Common Drug Review
Patient Group Input Submissions

elvitegravir/cobicistat/emtricitabine/tenofovir/alafenamide (Genvoya) for HIV-1 infection

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

CADTH received patient group input for this review on or before October 19, 2015
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.

CTAC

Section 1— General Information

Name of the drug CADTH is reviewing and indication(s) of interest	elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide (E/C/F/TAF)
Name of the patient group	CTAC
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
Email	[redacted]
Telephone number(s)	[redacted]
Name of author (if different)	[redacted]
Patient group's contact information: Email	[redacted]
Telephone	1-877-237-2822, extension 231
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Website	www.ctac.ca
Permission is granted to post this submission	Yes

1.1 Submitting Organization

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.

1.2 Conflict of Interest Declarations

CTAC received unrestricted organizational and/or educational grants from the following organizations in the 2014-2015 fiscal year: Abbott/Abbvie, Gilead Sciences, Janssen, and ViiV Healthcare.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

On October 8, 2015, CTAC delivered a national consultation webinar that provided an overview of the Common Drug Review patient input process and key findings from the E/C/F/TAF clinical trials. The consultation webinar was presented by Barbara Santosuosso, Policy Researcher at CTAC. CTAC members and organizational partners were invited to participate in the webinar. In addition, as we 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, we reached

out to principal investigators and asked that they inform trial participants about our patient input consultation.

In total, two participants attended the webinar. A link to the consultation webinar and web-based feedback survey was provided to webinar attendees and principal investigators by email and through CTAC's social media outlets (CTAC website, Youtube, Facebook, and Twitter). The survey was made available from Thursday October 8, 2015 to Monday October 19, 2015. In total, CTAC has compiled data from two survey respondents. Both respondents identified themselves as HIV-positive. One respondent identified as a 50 year old male, and the other respondent identified as two-spirited, aged 47. Both respondents reside in Ontario and are on treatment. One respondent has been on treatment for six years and the other has been on treatment for over eight years (and prior to HAART used traditional medicine). In addition to the results of the survey, survey data used in submissions for Stribild, Tivicay, Triumeq, and Prezcobix, have been used to inform and support this patient submission.

2.2 Impact of Condition on Patients

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 2011, 71 300 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.

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 respondent, for example, noted that the biggest challenges are "ignorance about HIV and healthy living and stigma attached to infection". Another respondent noted, "I was quite depressed and suicidal early on in my infection, and my caregivers had to deal with this".

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, one respondent noted that his quality of life has improved significantly. The respondent stated, "…energy, quality of life, appetite, sleep and other anxieties greatly diminished as result of healthier living and immune system. I have also left a [sic] AISH (disability provincial Alberta) and returned to work full time". Many people living with HIV experience fatigue, both before and after they initiated treatment, making it difficult to maintain diet, exercise routines, and even to work. A few respondents stated that their quality of life in these areas has improved as a result of treatment, including one respondent who said, "*Quality of life has improved because I am not as fatigued as previously*". Another respondent noted, "*I feel 'Non-toxic' again. Finding out I was HIV+ and living with a very high viral load did a number on my self-esteem and my ability to socialize and engage fulsomely. I am also considered a rapid progressor so I would likely have died by now without treatment*".

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. There have been a few respondents as well as caregivers who have noted the substantial impact that the social determinants of health, particularly living conditions, have had on managing their HIV, including:

"Affordable access to treatment is currently an issue a lot of PHA'S in Manitoba (Particularly those without some form of co-insurance) struggle with. This has resulted in additional stress, particularly when viral load is now considered a co-factor in non-disclosure cases".

"I required compassionate access to treatment at the beginning of taking treatment because I had been self-employed and my income taxes were not up to date. Trillium Drug Benefits are only available if your financial ducks are all in a row."

"Moving from Alberta to Manitoba was a traumatic experience because of the change of reality in formularies and coverage. It took additional support to work through some of these issues."

"back in 2006 i had left Ontario for more than 3 months, i had 50 platelets and 90 cd4 count and ohip did not allow me access. I came back to the province without a home. I had no support to adhere, i was physically weak to make it to docs.[sic]"

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.

2.3 Patients' Experiences With Current Therapy

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.

