CADTH

CADTH COMMON DRUG REVIEW

Patient Input

NALTREXONE HYDROCHLORIDE AND BUPROPION HYDROCHLORIDE (CONTRAVE)

(Bausch Health, Canada Inc.)

Indication: An adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of: 30 kg/m2 or greater (obese) or 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbidity (e.g., controlled hypertension, type 2 diabetes mellitus, or dyslipidemia).

CADTH received patient input from:

Canadian Spondylitis Association

Obesity Canada

May 17, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Contrave (naltrexone hydrochloride and bupropion hydrochloride)** **Chronic weight management in adults**
Name of the Patient Group	**Canadian Spondylitis Association**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	**execdirector@spondylitis.ca**
Telephone Number	**705-715-2162**

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

The Canadian Spondylitis Association is registered with CADTH.

The website is: www.spondylitis.ca

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Perspectives were gathered through a survey offered in April through May 2019 by the Canadian Spondylitis Association to the Spondyloarthritis community. Additional input was gained through one-on-one discussions. There was a total of 61 individuals diagnosed with a Spondyloarthritic condition and who have been diagnosed with obesity participated and 5 individual discussions were held. All participants reside in Canada. There were 49 female and 12 males who responded on-line and 5 females in person.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Many individuals living with Axial and/or Peripheral Spondyloarthritis also live with, and struggle with, obesity largely due to side effects of the medication they are prescribed, inactivity for various reasons, including pain, or a combination of both.

Axial and peripheral spondyloarthritis diseases are chronic and people diagnosed will live with these diseases and complications for the majority of their lifetime.

Living with a SpA condition alone is a challenge for many. Common complications include pain, depression & anxiety, and fatigue to name only a few. Non-pharmacologic treatment is as important for managing these conditions as pharmacologic. Exercise and being active are key to helping manage conditions. However, for many patients, because of side effects are unable or unmotivated to be active causing weight gain eventually leading to obesity. For those who are obese, exercise and being active is difficult, if not impossible. They become stuck in a vicious cycle that they can't get out of. Additionally, maintaining a healthy weight (lighter is better) places less pressure on joints and is a goal all patients should strive to achieve for better outcomes.

Comments include:

> **"I hate being so over-weight. My Rheumatologist keeps telling me I need to lose weight. It's hard when you can't bend and are in constant pain. My hips, lower back, knees and feet hurt the most. I hate looking at myself. I was never over weight when I was younger. It's very hard to find a man who wants a relationship with me. I feel very depressed. I want to look good and feel good about myself. I want to be able to exercise and be active. Its easy for my doctor to say I need to lose weight. Sometimes doctors just don't understand the constant fatigue I deal with every day. Please I need this medication."**

> **"Because of my AS, movement, although vitally important to engage in, has become more difficult. Being in pain daily is an antagonist to working out. When the only things that distract me from my pain are fleeting moments of pleasure from food, debilitating, self-loathing and hatred of the mirror are inevitable. I am getting married in 2 months and the usual anxieties of such an event revolve around "will I be experiencing a flair that days?", "will my back hold up?" or "I need to make sure someone reminds me to take my medication on time so that I can actually consummate my marriage". The impact of my illness on my weight in turn my self-esteem is insurmountable."**

> **"I have gained most of my weight because of meds and not being to move as much as I should"**

"I have no energy for anything. My dogs needs daily walks that I can't complete. I hurt everywhere. I used to weigh 153 at 5'8". Now I weight 255. No quality of life. I hardly eat due to no appetite. Can't loose the weight."

"Struggle to put socks and shoes on. Struggle to clip toe nails. Have developed osteoporosis in both knees, with the extra weight I have more pain. Along with the weight my stomach muscles have separated and push upwards. Stomach is large and hard. . Struggle to get off of low chairs or toilets."

"I've struggled with obesity my whole adults life. It's limited my willingness to have fun and enjoy life. I also have chronic issues with depression, and often use food to self sooth."

"I am in pain every day because of my AS. I gained over 50lbs since the disease started. I used to overweight, but healthy and very strong and active. Now, the pain is making it harder to exercise and the weight is making the pain worse. Arthritis is scary, but my weight is putting me in much more distress right now because it feels like I have less and less control over my life, my pain and my health."

