CADTH

CADTH COMMON DRUG REVIEW

Patient Input

dolutegravir / lamivudine (Brand Name TBC)

(ViiV Healthcare)

Indication: HIV-1 infection

CADTH received patient input from:

Canadian Treatment Action Council (CTAC)

March 14, 2019

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**dolutegravir/lamivudine, HIV Infection**
Name of the Patient Group	**Canadian Treatment Action Council (CTAC)**
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.

The Canadian Treatment Action Council (CTAC) is Canada's national non-governmental organization addressing access to treatment, care and support for people living with HIV and hepatitis C. CTAC's organizational goals are to meaningfully engage community members, service providers, policymakers and other relevant stakeholders to identify, develop, and implement policy and program solutions. CTAC understands that treatment access should be considered in its holistic form, encompassing the range of treatment, care and support needs required to reach the most successful treatment experience possible for people living with HIV and/or viral hepatitis co-infection. Full CTAC membership is reserved for: a) individual people living with HIV (including HCV co-infection); b) organizations, groups or projects with a substantial HIV mandate (including HCV co-infection). Associate CTAC membership is open to any individual, organization, group or project that supports CTAC's mandate and objectives

Website: http://www.ctac.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.

On February 7, 2019, CTAC delivered a patient input consultation workshop in Toronto that provided an overview of the Common Drug Review patient input process and key findings from the

dolutegravir/lamivudine clinical trials. Rounak Khan (Director of Community Engagement at CTAC), and Amanda Fletcher (Director of Policy, Research, and Development at CTAC) delivered the consultation workshop. People living with HIV were invited to participate in the workshop. We also recognize that CDR patient input submissions are much stronger if the voice of people who have had (or believe themselves to have had) experience with the new therapy under consideration are included. As such, we attempted to invite those to the workshop who had experience with any of the components within this 2-drug combination, or the new combination itself. CTAC also administered a web-based survey that was advertised on CTAC's website, and emailed to CTAC members and partners. The survey was made available from Thursday February 14, 2019 to Monday March 4, 2019.

Nine participants attended the workshop, and three individuals completed the online survey. In total, CTAC has compiled data from all twelve individuals. All of the respondents identified themselves as HIV-positive. Eight participants identified as male. Four participants identified as female. CTAC had a wide age range of individuals that participated in either the workshop, or the online survey. One participant was in their 20's, one participant was in their 30's, one participant was in their 40's, 6 participants were in their 50's and three participants were in their 60's. All of the participants are on treatment for HIV. The number of years in treatment varied from 5 years to approx. 34 years. In addition to the results of the survey and workshop, survey data collected for a patient submission on dolutegravir, and dolutegravir rilpivirine have been used to inform and support this patient submission.

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?

HIV is a serious, life-threatening illness that threatens the immune system. Over time, if left untreated, HIV can compromise a person's immune system to the point that the body may no longer be able to fight off opportunistic infections. As of 2016, 63,110 Canadians are living with HIV (Public Health Agency of Canada). Access, administration of and adherence to highly active antiretroviral treatment (HAART) can control the progression of a person's HIV. In most cases, people taking HAART achieve an undetectable viral load (or viral suppression), the point at which there is so little HIV in the bloodstream (<50 copies/mL) that it cannot be detected by conventional medical technologies. Viral suppression is linked to marked improvement in long-term health outcomes and drastically reduces the possibility of transmitting HIV to sexual partners.

While achieving and maintaining an undetectable viral load via HAART means HIV-positive people can live long lives and manage their HIV as a chronic illness, people living with HIV experience the effects of "accelerated aging". According to Centers for Disease Control and Prevention (CDC) HIV/AIDS surveillance data from 1985 to 2010, people with HIV are living longer, where more than 35% are aged 50 or older. As people living with HIV are aging, they are also more susceptible to inflammation and non-infectious co-morbidities, including bone fractures and renal failure, at earlier ages. From the literature, co-morbidities, such as kidney, liver, and cardiovascular disease, are more common in people living with HIV than the general population. Increased risk of experiencing co-morbidities is due to several risk factors, including co-infection and antiretroviral treatments themselves. In a study,

people living with HIV between ages 41-50 are 16 times more likely than the general population to develop renal failure, and 46 times more likely to develop renal failure when over 60 years of age. When considering bone fracture risk, HIV+ people between the ages 40-60 are 12-16 times more at risk than those uninfected with HIV (Guaraldi G, et al. Outcomes Res. 2013 Sep 23;5:481-8).

