cholestyramine, Crestor, and blood pressure medication. If I forget to take ursodeoxycholic acid then I notice the difference. I also have GERD which requires medicine as well as osteoporosis.” – PBC patient*

## Impact on Caregivers

As with many forms of liver disease, the slow deterioration of those with PBC results in caregivers needing to take over more and more of the household and financial responsibilities. Due to chronic fatigue as well as other symptoms like itching, diarrhea and nausea, patients may not want to leave the house or participate in family activities or social engagements which leaves them physically and socially isolated. This can cause stress with spouses and families.

*“The fatigue stops me from being active like I once was. I don't think my family and friends understand what my body truly feels like. Don't feel like socializing as I used to. It's always in your head: is this from pbc? How far along am I?” – PBC patient*

*“I find myself withdrawing from my friends and family. I don't participate in as many functions as I used to. I am scared to get sick as I have had 3 sinus/chest infections in 4 months because one of my children had a runny nose.” – PBC patient*

*“I'm tired, need quite a bit of rest, upper abdominal discomfort and itchiness. I find extra events like Christmas, birthdays, special occasions that require more energy I don't look forward to anymore. Being tired all the time can leave my family frustrated as I don't what to do any thing that I feel may be too much.” – PBC patient*

*“I am no longer able to make plans, as I really don't know from one day to the next how I will feel. I've really found out who will stand by me on my bad days and be a support when I need someone. As it is an invisible disease so many people haven't a clue how it affects ones life.” – PBC patient*

When patients develop more advanced disease, caregivers must help coordinate doctor's appointments, tests, medications as well as trying to provide emotional support and manage the household. They experience added stress from frustration and fear of what the future may hold.

*“I can no longer work and have so many appointments and tests to manage. People get tired of it after awhile and no longer offer any assistance. I was diagnosed at Stage 3, so I'm pretty advanced. I have portal hypertension, along with varices. I have to have regular endoscopies to monitor these. Regular ultrasounds and CT scans are another two tests that are repeated frequently.” – PBC patient*

*“My husband is in the advanced stages of PBC. This requires a regular 4-6 month endoscopy procedure to band vessels in the esophagus & stomach in an effort to prevent major bleed outs (he has lost 4-6 units of blood with each bleed out). I know that the chances of receiving a transplant, at his age (67 years) is not a possibility.” – caregiver for PBC patient*

## Information about the Drug Being Reviewed

### Information Gathering

The information in this section was compiled from clinical trial data, feedback from a PBC Multi-disciplinary Roundtable as well as from online surveys completed by PBC patients.

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

*Based on no experience using the drug:*

OCA can be used as a single therapy or in combination with UDCA to boost response. For patients who have not responded or are unable to take UDCA, OCA offers a much-needed alternative treatment option although some are still concerned about both side effects and cost.

“My liver enzymes are currently increasing so having something to take in addition to Urso would be fantastic. If it also helped to reduce some of the symptoms that would be even better. Although Urso has until now kept my enzymes relatively normal, it has never helped the fatigue.” – PBC patient

“I think it should be approved. For some patients who don't respond to the other med (Ursodiol) and or for whom it doesn't work or not well enough. My dad I believe is one of those people. I am fortunate for me it works so I would not at this time need the OCA but know others who might benefit for sure.” – PBC patient

“I would like to try this drug to see if it is easier for me to tolerate than URSO and if it would improve my quality of life. I would like to know what the side effects are as I have heard that it increases itching.” – PBC patient

“I have read many first hand comments about OCA, and it seems that it makes the fatigue and itching worse. I am at the point where I want to discontinue treatment and just enjoy whatever time I have left. It hasn't been proven that Urso slows the disease, and that it only makes your enzyme levels be in the normal range. It seems pointless to spend thousands of dollars on a drug that really doesn't do anything.” – PBC patient

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

Obeticholic acid or OCA increases bile flow from the liver and suppresses bile acid production in the liver. Reducing the amount of bile back-up in the liver helps to slow down the progression of PBC and improves the condition of the liver as indicated by lower levels of bilirubin and alkaline phosphatase (ALP). Reductions in these important indicators of liver health correspond to a decreased risk of liver failure and death and reduce the possibility of the person requiring a liver transplant. In clinical trials, patients who had not previously responded to UDCA, showed a positive response to OCA with a reduction in ALP and bilirubin levels. The main side effects patients experienced were itching (pruritus), fatigue, abdominal discomfort and a decrease in HDL ('good cholesterol') and an increase in LDL ('bad cholesterol').