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Respondents have tried a variety and often several treatments to try and lose weight including commercial programs (Weight Watchers, Jenny Craig, etc.), physical activity and mental health intervention (33%33% and 25% respectively). Some have tried behavioural interventions, medically supervised nutrition intervention (16%, 18% respectively). Two individuals tried Bariatric surgery.

Comments include:

"I have tried too many treatments to possibly count".

"I've had gastric by-pass surgery in January 2017. It was successful. Now two years later, I am struggling with emotional eating and starting to regain weight?

"I try different diets and programs. Some work, some don't. If I do lose weight, it's not enough to really help me. And the weight doesn't stay off long-term. It's like a yo-yo and is very frustrating. Sometimes I just want to give up on life"

When asked about outcomes from losing weight, the majority of people commented that weight loss would allow them to improve their mental and physical quality of life. Losing weight would help reduce or relieve pain and fatigue, improve mobility and break the cycle they are stuck in.

Comments include:

> **"My rheumatologist keeps blaming my weight for everything I experience and there is nothing else he can do – maybe if I were to lose weight, I may have less pain and symptoms, but I doubt the weight will cure me of all the pain from my AS. I wish he would look beyond my weight and believe me how bad of shape I'm in and how much my condition has progressed".**
>
> **"I just want to look at myself in the mirror and stop criticizing my body. I want to see the person I once was before AS. I have lost who I once was because of this disease and becoming obese".**
>
> **"To be happy and pain free. To know what I can be okay and look and feel better".**
>
> **"Finding my life again and doing what I need to improve my health".**

People commented on the affordability of various programs and over the counter medications. Unless people are fortunate to have private insurance medications for weight management aren't an option. When having to choose between paying for medication for weight loss or non-pharmacologic treatments (physiotherapy, massage therapy, chiropractor, yoga, float therapy etc.); all extremely important for managing SpA conditions, patients put the latter before paying out of pocket for weight loss treatments. For many, patients can't afford many of the non-pharmacologic treatments even with some costs being covered by private insurance.

5. Improved Outcomes

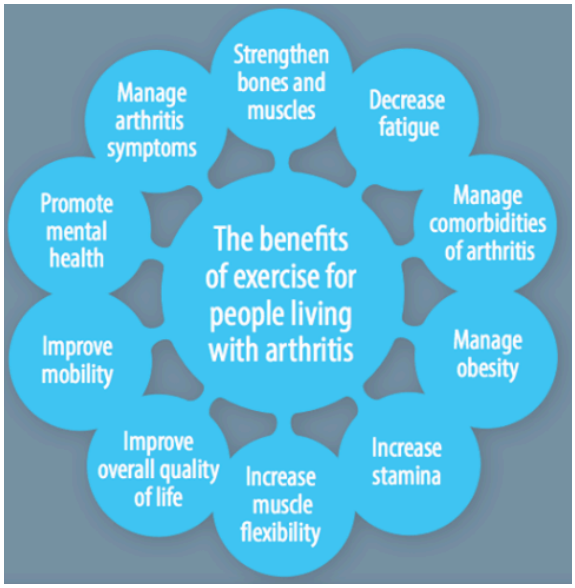
CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

Outcomes to consider when evaluating a new medication needs to include the class of medications and the health benefits to the patient and to the healthcare system. Since 1999, there are only two other medications in addition to Contrave approved in Canada for obesity. Newer medications often come with less side effects and better efficacy than the older therapies. Contrave also provides a patient support program that to many is a benefit and adds to the patient being successful.

Many SpA patients are prescribed multiple medications to manage their SpA condition. And on average SpA patients live with four additional complication in which they take medication to manage. For these reasons, patients do look for medications with fewer side effects.

Contrave provides an option for patients to help manage and take control of their obesity. A reduction in weight to a healthy BMI will impact patient's daily life and quality of life. Positive improvement to the patient will only benefit family and caregivers. Additionally, conquering obesity has an impact on the healthcare system in general.

Additionally, studies have confirmed, the heavier patients are, the less effective medications are; therefore, impacting outcomes for the patient.



6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies' patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

There was one respondent who had positive outcomes on Contrave. She had it covered through private insurance. If they did not have private insurance the person would not have been able to pay for it out of pocket because they have to pay out of pocket for so many other treatments not covered through private insurance or the government (physiotherapy, massage therapy).

