Common Drug Review
Pharmacoeconomic Review Report

August 2016

Drug	Emtricitabine/tenofovir alafenamide (Descovy)
Indication	In combination with other antiretrovirals (such as non-nucleoside reverse transcriptase inhibitors or protease inhibitors) for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adult and pediatric patients 12 years of age and older (and weighing ≥ 35 kg)
Reimbursement request	For use in combination with other antiretrovirals for treatment of treatment-naive and virologically suppressed HIV-1 infected adult and pediatric patients 12 years of age and older.
Dosage form(s)	emtricitabine/tenofovir alafenamide (200/10 mg) and emtricitabine/tenofovir alafenamide (200/25 mg) fixed-dose combination (oral tablet)
NOC date	April 29, 2016
Manufacturer	Gilead Sciences Canada, Inc.

Redactions: Confidential information in this document has been redacted at the request of the manufacturer in accordance with the *CADTH Common Drug Review Confidentiality Guidelines.*

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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ABBREVIATIONS

3TC	lamivudine
ABC	abacavir
ART	antiretroviral therapy
ARV	antiretroviral
ATV	atazanavir
CDR	CADTH Common Drug Review
COBI	cobicistat
DHHS	US Department of Health and Human Services
DRV	darunavir
DTG	dolutegravir
EVG	elvitegravir
FTC	emtricitabine
ODB	Ontario Drug Benefit
RAL	raltegravir
TAF	tenofovir alafenamide fumarate
TDF	tenofovir disoproxil fumarate

SUMMARY

Background

Emtricitabine/tenofovir alafenamide fumarate (FTC/TAF) (200 mg/10 mg and 200 mg/25 mg) is a fixed-dose combination of two nucleoside reverse transcriptase inhibitors (NRTIs) indicated for use in combination with other antiretroviral therapies (ARTs) for the treatment of HIV type 1 infection in adults and pediatric patients 12 years of age and older (and weighing ≥ 35 kg).[1] It is available as 200 mg/10 mg and 200 mg/25 mg film-coated tablets; the recommended dose is one 200 mg/10 mg tablet daily when used in combination with a ritonavir- or cobicistat (COBI)-boosted protease inhibitor. Otherwise, the recommended dose is one 200 mg/25 mg tablet daily.[1] The manufacturer submitted a price of $28.57 per tablet regardless of strength, which is slightly lower (by $0.51) than the unit cost of FTC/tenofovir disoproxil fumarate (TDF), the backbone component that FTC/TAF is expected to replace.

The manufacturer is requesting that FTC/TAF be listed in combination with other ARTs for treatment of treatment-naive and virologically suppressed HIV-1 infected adult and pediatric patients 12 years of age and older.[2]

Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost analysis comparing the costs of all recommended and alternative antiretroviral (ARV) regimens as outlined in the 2015 US Department of Health and Human Services (DHHS) *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*.[2,3] The manufacturer's approach assumes that FTC/TAF would supplant FTC/TDF as the backbone component of several of ARV regimens; as such, the manufacturer compared the daily cost of these regimens with FTC/TDF as the backbone drug versus FTC/TAF as the backbone drug.[2] The following recommended regimens were included in the analysis: dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) (50 mg/600 mg/300 mg daily); DTG (50 mg daily) + FTC/TDF (200 mg/300 mg daily); elvitegravir (EVG)/COBI/FTC/TDF (150 mg/150 mg/200 mg/300 mg daily); raltegravir (RAL) (400 mg twice daily) + FTC/TDF (200 mg/300 mg daily); and darunavir (DRV) 800 mg daily boosted with 100 mg ritonavir + FTC/TDF 200 mg/300 mg daily.

Additionally, the manufacturer included the following alternative regimens in its analysis: efavirenz (EFV)/FTC/TDF (600 mg/200 mg/300 mg daily); rilpivirine (RPV)/FTC/TDF (25 mg/200 mg/300 mg daily); atazanavir (ATV) (300 mg daily) boosted with 100 mg ritonavir + FTC/TDF (200 mg/300 mg daily); and DRV (800 mg daily) boosted with 100 mg ritonavir + ABC/3TC (600 mg/300 mg daily). Only drug costs were considered, as the manufacturer assumed that other resource use components would be equivalent among all ARV regimens.[2] Drug costs were obtained from the Ontario Drug Benefit (ODB) formulary.[4] Mark-ups and dispensing fees were excluded.