As a chronic illness, HIV can present a number of complications, and these can vary from day to day and from patient to patient. At CTAC, we know that many people living with HIV experience negative mental health outcomes, either as side effects from treatment, or from facing stigma, discrimination, and related stress. One participant explained how their depression can have an effect on whether they adhere to their medication, *"When depressed it is sometimes hard to just push yourself to pick up your pills."* Another participant from our dolutegravir rilpivirine survey noted that there are also issues with stigma in the medical community, *"Local doctors feel ill-equipped to treat HIV due to inexperience because of low patient caseloads with the condition. Stigma also play into it I think. Unless they're familiar, doctors still see HIV as something more difficult to live with than it actually is."* Another participant from our dolutegravir rilpivirine survey discussed the challenge of managing HIV while residing in a rural area, *"I live in a rural area and have to travel about 100 km. each way for my doctor's appointments. I only see my doctor about every six months. Obviously if I had to travel that far more often it would be a challenge. For those who don't have the support of family this could definitely be an obstacle."*

In 2011, the Canadian AIDS Society released a study that estimated a $1.3 million total economic loss per Canadian living with HIV (analyzing statistics current through 2008). This includes a $670,000 average loss per HIV-positive person in labour productivity and a $380,000 average loss in quality of life. As a result of being on HIV treatment, many participants described noticeable improvements in their quality of life and ability to engage in daily activities. Discussing the overall impact of treatment on his life, one participant stated, "*Up until this treatment I had been experiencing many side effects and resistance to the medications I was taking. My energy level has been high, although lowering somewhat lately (probably because of aging). As a result, home life is better in that there is not the constant worry of illness seriously affecting the quality of life."* When asked whether treatment had improved their quality of life another participant answered, "*My quality of life has improved as medications have improved- it's much easier having to take 1 pill a day, compared to dozens back in the beginning."*

Many people living with HIV experience intersecting vulnerabilities conditioned by the social determinants of health – the social and structural conditions in which people are born, live, work and age, shaped by the distribution of money, power and resources at the local, national and international levels. The following stories from respondents reflect the substantial impact that the social determinants of health, particularly employment and the accessing of public health benefits, have had on managing their HIV:

"My challenges are not treatment related, but more about how I am treated because I work periodically and I access Trillium. The Trillium plan is a barrier for people who work part time or periodically. Aids organizations and the government itself often assume that people will go onto ODSP or have private drug plans." [respondent from dolutegravir rilpivirine survey]

"I am worried about the fact that HIV is now viewed as chronic, manageable disease. I still have good and bad days but, if HIV is now seen as something other than a disability, will I be forced to go back to work, even when I'm not well?"

As a result, HIV is a complicated illness that requires treatment options that can be tailored to individual needs, delivered in innovative capacities that bolster access to treatment, care and support, such as treatment outreach programs, low-threshold health care services, adherence programs and social supports.

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).

HIV is a complex illness and people living with HIV have varying responses to treatments that are currently available. Most people living with HIV are able to work with their physicians to find a therapeutic regimen that achieves viral suppression. However, some people living with HIV are not able to achieve viral suppression, despite trying multiple treatment regimens. Additionally, treatment adherence (taking medication when prescribed, as prescribed) is necessary for treatment to be effective; non-adherence can lead to drug class resistance, requiring the adoption of a new regimen selected from fewer available treatment options. As a result, having the maximum possible treatment options available is of clinical importance.