The patient did not experience any side effects. The benefit was significant weight loss giving back improved mobility, self-confidence and the ability to do day-to-day activities not possible or very difficult at heaviest weight. The individual continues to be motivated to eat healthy and exercise with the goal to achieve and maintain a BMI in the normal range.

When informed of Contrave, the patients are excited to learn there is a new treatment option for obesity.

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

Not relevant

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

Spondyloarthritis conditions are chronic inflammatory diseases that are often painful & debilitating. The diseases are progressive and early diagnosis, pharmacologic and non-pharmacologic treatment intervention are critical to helping manage the life time journey for patients living with chronic illness. SpA patients often have more than one spondyloarthritic disease and on average live with 4 or more comorbidities/complications that complicate quality of life; including physical and mental aspects.

In a survey we conducted in 2018, among the most common complications experienced by patients are pain, depression & anxiety and fatigue. Unfortunately, the survey did not ask about obesity and in hindsight was a miss as what we've learned is that a significant number of people are overweight or obese adding an additional complication in the vicious cycle, they seem to live in.

SpA Diagnosis (and often complications)
+
pain
+
Depressed/anxiety
+
Fatigue
+
Sleep issues
=
Inactive lifestyle
+
Unhealthy/ emotional eating
=
Obesity

If the complication of being obese can be removed, the patient will feel better about themselves, have less pain, be able to exercise and likely want to eat better feeling the benefit of losing weight and impact on their joints.

There have not been any new treatment options for the management of obesity since 1999. New and innovative therapies with often have few side effects and better efficacy than older agents. Patient support programs are valuable and can influence patients to stay on track. Canadians need to have access to all treatment options that can positively impact health outcomes.

In addition to improved physical health, exercise has many psychological benefits. Pain can seem more pronounced when one is unhappy or upset and exercise can help reduce depression. Self-esteem and self-confidence are likely to improve the ability to relax, improve mood and wellbeing, and promote a good body image. Exercise also provides a good outlet for dealing with stress and anxiety.

Appendix: Patient Group Conflict of Interest Declaration

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To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   The submission was completed in its entirety by the Canadian Spondylitis Association with no outside assistance or influence.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   Data collection and analysis was completed in its entirety by the Canadian Spondylitis Association through survey monkey and telephone interview.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: **Wendy Gerhart**
Position: **Executive Director**
Patient Group: **Canadian Spondylitis Association**
Date: **May 17, 2019**

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Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Contrave**
Name of the Patient Group	**Obesity Canada**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Obesity Canada-Obésité Canada, previously known as the Canadian Obesity Network-Réseau canadien en obésité, is Canada's authoritative voice on evidence-based approaches for obesity prevention, treatment and policy. Currently, Obesity Canada-Obésité Canada has more than 20,000 professional members and over 25,000 patient supporters.

Our mission is to improve the lives of Canadians affected by obesity through the advancement of anti-discrimination, prevention and treatment efforts.

Our goals are to address the social stigma associated with obesity, change the way policy makers and health professionals approach it and improve access to evidence-based prevention and treatment resources.

Website: https://obesitycanada.ca/

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include when the data were gathered; if data were gathered in Canada or elsewhere; demographics of the respondents; and how many patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Obesity Canada engaged persons living with obesity through an online survey and individual interviews. We conducted the survey between April 23 - May 14 2019 . The survey reached persons living with obesity from across provinces and territories. The survey was sent through a newsletter to 4300 people. We obtained 45 survey responses.

Considering that Contrave is currently not accessible to many Canadians living with obesity, it was challenging for Obesity Canada to find individuals that have had experience with this medication. Out of the 4300 persons that were surveyed, many could not complete it because they have not tried this medication.

Furthermore, since obesity is a highly stigmatized disease, many persons living with obesity do not want to share their experiences with obesity treatments for fear of blame and shame. Often, patients living with obesity feel that they have failed the treatments rather than the treatment having failed them. This internalized self-stigma hinders participation of individuals with obesity from participating in research, surveys, or consultations. Many persons with obesity do not disclose that they are on a particular obesity treatment for fear of being shamed for not being able to just manage their weight on their own through diet and exercise.