FTC/TAF and FTC/TDF were considered to have similar efficacy and safety (thereby justifying the use of a cost analysis) based on the following phase 3 studies: two double-blind, active-controlled non-inferiority trials that compared EVG/COBI/FTC/TAF with EVG/COBI/FTC/TDF in treatment-naive adult patients (studies 104 and 111);[5,6] one double-blind, active-controlled non-inferiority trial that compared patients on a FTC/TDF + third drug regimen versus those who switched to a FTC/TAF drug + third agent regimen (study 1089);[7] and an open-label, active-controlled non-inferiority trial that compared patients who switched to EVG/COBI/FTC/TAF from a pre-existing regimen (FTC/TDF + a third drug) with those who remained on their pre-existing regimen, in virologically suppressed adults (i.e., treatment-experienced patients) (study 109).[8] Bioequivalence was demonstrated for FTC/TAF and EVG/COBI/FTC/TAF, which

supported the use of evidence from the clinical development program of EVG/COBI/FTC/TAF for the comparison of FTC/TAF with FTC/TDF. The conclusion of non-inferiority for the primary outcome of virological success was defined based on the proportion of patients with plasma HIV-1 ribonucleic acid (RNA) < 50 copies/mL at 48 weeks. Additional information on efficacy and safety in specific subgroups of patients — i.e., adolescents and patients with renal impairment — was obtained from two open-label cohort studies (studies 106 and 112) for the primary outcome of virological success at 24 weeks.[9,10] The manufacturer noted that the analysis is applicable only to adults and adolescents whose treatment aligns with HIV-1 treatment regimens for adult patients.[2]

As the submitted price of FTC/TAF is slightly lower (by $0.51) than that of FTC/TDF, based on the publicly available price of FTC/TDF on the ODB formulary,[4] there may be modest cost savings associated with replacing FTC/TDF with FTC/TAF. However, TDF- or TAF-containing regimens are not the lowest-cost regimens available. Of the DHHS-recommended regimens, the single-tablet regimen DTG/ABC/3TC is the least costly, while RAL + FTC/TDF (FTC/TAF) is the most expensive.

Key Limitations

- **Lack of comparative clinical information for FTC/TAF + third drug (or EVG/COBI/FTC/TAF) versus other ARV regimens in adolescent patients:** There are no head-to-head comparative trials for FTC/TAF + third drug (or EVG/COBI/FTC/TAF) compared with other ARV regimens for adolescent patients, and the manufacturer did not report an indirect comparison. Thus, there is uncertainty regarding comparative clinical effectiveness and harms in this population.

  The efficacy and safety of EVG/COBI/FTC/TAF for the primary outcome of virological success at 24 weeks in treatment-naive adolescent patients (12 to 18 years of age) was assessed in one phase 3 open-label cohort study (study 106).[9] In this study, 91.3% of patients achieved virologic success at 24 weeks.[9] However, this study was limited by a small sample size (N = 23).

  As noted by the clinical expert consulted by the CADTH Common Drug Review (CDR) for this review, most adolescents acquire HIV-1 infection through vertical transmission (i.e., mother-to-child). As such, adolescents will likely have exposure to ARV treatments either through transmission or previous treatment. There is no clinical information for FTC/TAF + third drug (or EVG/COBI/FTC/TAF) in treatment-experienced adolescents.

- **Lack of comparative clinical information for FTC/TAF as part of initial ARV regimens other than EVG/COBI/FTC/TDF:** The clinical expert consulted by CDR noted that FTC/TAF would likely be used in combination with either DTG, RAL, ritonavir-boosted darunavir (DRV/r), or DRV/COBI. However, there are no clinical data comparing FTC/TAF and FTC/TDF in regimens other than EVG/COBI in treatment-naive patients. Because the comparative clinical effectiveness and safety of FTC/TAF-based regimens and DHHS-recommended ARV regimens for initial therapy have not been demonstrated (other than against EVG/COBI/FTC/TDF), there is uncertainty regarding comparative cost-effectiveness and the appropriateness of a cost analysis founded on an assumption of equivalent efficacy and safety.

Issues for Consideration

- It should be noted that the safety and effectiveness of FTC/TDF has not been established in patients younger than 18 years of age. As such, FTC/TAF provides an additional option for pediatric patients requiring ARV therapy.
- There is variability in the price of ARTs across CDR-participating drug plans, including the price of FTC/TDF. This has an impact on the comparative cost analysis for FTC/TAF.