Findings from our workshop and online survey indicate that, of the twelve respondents who identified as living with HIV, all are currently on treatment for their HIV. Their length of time on their current therapies was approximately 3-15 years for all participants, although minor changes have had to be made due to other health problems, or resistances that have developed. Considering our workshop and survey populations were primarily made up of long-term survivors (individuals who have been living with HIV for up to 34 years), this result demonstrates that there is relative stability with the new generation of HIV medications, but individuals living with HIV will change their treatment regimen after advancements in medications, or due to other health complications. This emphasizes the significant need for the availability of several HIV treatments.

All of the participants that came to the workshop, and completed the dolutegravir lamivudine online survey, indicated current or past use of regimens containing darunavir, dolutegravir, emtricitabine, rilpivirine, ritonavir, and/or tenofovir. Treatments ran the gamut from Prezista to Intelence, Triumeq, Isentress, Norvir, and/or Atripla with different combinations of the above being utilized. Participants noted that their current treatment was effective at suppressing their viral load, but that there had been side effects associated with older treatments that were given when they were first diagnosed. One participant noted that, *"When I was first diagnosed, my doctor forced me onto AZT. AZT made me extremely sick. I became anemic and had extremely low energy. The side effects were so bad, that I wanted to discontinue treatment."*

In the dolutegravir consultations, participants highlighted a number of areas where they had, or could benefit from, caregiver support. They all noted substantial impact on caregivers looking after patients living with HIV. One participant highlighted that the challenges his/her spouse faces in providing

support is surrounding disclosure. According to the participant, "*hiding from friends and some of our family members that I am HIV positive*" has been extremely difficult and hindered the ability to acquire a social safety net. Others noted service provider knowledge, staff time, funding, transportation and other associated costs as barriers to providing support and its impact on treatment adherence, mental health and other determinants of health. One participant noted, "*There are a lot of challenges associated with lack of knowledge about services and how to access them. Such as dental care, legal aid (writing of wills, living wills, how to access disability benefits etc...)*" In addition, more than one participant noted that difficulties understanding stigma and its impact, and navigating HIV-specific social services and institutional systems, including disability, insurance and mortgage, have presented specific challenges.

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?

Dolutegravir/lamivudine is a novel, once-daily, fixed dose combination therapy featuring two drugs that are already on the Canadian market: dolutegravir and lamivudine. The clinical trials for dolutegravir/lamivudine have shown that switching to this 2DR combination is associated with high HIV suppression rates, has a low potential for drug-drug interactions, and the potential for less long-term drug toxicity. These benefits were considered important for individuals managing lifetime use of HIV antiviral treatment. Many of the participants expressed interest in a drug with a new chemical composition that is potent against NNRTI resistant variants. One participant noted that, *"New meds offer hope, especially for those with multiple types of drug resistance."* Other participants, like this participant from our dolutegravir rilpivirine survey noted that, *"I don't see replacing the "devil" I know with the "devil" I don't know - at least on a personal basis. If I had to make changes - and that time could come since I've been on the present regime for quite some time."*

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?

None of the participants within the workshop, or who completed the online survey, had experience with the single-dose, combination drug doravirine/lamivudine.

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.

8. Biosimilar

If the drug in review is a biosimilar (also known as a subsequent entry biologic), please outline any expectations or concerns held by patients, caregivers, and families about the biosimilar. If the biosimilar was less expensive than the brand name drug, what would the impact be for patients, caregivers, and families?

9. Anything Else?

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

CTAC continues to acknowledge and appreciate CADTH and CDEC suggestions as to how to improve patient input submissions, and is motivated to discuss revisions, reform, and refinements to the patient input process that can better represent the patient voice as well as improve the work of not only submitting organizations, but also the CDR as a whole.

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.

   CTAC did not receive help from outside our patient group to complete this submission

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.

   CTAC did not receive help from outside our patient group to collect or analyze data used in this submission

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
ViiV Healthcare				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.

Name: Amanda Fletcher
Position: Director of Policy, Research, and Development
Patient Group: CTAC
Date: March 11, 2019