Finally, this is the first time that Obesity Canada prepared a patient submission for CADTH. Many of our patient supporters are not aware of medications that have been approved by Health Canada. Several persons started to complete the survey but stopped when they realized that the survey was a particular medication that they have even heard about. We got several requests for more information about this medication during the survey.

We conducted five interviews with persons living with obesity who have had direct experience with Contrave.

Since Obesity Canada is also the only professional organization dedicated to obesity research, prevention, management and policy, we also engaged scientists and clinical experts working in this area.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Obesity is a chronic relapsing disease, similar to diabetes or high blood pressure, characterized by abnormal or excessive fat accumulation that impairs health. There is consensus in the medical and scientific community that obesity is a chronic disease. Obesity Canada, the World Health Organization, the Canadian Medical Association, the American Medical Association (US), the World Obesity Federation, the European Association for the Study of Obesity, Obesity Medicine Association (US), the Obesity Society (US), The Obesity Action Coalition (US) all recognize obesity as a chronic disease.

Population health studies measure the prevalence of obesity using a crude measure called the Body Mass Index (BMI). Although this measure is helpful for population health surveillance, it is not a tool that can be used to clinically diagnose people with obesity. Obesity should be diagnosed by a qualified health professional using additional clinical tests and measures. Based on existing population surveillance studies, the prevalence of obesity in Canada has increased significantly over the past three decades. According to the 2017 Canadian Community Health Survey, **over 7.2 million adults have obesity**, and according to the 2017 Canadian Health Measures Survey, 26.9%, or more than one in four adults in Canada is living with obesity and may require medical support to manage their disease.

Over this time period, there has particularly been a dramatic (over 400%) increase in severe obesity (BMI >35 kg/m^2). This increase in severe obesity is largely attributable to the lack of effective obesity interventions at early stages of this progressive chronic disease.

As a leading cause of chronic diseases such as type 2 diabetes, non-alcoholic fatty liver disease, high blood pressure, heart disease, stroke, arthritis, many forms of cancer, and other important health problems, obesity can have serious impacts on those who live with it. It is estimated that one in 10 premature deaths among Canadian adults age 20 to 64 is directly attributable to obesity.[4]

Beyond its effects on overall health and well-being, obesity also affects people's' overall social and economic well-being due to the **pervasive social stigma associated with it**.[5] As common as other forms of discrimination — including racism — weight bias and stigma can increase morbidity and mortality.[6] Obesity stigma translates into significant inequities in access to employment, healthcare and education, often due to widespread negative stereotypes that persons with obesity are lazy, unmotivated, or lacking in self-discipline.[7,8]

Obesity has long been misunderstood, trivialized, and stigmatized as a simple "lifestyle" issue that can be effectively addressed by the mantra of "eat-less-move-more". This simplistic view of obesity disregards both the lived experience of persons with obesity as well as the vast body of scientific evidence showing that, like other chronic diseases, obesity is a rather heterogeneous condition resulting from the complex interaction of a multitude of socio-psycho-biological factors that promote excessive weight gain and ultimately impair health.

Most importantly, once established, powerful neuro-hormonal factors effectively defend our bodies against weight loss, thereby often making obesity a life-long problem, where weight regain (or relapse) is the rule rather than the exception.

In Canada, specifically, the lack of recognition of obesity as a chronic disease by provincial and territorial governments has a significant impact for adults in Canada. Only a few provincial governments have focused their attention on health promotion among children and families and most have not implemented obesity treatment programs for Canadians living with obesity.

The pervasive weight bias in our society is a major barrier to access to obesity care. **Obesity Canada's report card on access to obesity treatments** show that:

1. there is a profound lack of interdisciplinary teams for obesity prevention and management at the primary care level in Canada;
2. Anti-obesity medications are not covered by provincial public drug benefit programs or any of the Federal public drug benefit programs, and that
3. there are significant disparities in the access to bariatric surgery, with only 1 in 171 (0.58%) adults living with severe obesity having access to surgery every year. In many provinces and territories, wait times for bariatric surgery can go up to 5 years.

Due to lack of availability of access to evidence-based treatments in the health system, Canadians affected by obesity are left to navigate a complex landscape of weight-loss products and services, many of which lack a scientific rationale and openly promote unrealistic and unsustainable weight-loss goals.