*“My liver enzymes were reduced back to the normal range, they had been slowly climbing previously, I believe my liver is now healthier. Before participating in the OCA Clinical Trial (Phase 3) my ALP was between 4-5 times the normal range, they are now within the normal range. The only side effect that I experienced was itching at the beginning, after a few weeks the itching resolved.”*  
– PBC patient

## Additional Information

PBC is a chronic autoimmune disease for which there is no cause or cure. It attacks predominantly women in the prime of their lives when they are striving to meet high demands from careers, families and other responsibilities. This disease slowly robs them of their energy, quality of life and eventually may take their lives.

For the past 20 years, PBC patients have had one drug therapy option. UDCA can slow down the progression of the disease but is only effective for about 40-50 percent of those who take it. The remainder do not respond (their liver enzyme levels continue to rise indicating ongoing damage) or cannot tolerate it. Alternative treatments including bile acid therapy, immunotherapy or antivirals are not effective. OCA represents the first new alternative treatment for thousands of PBC patients. Although it may come with some of the same side effects of UDCA (e.g. fatigue, itching), many patients would like to be able to try this therapy either now or in the future. Those that are in the early stages of their disease and are responding to UDCA, still see the value of having this option available for others.

*“This medication works, the most significant side effect was increased itching however the itching did resolve itself within 1-3 weeks. I would rather live with the side effect than without this medication as I believe I am alive today because I was fortunate enough to be chosen to participate in the OCA Phase 3 Clinical Trial. Please fast track this medication for those living with PBC that do not respond to the only drug currently available for PBC, UDCA.” —PBC patient*

*“I am a liver transplant recipient. I felt compelled to fill out this survey, because I feel so strongly about getting additional drugs to help with managing PBC. It was such a terrible ordeal for me to live with PBC and the Urso didn't work for me. Please okay this medication to help others live healthier lives with liver disease.” – PBC patient*

*“Since Urso is currently the only treatment, we badly need more options for those who cannot tolerate Urso, and for those who find Urso doesn't work.” – PBC patient*

The Canadian Liver Foundation believes that liver disease patients and their doctors should have access to the most effective treatment options regardless of location and financial status. OCA offers a viable treatment option for those for whom UDCA does not work and therefore gives them the opportunity to reduce their risk of developing the most severe consequences of advanced liver disease including liver failure. This drug could be life-saving for these patients but without coverage, it would be inaccessible due to the cost. Based on the fact there are currently no other treatment options for patients who do not respond UDCA and the fact that OCA can significantly improve quality of life for these under-served patients and reduce the need for liver transplants (thereby saving costs to the acute care system), we recommend that OCA be made available to all patients who need it without restriction.



## Canadian PBC Society

### General Information

<b>Name of the drug CADTH is reviewing and indication(s) of interest</b>	Obeticholic Acid, for the treatment of primary biliary cholangitis (PBC)
<b>Name of the patient group</b>	Canadian PBC Society
<b>Patient group's contact information:</b>	
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Website	<a href="http://pbc-society.ca/">http://pbc-society.ca/</a>
<b>Permission is granted to post this submission</b>	Yes

### Submitting Organization

The Canadian PBC Society was founded in 2003 as a registered national charity. As a support group for people living with Primary Biliary Cholangitis, our mission is to provide compassionate support, to develop and deliver information and education programs, to raise disease awareness, and to raise funds for research into PBC causes, treatment and a cure.

We are a totally volunteer, non-profit organization, with a membership base of PBC patients, their families and caregivers across the country.

### Conflict of Interest Declarations

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

- We have received unrestricted grants and event sponsorships from Intercept Pharmaceuticals in both 2016 and 2017.

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

- N/A

### Condition and Current Therapy Information

#### Information Gathering

The information used to complete the section below was gathered via the following:

- In-person conversations gathered in Toronto, Edmonton & Vancouver during our PBC Self
- Management Workshops in June & November, 2016
- Electronic survey sent via email and completed by 120 people with PBC in December 2016

#### Impact of Condition on Patients

PBC is a chronic, progressive and incurable liver disease which has only one drug treatment currently available. This treatment is effective only for approximately 60% of patients in Canada, leaving 40% of patients in a devastating position with this complex

disease. Unfortunately, left untreated – or ineffectively treated – PBC ultimately progresses to cirrhosis and the need for life-saving liver transplantation – or, failing transplantation, death.

PBC generally affects women between the ages of 40 and 60, but is also seen in younger women and men; the ratio is known to be 9 females to every 1 male patient.

PBC causes debilitating fatigue. The fatigue, which is independent of the amount of sleep, has been described as “walking through custard” or “wearing a lead blanket” and renders simple daily tasks impossible.

- People with PBC-related fatigue find it difficult or impossible to: hold a job, drive a car, care for children, make dinner, clean house, participate in physical and social activities, maintain personal relations.
- People with PBC need help preparing meals (46%); cleaning home (56%); shopping for groceries (49%); driving (38%); and bathing/dressing (11%).