- The patent for Truvada (FTC/TDF) will expire in 2024; therefore, generic entrants for FTC/TDF are not anticipated for a number of years.[11] While the availability of regimens in co-formulated fixed-dose combinations offers potential benefits to patients in terms of convenience and adherence, it presents challenges to generic entrants as individual drug patents expire.
- Input received from one patient group highlighted patients' concerns regarding adverse events associated with ARV regimens, the availability of treatment options, and regimens that support adherence to treatment. Based on the manufacturer's submission, there is a lack of data on the comparative safety of FTC/TAF versus other ARV regimens, although it has potential advantages over FTC/TDF with respect to renal and bone health. As FTC/TAF is likely to be used in place of FTC/TDF in combination with a third ARV, it does not offer any advantages in terms of pill burden or convenience.

Conclusions

At a daily cost of $28.57, FTC/TAF is slightly less expensive than FTC/TDF, based on the price of FTC/TDF in the ODB formulary.[4] However, at the submitted price, treatment with FTC/TAF costs $0.87 more per day compared with the lowest publicly available price for FTC/TDF in Canada. Additionally, among the DHHS-recommended and alternative regimens, TDF- or TAF-containing regimens are not the lowest-cost regimens available. The cost comparison for adolescents is of uncertain validity, as there was no comparative evidence for FTC/TAF in this population.

APPENDIX 1: COST COMPARISON

The comparators presented in the tables below are based on recommended and alternative regimens for treatment-naive patients in the US Department of Health and Human Services (DHHS) *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adolescents and Adults* (2016),[12] and have been confirmed by the clinical expert consulted by the CADTH Common Drug Review (CDR) for this review. The guidelines do not make specific recommendations for treatment-experienced patients; however, as noted by the clinical expert, these regimens are most often used in treatment-experienced patients as well.

Costs in Table 1 and Table 2 are manufacturer list prices, unless otherwise specified. Existing Product Listing Agreements are not reflected in the tables and as such may not represent the actual costs to public drug plans.

TABLE 1: COST COMPARISON TABLE FOR HIV ANTIRETROVIRAL AGENTS IN TREATMENT-NAIVE ADULT PATIENTS

Drug/Comparator	Strength	Dosage Form	Price ($)	Recommended Use	Daily Cost ($)	Freq. of Use (/Day)	No. Pills (/Day)
FTC/TAF-Based Regimens[a]							
Dolutegravir (Tivicay) + Emtricitabine/tenofovir alafenamide	50 mg 200 mg/25 mg	Tab	18.6665 28.5710[b]	50 mg daily 1 tablet daily	47.24	1	2
Raltegravir (Isentress) + Emtricitabine/tenofovir alafenamide	400 mg 200 mg/25 mg	Tab	13.9050 28.5710[b]	400 mg twice daily 1 tablet daily	56.38	2	3
Darunavir (Prezista) with ritonavir (Norvir) + Emtricitabine/tenofovir alafenamide	800 mg 100 mg 200 mg/10 mg	Tab	21.7160 1.5183 28.5710[b]	800 mg daily 100 mg 1 tablet daily	51.81	1	3
Darunavir/cobicistat (Prezcobix) + Emtricitabine/tenofovir alafenamide	800 mg/150 mg 200 mg/10 mg	Tab	23.1720[c] 28.5710[a]	1 tablet daily 1 tablet daily	51.74	1	2
DHHS-Recommended Antiretroviral Regimens[12]							
INSTI-Based							
Dolutegravir/abacavir/Lamivudine (Triumeq)	50 mg/600 mg/300 mg	Tab	41.3834	1 tablet daily	41.38	1	1
Dolutegravir (Tivicay) + Emtricitabine/tenofovir disoproxil (Truvada)	50 mg 200 mg/300 mg	Tab	18.6665 29.0797	50 mg daily 1 tablet daily	47.75	1	2
Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil (Stribild)	150 mg/150 mg/ 200 mg/300 mg	Tab	46.3894	1 tablet daily	46.39	1	1
Raltegravir (Isentress) + Emtricitabine/tenofovir disoproxil (Truvada)	400 mg 200 mg/300 mg	Tab	13.9050 29.0797	400 mg twice daily 1 tablet daily	56.89	2	3
Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide (Genvoya)	150 mg/150 mg/ 200 mg/10 mg	Tab	46.3893[d,e]	1 tablet daily	46.39	1	1
PI-Based							
Darunavir (Prezista) with ritonavir (Norvir)	800 mg 100 mg	Tab	21.7160 1.5183	800 mg daily 100 mg	52.31	1	3