"The engendered bias and discrimination are rampant in healthcare, where obesity continues to be grossly misunderstood and is not treated with the same fundamental dignity and rigor as other diseases. We deserve and demand better," says Lisa Schaffer, obesity advocate and chair of Obesity Canada's Public Engagement Committee. "As one of millions of Canadian living with obesity, I find it reprehensible that our healthcare systems have not made any significant improvements in access to care."

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Like many other chronic diseases, obesity is a manageable disease. In 2006, the first evidence-based Canadian clinical practice guidelines on the prevention and management of obesity in adults and children were released.[9] More than 10 years after the release of the first Canadian obesity guidelines, there remains a gap in access to obesity care in Canada. [13] Obesity has not received official recognition as a chronic disease by the federal government or any of the provincial/territorial governments, despite the Canadian Medical Association and the World Health Organization's declarations. [14,15] The lack of recognition of obesity as a chronic disease by public and private payers, health systems, the public, and the media has a trickle-down effect on access to treatment. Obesity continues to be treated as a self-inflicted risk factor, which affects the type of interventions and approaches that are implemented by governments or covered by health benefit plans. [16]

While our current health system theoretically allows for most people with obesity to receive health care in a structured and systematic way, compelling evidence indicates that obesity is "not effectively managed within our current health system".[13,18] Canadian health professionals feel ill-equipped to support patients with obesity. [19-21] In addition, despite the important role health professionals can play in obesity management, they are an underutilized resource; most Canadians do not look to them for advice.

A startling 89% of Canadians with obesity have never asked any licensed healthcare professional (family doctor, dietitian, pharmacist, etc.) about obesity. [23] Rather, consumers turn to a multi-billion-dollar commercial weight-loss industry.

Many products and services offered in this space are unregulated and untested, but entice consumers with promises of significant and easy weight loss. While some approaches may actually achieve significant weight loss, more than 95% of diets and other approaches fail and result in weight regain, often to an even higher weight. An inability to lose and/or maintain weight loss perpetuates a vicious cycle of "yo-yo dieting," which too often results in frustration, depression, poor self-esteem, and further weight gain.[23]

Obesity management has evolved and there is now a general acceptance that obesity care should be individually tailored to patients' needs using interprofessional approaches.[24-26] Simplistic obesity interventions and approaches (e.g. eat Less and move More) are not enough. Patients living with obesity expect primary care professionals to assess and address the root causes of their obesity rather than giving simplistic advice to "eat less, move more".[27]

Understanding the perspectives of patients living with obesity is vital to achieving patient-centred care in primary care and improving health outcomes.[27] Since the release of the clinical practice guidelines, there has been significant advances in new therapeutic treatments and approaches. Our understanding of the homeostatic and pathologic mechanisms underlying the development and maintenance of excess adiposity have helped scientists to identify new therapeutic interventions. [28] In recent years, for example, Health Canada has approved two medications for the treatment of obesity in adults.[29]

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

With outcomes for obesity treatment, patients look for a number of outcomes but many go beyond simple weight loss efficacy. Many patients are looking for quality of life measures for things that they have been limited in due to their obesity. Outcomes related to improvement in related comorbidities (diabetes, hypertension, sleep apnea) as well as outcomes related to everyday life such as productivity, energy levels, sleep, activity and mental health. While weight loss is typically the primary outcome measure for the efficacy of an anti-obesity therapy, from a patient's' viewpoint it goes much deeper and the weight loss is viewed as a needed step to the

more meaningful quality of life outcomes. For example, one participant described the non-weight loss outcomes as follows:

> ***"I need to lose weight so I can have the energy and mobility to play with my kids/grandkids" or "I am so preoccupied with worrying about my weight that my productivity and mental health suffer, if I can lose some weight, everything else will get better." So from a patient's view, the actual weight loss is less important than the impacts on the other outcomes.***

If new treatments provided positive impact on these outcomes, the quality of life of patients, caregivers and families would be drastically different. Obesity is a disease that impacts virtually all aspects of an individual's daily life. Improvement in sleep, productivity, energy levels, reduced stress of other conditions, improved mental status would all make a significant difference. These outcomes will also positively impact social aspects of life where individuals living with obesity would be better equipped and more comfortable engaging in social situations.