*Patient testimonials:*

"I'm exhausted often and even when I get a good night's sleep I am tired by noon"

*"My husband has picked up more household tasks like shopping, helping with housework and cooking"*

*"Quality of life is not the same as five years ago. I am tired all the time. My back and arms are itchy and disturb my sleep. It is very hard to motivate myself to do errands or home projects"*

*"I feel like a burden to my family as they often have to help me out."*

**Social isolation and depression** are two of the most common problems facing those living with PBC today. PBC fatigue may result in people feeling imprisoned within their home – frequently resulting in a loss of contact with friends, family, coworkers and community.

*Patient testimonials:*

*"PBC has left me with no energy to do daily tasks as well as extra activities I may want to do with my friends and family. I always am pushing myself to do things that I want to do leaving me feeling exhausted and sore"*

*"I have lessened my social interactions considerably from not feeling well and I am embarrassed by my weight and over all appearance as I look and feel tired all the time"*

*"Fatigue, insomnia and pain leave me with a challenge planning anything including meals. I am finding cognitive impairment is becoming worse and is starting to frighten me. I have much fewer friends, gained 75 lbs and feel crummy most of the time"*

The social effects of PBC are also significant. It is common for PBC sufferers (34%) to **cancel a social, work or family function** due to PBC related symptoms; additionally, studies have shown that one in three PBC patients suffers from **mental health issues or depression**.

*Patient testimonials:*

*"I can't plan things in the future as I know I likely won't be feeling well enough to go"*

*"Socializing with friends is too much at times."*

**Fear, stress and anxiety** concerning how their PBC will progress was expressed by several respondents.

*Patient testimonials:*

*"There is always a cloud of fear lingering above my head. Will I be able to go to work tomorrow? Will I need a transplant? Will I live to see my grandchildren?"*

*"Forever wondering how long I've got left"*

*"Anxiety is [my worst] problem. I have a lot of problems [with] sleep"*

*"My symptoms have impacted my ability to do activities with my young son. We were physically active together before and now I no longer am able to participate. This is an impact that I struggle often with. His mom is now often too tired to do activities or having naps. He's understanding but I still see the disappointment in his eyes. I wish he didn't have to grow up with a sick mother"*

Some patients experience **cognitive dysfunction due to fatigue.**

*Patient testimonials:*

*"Fatigue and brain fog are the worst symptoms. I don't sleep well and some days it is hard to get out of bed"*

*"Chronic fatigue and loss of cognitive function. I can no longer do my job as a geologist because I cannot focus nor remember information to do my job effectively. I'm about to go on long term disability"*

For those who are employed (41%), many report **missing work because of PBC** (51%) and a significant group of those report feeling that PBC has or would **negatively impact their coworkers' attitudes** towards them (44%).

*Patient testimonials:*

*"I no longer work from fatigue"*

*"Having to take early retirement...abandoning much loved hobbies...limiting time spent with grandchildren...feeling guilty that I'm not pulling my weight"*

*"It's the exhaustive fatigue, I've had to leave my job and go on disability. Its' struggling to even do the basics of living."*

*"I am so tired now I don't know how much longer I can continue to work"*

**In addition to debilitating fatigue, another major symptom of PBC is itch.**

The itch experienced by PBC sufferers goes far beyond the itch associated with a topical rash or insect bite. The itch is described as experiencing "a thousand ants crawling on the inside of your skin".

Often worse at night, the itch might prevent or interrupt sleep, further contributing to the debilitating fatigue. Continuous scratching does not relieve the itch, but may be the cause of dangerous skin infections.

The unrelenting itch and its effects has PBC patients requesting compassionate liver transplants related to feelings of suicide and PBC patient suicides have been reported. PBC itch that does not respond to medication is an indication for liver transplant.

*Patient testimonials:*

*"Skin is wrecked; scabbed and scarred. Exhausted. Scratch non-stop. Practically narcoleptic. Can't keep up with the kids or the house. Miss work when fatigued. Friendships are drifting away"*

*"I am no longer able to function as I used to be able to. I itch everywhere, I bloat, I can't sleep even though I am exhausted all the time."*

**PBC often comes with co-morbidities and/or associated medical interventions.**

People with PBC often have several autoimmune diseases, and find themselves routinely seeing multiple specialists, taking invasive and benign tests and experiencing overlapping symptoms. These overlapping

symptoms may have delayed diagnosis of PBC for years, as a patient's symptoms are not taken seriously or mistakenly attributed to other diseases such as multiple sclerosis, depression, alcoholism, and menopause - just a few examples.