Drug/Comparator	Strength	Dosage Form	Price ($)	Recommended Use	Daily Cost ($)	Freq. of Use (/Day)	No. Pills (/Day)
+ Emtricitabine/tenofovir disoproxil (Truvada)	200/300 mg		29.0797	1 tablet daily			
DHHS Alternative Antiretroviral Regimens							
NNRTI-Based							
Efavirenz/tenofovir disoproxil/emtricitabine (Atripla)	600 mg/200 mg/ 300 mg	Tab	43.7833	1 tablet daily	43.78	1	1
Emtricitabine/rilpivirine/ tenofovir disoproxil (Complera)	200 mg/25 mg/ 300 mg	Tab	43.3428	1 tablet daily	43.34	1	1
PI-Based							
Atazanavir (Reyataz) with ritonavir (Norvir) + Emtricitabine/tenofovir disoproxil (Truvada)	300 mg 100 mg 200 mg/300 mg	Cap	22.4330[f] 1.5183 29.0797	300 mg daily 100 mg 1 tablet daily	53.03	1	3
Darunavir/cobicistat (Prezcobix) + Abacavir/lamivudine (Kivexa)	800 mg/150 mg 600 mg/300 mg	Tab	23.1720[c] 23.9498	1 tablet daily 1 tablet daily	47.12	1	2
Darunavir (with ritonavir) + Abacavir/lamivudine (Kivexa)	800 mg (100 mg) 600 mg/300 mg	Tab	21.7160 1.5183 23.9498	800 mg daily 100 mg 1 tablet daily	47.18	1	3

DHHS = Department of Health and Human Services; DRV/r = ritonavir-boosted darunavir; DRV/c = cobicistat-boosted darunavir; DTG = dolutegravir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitors; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir; TAF = tenofovir alafenamide fumarate.

Note: All prices are from the Ontario Drug Benefit formulary (accessed April 2016),[4] unless otherwise indicated.

[a] Based on feedback from the clinical expert, FTC/TAF will be used in combination with either DTG, RAL, DRV/r or DRV/c. FTC/TAF-based regimens have not yet been added to the DHHS guidelines.

[b] Manufacturer's submitted price.[2]

[c] Price submitted to the CADTH Common Drug Review, non-confidential.[13] Not available on any public drug plans.

[d] Delta PA, manufacturer's list price, accessed April 2016.

[e] Not available on any public drug plans.

[f] Saskatchewan Drug Benefit formulary (accessed April 2016).[14]

The comparators presented in Table 2 are based on the recommended regimens for initial therapy for HIV infection in children in the DHHS guidelines for the use of antiretroviral (ARV) drugs in pediatric HIV-1 infection (2016).[15] Patients aged 12 to 18 years may be prescribed treatment regimens based on the pediatric guidelines included below or the guidelines for adolescents and adult patients (included in Table 1).

TABLE 2: COST COMPARISON TABLE FOR ANTIRETROVIRAL DRUGS IN ADOLESCENT PATIENTS WITH HIV INFECTION (AGED 12 TO 18 YEARS) — DHHS-RECOMMENDED AND ALTERNATIVE REGIMENS

Drug/Comparator	Strength	Dosage Form	Price ($)	Recommended Use	Daily Cost ($)	Freq. of Use (/Day)	No. Pills (/Day)
Preferred Antiretroviral Regimen Options[b]							
FTC/TAF - based regimens							
Atazanavir (Reyataz) with ritonavir (Norvir) + Emtricitabine/tenofovir alafenamide[b]	300 mg 100 mg 200 mg/10 mg	Cap Tab	22.4330[c] 1.5183 28.5710[a]	300 mg daily[d] 100 mg daily 1 tablet daily	53.03	1	3
Dolutegravir (Tivicay) + Emtricitabine/tenofovir alafenamide[b]	50 mg 200 mg/25 mg	Tab	18.6665 28.5710[a]	50 mg daily[d] 1 tablet daily	47.75	1	2
Darunavir (with ritonavir) + Emtricitabine/tenofovir alafenamide[b]	800 mg (100 mg) 200 mg/10 mg	Tab	21.7160 1.5183 28.5710[a]	800 mg daily 100 mg 1 tablet daily	52.31	1	3
Other							
Atazanavir (Reyataz) with ritonavir (Norvir) + Abacavir/lamivudine (Kivexa)	300 mg 100 mg 600 mg/300 mg	Cap Tab	22.4330[c] 1.5183 23.9498	300 mg daily[d] 100 mg daily 1 tablet daily	47.90	1	3
Dolutegravir (Tivicay) + Abacavir/lamivudine (Kivexa)	50 mg 600 mg/300 mg	Tab	18.6665 23.9498	50 mg daily[d] 1 tablet daily	42.62	1	2
Darunavir (with ritonavir) +	800 mg (100 mg)	Tab	21.7160 1.5183	800 mg daily 100 mg	47.18	1	3