> ***"I rarely obsess about sugar/carbs and eating. That gives me room in my brain to consult my body about what I need rather than give in to the urges that overpower everything else. It's easier for me because I'm more than 50 lbs lighter and I can find clothes and gear that fit and chairs are easier."***

Typically when considering a therapy for obesity, patients tend to assess the trade-offs between the desired outcomes mentioned above and the potential side-effects of the therapy, the ease of use of the therapy, and the cost of the therapy. In many cases, the potential for moderate benefits of a therapy will outweigh many manageable side effects. Cost seems to be the most significant determining factor in choosing a therapy for obesity.

More than 95% of survey respondents indicated that anti-obesity medications need to be covered under public and private insurance plans just like treatments for any other chronic disease state.

> ***"It really is a struggle because the medications and treatments that are evidence-based and available in Canada are really cost-prohibitive, no insurance covers obesity meds, at least mine doesn't, who can afford an extra car-payments worth each month for medication? This leaves us on our own or with the diet industry and over-the counter scams that prey on people's desperation, it really is unfair."***

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

Contrave targets an area of obesity that is a great challenge for individuals who live with the disease. Specifically, buproprion and naltrexone target both the homeostatic system (hunger and satiety) as well as the hedonic system (liking and wanting), which together largely determine eating behaviours and food intake. Particularly the subjective effect of Contrave on craving and wanting were noted by several of the respondents .

"I don't feel intense NEED to eat. I feel satisfied and am able to think about other things. It is slow weight loss not an immediate fix. I have the energy and time to live. Mood is stable so do not snap at people"

"It's helping me consult my body about eating rather than trying to control my thinking about eating (like diets do). This is the first weight loss I've experienced where I'm not obsessed with controlling eating and my thinking - rather it gives me room to explore my eating and my thinking."

For some benefits to the treatment are quite significant and impact quality of life a great deal.

"It as if a heavy burden was lifted allowing for some clarity and mental space being opened up. The constant obsession or thinking about food was replaced with the ability to focus on other areas of my life".

As noted in the recent **Obesity Canada 2019 Report Card**, the proportion of Canadians, even among those with private drug benefit plans, that have access to anti-obesity medications is less than 20%. Those who rely on public coverage for their prescription drug costs do not have access to these medications and are left paying for them out of pocket.

This lack of access was highlighted by many survey respondents:

"My experience with contrave has been a bittersweet one, for the first time I am seeing a medical management tool to help me control my disease that has been effective and had far reaching improvements in my quality of life, however, it is one I know I will have to give up soon and go back to my struggle with managing unsuccessfully on my own as it is cost prohibitive. There are not many families in this country (mine included) where there is an additional $200+ lying around each month. I have to make significant sacrifices for my family to try this medication but soon will come a time where it will no longer be fair or acceptable to the rest of my family to take that money and invest in myself....it feels very selfish and is putting my family in a bigger hole than we were already in."

"When choosing a treatment for obesity, the first thing I have to look at is the cost, even before I see what the potential outcomes might be, because

my drug plans do not cover obesity treatments so I would be out of pocket for anything. Even if the medication cured everything and made all my weight related issues go away, I would still consider the financial aspect of it first. I have responsibilities and obligations and do not have the disposable income to make this a non-issue."

"I have a very good extended health benefits plan through my job, but I was shocked to find out that Contrave or any other obesity treatment is deemed a "lifestyle" add on and not classified with other diseases. If I had Diabetes, I would have many potential options of medications to help manage at my disposal, but for my disease, nothing."

In this context it should be noted that, not unlike other treatments for chronic diseases (e.g. hypertension, depression, etc.), a specific medication will not work for or be tolerated by all patients living with obesity. Health care professionals who prescribe anti-obesity medications need to determine the effectiveness of these medications with their patients on a case by case basis.

"When I started taking Contrave I experienced frequent hot-flashes and nausea that made it pretty uncomfortable but what really made it unbearable was the development of Tinnitus which has persisted for two months after going off the medication."

Considering that there are **over 7 million Canadians living with obesity,** even if this medication does not work for every patient living with obesity, for those from whom it works, it has the potential to improve their health well being significantly. For example, based on current research, we know that a **weight loss of 5-10% can significantly improve the health and well-being** for individuals affected by obesity. [9] This level of weight loss can be achieved by over 60% of patients treated with Contrave, thus offering a potential treatment to a substantial number of Canadians affected by obesity.