From the survey, both respondents indicated current use of an integrase inhibitor (specifically, a Tivicay- based regimen). One respondent has currently been taking Tivicay with a Kivexa backbone for one year, and the other respondent has been currently taking Triumeq (Tivicay/Kivexa combination therapy) for the past two months. One respondent noted his experience with their current regimen as fairly positive, stating, "*My viral load has been undetectable since within one month of commencing treatment in 2009. Until my current ARV regimen, health complications resulting from the toxicity of previous Rx medications were hepatic and renal deterioration. Hypercholesterolemia and bone density loss are also suspected collateral damage*". The other respondent indicated that current therapy is,"*… very effective regardless of the awful side effects, I am still undectable [sic] just like with the previous treatment, it didn't take time to function, i [sic] was ok before but doctor pushed me to change meds]*". In terms of side effects, both participants indicated fatigue, nausea and diarrhea as the most common adverse events, and one respondent indicated insomnia and depression as additional side effects of current treatment. When asked how they cope with current side effects, one respondent indicated, "*I try to sleep and well*", while the other respondent stated, "*I take supplements*". When asked if being on HIV treatment has improved quality of life, one respondent indicated no impact, while the other stated a positive impact, particularly around "*…energy level, work life, home life, relationship with pet, etc…*".

Patient responses from the Stribild, Tivicay, Triumeq, and Prezcobix surveys also indicated several advantages and challenges with current therapy. One respondent from a survey on Stribild indicated taking a Viramune and Truvada based regimen, and noted cardiovascular events, including a stroke, gum disease, lipodystrophy, and fatigue as adverse events. The respondent stated that he has been managing these side effects through the following: *"I deal with them by staying physically active and living a balanced lifestyle. I do not drink alcohol or smoke cigarettes. I remain involved in social activities, family activities and push myself to go out and stay busy with projects. I do a lot of volunteer work".* Another respondent from the Tivicay patient input survey stated that s/he has experienced several gastrointestinal adverse events due to ritonavir, specifically "… *GI distress, diarrhea, gas, weight gain",* while a respondent who participated in the Triumeq patient input survey currently on a darunavir based therapy noted side effects as being "*minor*", and indicated that s/he was able to suppress their virus to undetectable levels.

Three previous respondents from the Prezcobix consultation noted experiencing adverse events as a result of their current treatment. One respondent who was taking a darunavir/ritonavir based regimen noted these adverse events as, *"High cholesterol...Loose stools…",*and indicated taking finofibrate and omega 3 as a way to alleviate these symptoms, while another respondent currently taking Complera noted, "*Fatigue- Trying to sleep early, but not working and changed my diet; zero Big stomach- tried changing diet-zero results".* The third respondent who is currently taking Isentress for the past four years noted "*wasting"* as a side effect, although mentioned that physical activity, particularly exercising at the gym, has helped alleviate this adverse event. For this respondent, while a benefit of being on treatment has been "*Less fear of catching opportunistic infections*", a challenge has been *"rehabilitation from sickness to health and back into the workplace".* The three respondents commented on the impact that being on treatment has had on their quality of life. One respondent stated that quality of life has remained the same since being on HIV treatment, while another noted

that his quality of life has improved, and the third respondent indicated a decrease in quality of life since being on HIV treatment and stated, "*…I'm more depressed than I used to be".*

2.4 Impact on Caregivers

From the E/C/F/TAF patient input consultation, both respondents indicated the impact that living with HIV has had on themselves, caregivers and/or service providers. One respondent stated, "*In the past, my biggest challenge has been to explain to my employer periodic requests to make adjustments to my work schedule in order to seek medical advice and treatment - especially when I had consultations and follow-ups with my family doctor, ID specialist, nephrologist, ENT specialist and GI specialist within the same general period of time. My health challenges were most certainly linked with side effects to my treatment at the time*". The other respondent noted that " *time, assistance with navigating the social safety net, acting as a resource person, providing support, these challenges are linked to side effects that did not let me make it to docs [sic]*".

Respondents from previous patient input surveys (Stribild, Tivicay, Triumeq, and Prezcboix) noted substantial impact on caregivers looking after patients living with HIV. In the Prezcobix consultation, one female respondent from Alberta noted, *"HIV/AIDS agencies in Fort McMurray are stressful because for clients to get emergency funding [sic]. They have to go through a lot, like having to go to Alberta works to see if they can fund the trip. When we travel to Edmonton, we pay for both travel and accommodation in hotels [sic]. Or make a day trip which is 12 hours to go and come back, and no stressful. It costs us $270 (bus fare, taxi fare, hotel and food)".* A second respondent stated that "*providing support*" was a challenge that caregivers and/or service providers face when providing care to a person living with HIV.