When diagnosis is delayed, the disease progresses untreated and may accelerate the need for liver transplantation.

*Patient testimonial:*

*"I've gone from a perfectly non-medicated healthy 67-year-old with annual visits to my GP to a tired, itchy, stay at home, with 4 specialists and life-long prescribed drugs"*

When PBC is advanced, complications such as variceal bleeding, portal hypertension, hepatocellular carcinoma, and jaundice may be present.

## Patients' Experiences With Current Therapy

As mentioned, Ursodiol is the only treatment currently available for PBC patients, 40% of whom do not respond to treatment.

It is currently effective in slowing the progression of the disease for the other 60% of people with PBC; however, it does not control the symptoms of PBC.

If PBC is diagnosed before liver cirrhosis has occurred and the patient responds to Ursodiol, then normal life expectancy is predicted. For the 40% of those with PBC who are considered non-responders to Ursodiol, disease progression is likely, leading to cirrhosis and the need for transplantation (30-50%) or death due to liver failure.

People diagnosed at a younger age are more likely to be non-responders, as are males. 1/40 people with PBC will need a liver transplant as compared to 1 in 65 Hepatitis C patients.

Ursodiol has several possible side effects including: diarrhea, nausea, dizziness, constipation, flu-like symptoms, stomach pain and hair loss.

*Patient testimonials:*

*"I regularly have stomach issues - indigestion, acid reflux, constipation, diarrhea...it's always something not working right in that department."*

*"I often experience nausea"*

*"20 second warning for diarrhoea attacks"*

*"Even if Ursodiol works for me I have side effects."*

*"I have significant hair loss as a result of being on Urso"*

## Impact on Caregivers

In discussions and through patient surveys, patients told us they experienced difficulty in performing simple day to day tasks and **relied heavily upon spouses and family members** to "take up the slack", "step up to the plate" and "completely support" them.

The majority of our respondents were women, who told us they depend upon spouses to manage the family responsibilities and to navigate ongoing time-consuming medical treatment - including visits to emergency rooms, specialist appointments, and routine scheduled physician appointments.

Many noted their worries about their inability to contribute to family income and the medical costs they incur – especially when it comes to placing a financial burden on their families.

In addition, they think about liver transplantation, often wondering: when will they need one? Will they qualify? Will they need to move to a major city? Will they have to sell their homes to pay for posttransplant treatment?

Like many liver diseases, PBC carries a stigma. Patients and their families often feel the need to keep their disease a secret to avoid negative judgements relating to drug or alcohol abuse, which lead to people believing that PBC was brought on by the patient's bad behaviour. This puts further stress on the family trying to hide the disease from their extended family, friends and community, while they struggle to cope with deteriorating health and finances.

## Information about the Drug Being Reviewed

### Information Gathering

The information used to complete the section below was gathered via the following:

- In-person conversations gathered in Toronto, Edmonton & Vancouver during our PBC Self Management Workshops in June & November, 2016;
  - Electronic survey sent via email and completed by 120 people with PBC in December 2016;
- And
- A webinar discussion on December 13, 2016 with Dr. Andrew Mason, Co-Director of the Centre of Excellence for Gastrointestinal Inflammation and Immunity Research at the University of Alberta

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

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

Currently, non-responders to Ursodiol are isolated and feel frustrated and doomed. With no other treatment option to date, they often simply give up hope of improving their lives.

With the introduction of obeticholic acid, PBC patients are excited at the possibility that their disease progression could be slowed and controlled, resulting in a better quality of life and give them the hope of a normal life expectancy.

The benefits of patients having their PBC managed with effective treatment are clear; as mentioned above, patients with their PBC under control are less likely to face debilitating and chronic fatigue, require less support from families and caregivers in their day-to-day lives, and will face improved mental health. This should result in increased productivity, continued employment and fewer health resources being utilized by PBC patients who are able to effectively have their disease managed through treatment.

In short, obeticholic acid offers patients, families and caregivers a chance to properly manage their (or their loved ones') disease, and offers hope that patients may be able to lead better and longer lives, with improved mental health and hope for the future.

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

We were not able to confirm if any of our members enrolled in an obeticholic acid clinical trial, as no members chose to reveal to this information to us. However, through our discussions with Dr. Andrew Mason, we learned about the initial effects of obeticholic acid; within a month of starting treatment, participants had experienced and sustained a 25% drop in ALP (alkaline phosphatase, one of the indicators of PBC disease). All other liver function tests improved (ALT, AST, GGT, Bilirubin) as well as whole liver improvement.

The initial trials showed an increase in itch (pruritus); however, once the dose was titrated the itchiness improved significantly. Still, it is felt that most people who need this drug will have an issue with pruritus.