Overall, patients, who have tolerated and responded well to Contrave were adamant about the personal benefits that they have derived from this medication:

"I hope that Contrave will continue to improve my quality of life by allowing me to no longer obsess over food and my weight. Take control of my cravings which would allow me to free up a massive amount of mental real estate. this will allow me to be more productive, more functional, a better father and husband, and allow me to enjoy life. This in turn will positively impact my physical health by allowing me to manage my weight better, improve function and reduce pain. Contrave has the potential to have such far reaching benefits to my quality of life that go way beyond any weight loss."

Anti-obesity medications such as Contrave have the potential to improve the health and well-being of many Canadians living with obesity. However, until we change the way Canadians affected by obesity, health professionals and policy makers understand obesity, we will not be able to effectively support Canadians living with obesity.

"There are many barriers to more comprehensive policy approaches for obesity prevention and management in Canada, but the real culprit is a lack of understanding of obesity as a chronic disease," said Dr. Arya M. Sharma, Professor, Faculty of Medicine, University of Alberta. "Ultimately, the lack of policy action means that individuals with obesity are responsible for managing their disease on their own, with little support from healthcare providers, employers and policy makers. We must address this lack of understanding of obesity in order to create real change at all levels of society or this social injustice will continue to exist."

There is a perception that if we make anti-obesity medications available to Canadians living with obesity, it will lead to large health care costs. This misconception is not based on an evidence-based understanding of obesity. Obesity is a heterogenous chronic disease. In other words, people gain weight for many different reasons. No one solution will work for all people with obesity. This is why Obesity Canada advocates for the need to do more research to find better solutions that work for different patients. The more treatment options we have, the better we can address the needs of individual patients.

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- **Access to testing: for example, proximity to testing facility, availability of appointment.**
- **Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?**
- **Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?**
- **How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.**

As can only be expected given the heterogeneity of obesity, individual responses to medication will vary. Currently there is no biomarker or other test that will predict individual tolerability or response to Contrave. However, as with other anti-obesity medications, early response is a strong indicator of long-term outcomes. Thus, it is possible to predict whether or not treatment with Contrave will benefit a given patient within the first few weeks of treatment. Generally speaking, if patients do not experience a 5% weight loss within the first 12 weeks of treatment, the medication should be discontinued (Stopping Rule - https://pdf.hres.ca/dpd_pm/00043849.PDF).

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

References

1. WHO. *Obesity: Preventing and Managing the Global Epidemic.* http://www.who.int/nutrition/publications/obesity/WHO_TRS_894/en/ World Health Organization;2000.
2. *Table 105-0501 – Health indicator profile, annual estimates, by age group and sex, Canada, provinces, territories, health regions (2013 boundaries) and peer groups, occasional. .* CANSIM Database: Statistics Canada;2013.
3. Stunkard AJ, Messick S. The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *Journal of psychosomatic research.* 1985;29(1):71-83.
4. Katzmarzyk PTA, C.I. Overweight and Obesity Mortality Trends in Canada, 1985-2000. *Canadian Journal of Public Health / Revue Canadienne de Sante'e Publique.* 2004(1):16.
5. Puhl R, Suh Y. Health Consequences of Weight Stigma: Implications for Obesity Prevention and Treatment. *Current Obesity Reports.* 2015;4(2):182-190.
6. Sutin AR, Stephan Y, Terracciano A. Weight Discrimination and Risk of Mortality. *Psychological Science (Sage Publications Inc).* 2015;26(11):1803-1811.
7. Forhan M, Ramos Salas X. Inequities in Healthcare: A Review of Bias and Discrimination in Obesity Treatment. *Canadian Journal of Diabetes.* 2013;37(3):205-209.
8. Ramos Salas X, Forhan M, Sharma AM. Diffusing obesity myths. *Clinical Obesity.* 2014(3):189.
9. Lau DCW, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. *CMAJ: Canadian Medical Association Journal Supplement.* 2007;176(8):S13.
10. Vallis M, Piccinini-Vallis H, Sharma AM, Freedhoff Y. Clinical Review: Modified 5 As: Minimal intervention for obesity counseling in primary care. *Canadian Family Physician.* 2013;59(1):27-31.
11. Rueda-Clausen C, Benterud E, Bond T, Olszowka R, Vallis TM, Sharma AM. Effectiveness of Implementing The 5As of Obesity Management™ in a Primary Care Setting. *Canadian Journal of Diabetes.* 2013;37(1):S282.
12. Canadian Obesity N. 5As of Obesity Management Framework and Resources. Vol 20132013.
13. *Report Card on Access to Obesity Treatment for Adults in Canada 2017.* http://www.obesitynetwork.ca/reportcard: Canadian Obesity Network;2017.
14. CMA. Canadian Medical Association recognizes obeisity as a disease. 2015; https://www.cma.ca/En/Pages/cma-recognizes-obesity-as-a-disease.aspx.
15. World Health O. *Obesity: Preventing and Managing the Global Epidemic.* Geneva: World Health Organization;2000.
16. Ramos Salas, X., Forhan, M. ; Caulfield, T.; Sharma, A.M.; Raine, K. A critical analysis of obesity prevention policies and strategies. *Canadian Journal of Public Health.* 2017 (In Press).
17. Brauer P, Gorber, Sarah Connor, Shaw, Elizabeth, Singh, Harminder, Bell N, Shane, Amanda R.E., Jaramillo, Alejandra, Tonelli, Marcello. Recommendations for prevention of