Drug/Comparator	Strength	Dosage Form	Price ($)	Recommended Use	Daily Cost ($)	Freq. of Use (/Day)	No. Pills (/Day)
Abacavir/lamivudine (Kivexa)	600 mg/300 mg		23.9498	1 tablet daily			
Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide (Genvoya)	150 mg/150 mg/ 200 mg/10 mg	Tab	46.3893[e,f]	1 tablet daily	46.39	1	1
Alternative Antiretroviral Regimen Options[g]							
Efavirenz + Lamivudine/zidovudine (Combivir, generics)	600 mg 300/150 mg	Tab	3.8030 2.6103	600 mg once daily One tablet twice daily	9.02	2	3
Raltegravir + Lamivudine/zidovudine (Combivir, generics)	400 mg 300 mg/150 mg	Tab	13.9050 2.6103	400 mg twice daily One tablet twice daily	33.03	2	4

3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV/r = ritonavir-boosted atazanavir; COBI = cobicistat; DHHS = US Department of Health and Human Services;[15] DRV/r = ritonavir-boosted darunavir; DTG = dolutegravir; EFV = efavirenz; FTC = emtricitabine; NRTI = nucleos(t)ide reverse transcriptase inhibitor; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide fumarate; ZDV = zidovudine.

Note: All prices are from the Ontario Drug Benefit formulary (accessed April 2016),[16] unless otherwise indicated.

[a] Manufacturer's submitted price.[2]

[b] DHHS guidelines for the use of ARV drugs in pediatric HIV infection recommend the use of 2 NRTIs + a third drug.[15] Among children aged 12 years and older who are not sexually mature, the preferred 2 NRTI backbone would be ABC/3TC or FTC/TAF, and the preferred third drug is ATV/r, DTG, DRV/r, or EFV/COBI.[15] Adolescents older than 12 years who are sexually mature are treated as per the adult guidelines.

[c] Saskatchewan Drug Benefit Formulary (accessed April 2016).[14]

[d] Based on a patient weight of 40 kg.

[e] Delta PA, manufacturer's list price, accessed April 2016.

[f] Not available on any public drug plans.

[g] DHHS guidelines for the use of ARV drugs in pediatric HIV infection recommend the use of 2 NRTIs + a third drug.[15] Among children aged 12 years and older, the alternative 2 NRTI backbone would be ZDV plus either ABC or FTC. As FTC is not available in a fixed dose with ZDV, and is not approved for use as a single drug in patients younger than 18 years in Canada, ZDV/3TC was used as the backbone drug in the cost table. Additionally, the alternative third drug would be EFV, RAL, or RPV (also not approved for patients younger than 18 years in Canada).