Other respondents from previous patient input surveys highlighted that staff time, funding, transportation and other associated costs, acted as barriers to providing support and had a negative impact on patient treatment adherence, mental health and other determinants of health. One caregiver stated, "*I think caregivers and/or service providers, including myself, struggle against messaging that strictly biomedical answers are appropriate for the treatment of HIV+ people. While the treatment advances have proven benefits, I feel a holistic approach will prove more beneficial than simply a biomedical one. I think there are many intersecting factors which must be addressed which treatment on its own cannot. I am not sure if this is linked to side effects or adverse reactions, however these issues fall victim to the same messaging. It is my personal experience that discussing treatment options in certain situations is a non-issue when the person doesn't know where their next meal is coming from or where they are sleeping that night, two serious problems in much of the HIV+ population".*

On respondent also noted the difficulties associated with being obliged to seek services from specialists: "*At times it is confusing as the various specialists involved do not communicate with each other and each physician manages my dossier as a separate entity, when in fact, all of the health issues necessitating a specialist are inter-related",* while another two respondent indicated *"understanding the episodic nature of the illness even when on treatment and allowing for the flexibility to work hours that meet that*" as a challenge for caregivers and "*…side effects can make sticking to treatment difficult. I think caregivers look to their loved one's adherence to treatment as assurance of their wellness and endurance. Therefore side effects can have major implications for caregivers in terms of peace of mind.*"

Section 3 — Information about the Drug Being Review

3.1 Information Gathering

The information in this section was gathered in the same means described in section 2.1.

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

a) Based on no experience using the drug:

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

Of the two survey participants, none currently were taking or had even taken E/C/F/TAF either by compassionate supply or as part of a clinical trial. When asked if they would consider taking E/C/F/TAF instead of their current treatment regimen, one respondent indicated: "I would only consider taking it on the advice of my ID specialist. As my current HAART is now available in the single-tablet regimen Triumeq, my doctor will be switching me over to the new co-formulation at my next prescription renewal. There is no compelling reason to change to another therapy when the one I am on is effective and has a

better safety profile than previous therapies", regardless of the "…understanding that the side effects are about the same". The other respondent also noted, "no, I am not into new challenges", and indicated disinterest in switching regimens to find out if the tolerability profile of E/C/F/TAF is similar to current or past regimens. Both also indicated that if they did switch to E/C/F/TAF, they would expect that their quality of life would remain the same.

Of the 10 survey participants who participated in the Stribild patient input consultation (E/C/F/TDF), none were currently taking a Stribild for their HIV treatment. Four respondents said they would consider taking Stribild either now or in the future, if a therapeutic change was necessary; however, three participants indicated that they would not consider Stribild due to concerns about its safety, tolerability, and/or efficacy. Two respondents stated they would not consider Stribild because they had previously taken regimens that had included tenofovir disoproxil fumurate (TDF) and had experienced negative side effects. One respondent said she would need to see more longer-term studies of Stribild's safety and efficacy, especially to get a clearer picture of effectiveness and side effect profiles in women.

It is important to note that since the patient input consultation on Stribild, more real-world evidence about its safety, efficacy, and tolerability has become available, particularly around TDF. While TDF is highly effective in viral suppression, and for that reason, is one of the most commonly used and recommended HIV treatments in clinical trials and in several regimens, there has been concern about TDF use and its association with new or worsening kidney impairment or serious kidney disease, as well as decreased bone mineral density in a small minority of people. Three out of four of the components of E/C/F/TAF are present in the Stribild, with the difference being that Stribild contains TDF and E/C/F/TAF contains tenofovir alafenamide. TAF, a prodrug of tenofovir, not only requires a lower dosage than TDF, is smaller in pill size (due to lower concentration), and has potent antiviral activity, but it also has a different pathway than TDF. Because TAF is not concentrated in the blood as is TDF, early findings indicate that TAF will not affect kidney or bones the way TDF does and might kill the HIV virus better. TAF has favourable virologic outcomes when compared to Stribild and other TDF- containing regimens, significantly less effect on spinal and hip bone mineral density(BMD) (and in some cases, resulted in BMD gains), and significant improvements in multiple tests of renal function.

While people living with HIV continue to experience increased life expectancies, trends also indicate that a growing portion of new HIV diagnoses in Canada are among adults aged 50 and older (PHAC, 2012). As people living with HIV get older, the risk of developing co-morbidities also increases (and at earlier ages). As a result, it is becoming more imperative that new treatments not only have potent antiviral activity, but also address the unmet needs of people living with HIV, particularly around minimizing the potential risks associated with such co-morbidities, including the negative effects of polypharmacy. All things considered, we strongly recommend that E/C/F/TAF be listed for treatment of HIV-1 infection. E/C/F/TAF has the potential to reduce the burden of HIV (especially as people age), reducing strain on the health care system and supporting people living with HIV as they lead healthy, active lives and fully contribute to society.

Section 4 — Additional Information

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 the CDR as a whole.