weight gain and use of behavioural and pharmacologic interventions to manage overweight and obesity in adults in primary care. *Canadian Medical Association Journal.* 2015(3):184.
18. Block JP, DeSalvo KB, Fisher WP. Are physicians equipped to address the obesity epidemic? Knowledge and attitudes of internal medicine residents. *Preventive medicine.* 2003;36(6):669-675.
19. Janke EA, Ramirez ML, Haltzman B, Fritz M, Kozak AT. Patient's experience with comorbidity management in primary care: a qualitative study of comorbid pain and obesity. *Primary Health Care Research & Development.* 2016;17(1):33-41.
20. Greener J, Douglas F, van Teijlingen E. More of the same? Conflicting perspectives of obesity causation and intervention amongst overweight people, health professionals and policy makers. *Social Science & Medicine.* 2010;70:1042-1049.
21. Kirk SFL, Price SL, Penney TL, et al. Blame, Shame, and Lack of Support: A Multilevel Study on Obesity Management. *Qualitative health research.* 2014;18(4):501.
22. Tytus R. Weight Loss Practices of Adults in Canada. 1st Canadian Obesity Summit; 2009; Kananaskis, Alberta.
23. Freedhoff Y, Sharma AM. "Lose 40 pounds in 4 weeks": Regulating commercial weight-loss programs. Vol 1802009:367.
24. Sharma AM. M, M, M & M: a mnemonic for assessing obesity. *Obesity Reviews.* 2010(11):808.
25. Sharma AM, Kushner RF. A proposed clinical staging system for obesity. *International journal of obesity.* 2009;33(3):289-295.
26. Dietz WH, Solomon LS, Pronk N, et al. An Integrated Framework For The Prevention And Treatment Of Obesity And Its Related Chronic Diseases. *Health affairs.* 2015;34(9):1463 1468p.
27. Torti J, Luig T, Borowitz M, Johnson JA, Sharma AM, Campbell-Scherer DL. The 5As team patient study: patient perspectives on the role of primary care in obesity management. *BMC Family Practice.* 2017;18(1):19-19.
28. Wharton S. Review: Current Perspectives on Long-term Obesity Pharmacotherapy. *Canadian Journal of Diabetes.* 2016;40:184-191.
29. Wharton S, Lee J, Christensen RA. Weight loss medications in Canada - a new frontier or a repeat of past mistakes? *Diabetes, Metabolic Syndrome And Obesity: Targets And Therapy.* 2017;10:413-417.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. **Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.**

   We consulted with other patient associations who have submitted patient input before.

2. **Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.**

   Obesity Canada has access to obesity researchers working in a variety of disciplines. For this submission we reached out to researchers who helped prepare the Obesity Canada Report Card on Access to Obesity Treatments for Canadian Adults. We also engaged several clinicians and scientists to obtain research on weight bias and discrimination, clinical practice guidelines, and obesity management.

3. **List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.**

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bausch Health has provided unrestricted donations and sponsorships for professional research and education events to Obesity Canada.				X

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

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Patient Group: Obesity Canada
Date: May 17, 2019