APPENDIX 1: REVIEWER WORKSHEETS

TABLE 3: SUMMARY OF MANUFACTURER'S SUBMISSION

Drug Product	FTC 200 mg/TAF 10 mg; FTC 200 mg/TAF 25 mg
Treatment	FTC/TAF 200 mg/10 mg taken orally once daily in combination with an HIV-1 protease inhibitor that is administered with either ritonavir or cobicistat, otherwise FTC/TAF 200 mg/25 mg
Comparators	Main comparison: FTC/TDF 200 mg/300 mg daily In this context, a broader comparison against all recommended and alternative regimens based on the DHHS guidelines for adolescents and adults was also considered: **Recommended regimens:** • DTG/ABC/3TC 50 mg/600 mg/300 mg daily • DTG 50 mg daily + FTC/TDF 200 mg/200 mg daily • EVG/COBI/FTC/TDF 150 mg/150 mg/200 mg/300 mg daily • RAL 400 mg twice daily + FTC/TDF 200 mg/300 mg daily • DRV 800 mg daily boosted with ritonavir 100 mg + FTC/TDF 200 mg/300 mg daily **Alternative regimens:** • EFV/FTC/TDF daily 600 mg/200 mg/300 mg daily • RPV/FTC/TDF daily 25 mg/200 mg/300 mg daily • ATV 300 mg daily boosted with ritonavir 100 mg + FTC/TDF 200 mg/300 mg daily • DRV 800 mg daily boosted with ritonavir 100 mg + ABC/3TC 600 mg/300 mg daily
Study Question	"To conduct a cost-minimization analysis of FTC/TAF versus Truvada, comparing daily drug acquisition prices from a government perspective, in patients with HIV-1 infection."
Type of Economic Evaluation	Cost comparison (drug costs only)
Target Population	Patients with HIV-1 infection
Perspective	Health care system
Outcomes Considered	Virological success, defined by the proportion of patients with plasma HIV-1 RNA < 50 copies/mL at week 48
Cost	• Cost of FTC/TAF 200 mg/10 mg and FTC/TAF 200 mg/25 mg from the manufacturer • Cost of other ARTs obtained from the Ontario Drug Benefit,[4] based on 2015 Canadian dollars • Health care resource use and those associated with adverse events were not included (assumed to be equivalent) • All costs excluded markup and dispensing fees
Clinical Efficacy	• Five phase 3 trials which were part of the clinical development program for EVG/COBI/FTC/TAF (Genvoya) • One phase 3 trial that compared patients on FTC/TDF-based regimens who were randomized to either remain on treatment or were switched to FTC/TAF
Time Horizon	Daily

Results for Base Case	• The manufacturer priced FTC/TAF 200 mg/10 mg and FTC/TAF 200 mg/25 mg at a $0.51 discount per tablet compared with FTC/TDF 200 mg/300 mg, based on the publicly available price for FTC/TDF on the Ontario Drug Benefit formulary.[4] As such, there may be modest cost savings associated with replacing FTC/TDF with FTC/TAF. • Compared with the lowest publicly available price for FTC/TDF identified by CDR (on the Saskatchewan Drug Plan formulary),[14] FTC/TAF-based regimens are $0.87 more costly per day than FTC/TDF-based regimens. • Of the DHHS-recommended regimens, DTG/ABC/3TC is the least costly ($41.38 daily), while RAL + FTC/TDF (or FTC/TAF) is the most expensive regimen ($56.38 daily).

3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ATV = atazanavir; CDR = CADTH Common Drug Review; COBI = cobicistat; DRV = darunavir; DHHS = US Department of Health and Human Services; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; RAL = raltegravir; RNA = ribonucleic acid; RPV = rilpivirine; TAF = tenofovir alafenamide fumarate; TDF = tenofovir disoproxil fumarate.

Manufacturer's Results

The manufacturer conducted a cost comparison analysis for the indicated population (i.e., adolescent and adult patients).[2] As reported below in Table 4, the manufacturer compared the daily cost of recommended and alternative regimens as per the 2015 DHHS guidelines — both with emtricitabine/tenofovir alafenamide fumarate (FTC/TAF) and FTC/tenofovir disoproxil fumarate (TDF) as the backbone drug. As the price of FTC/TAF submitted to the CADTH Common Drug Review (CDR) is slightly lower than the current list price of FTC/TDF on the Ontario Drug Benefit (ODB) formulary, there may be modest cost savings associated with the use of FTC/TAF over FTC/TDF.

TABLE 4: MANUFACTURER'S BASE-CASE ANALYSIS

Regimen	Unit Costs (with FTC/TDF Backbone Where Applicable)	Total Daily Regimen Cost	Unit Costs (with FTC/TAF Backbone Where Applicable)	Total Daily Regimen Cost	Incremental Cost of FTC/TAF-Based Regimens Versus FTC/TDF-Based Regimen
Recommended Regimens					
DTG/ABC/3TC	DTG/ABC/3TC (STR: $41.38)	$41.38	N/A	N/A	N/A
DTG + FTC/TDF	DTG ($18.67) + FTC/TDF ($29.08)	$47.75	DTG ($18.67) + FTC/TAF 200 mg/ 25 mg ($28.57)	$47.24	–$0.51
EVG/COBI/FTC/ TDF	EVG/COBI/FTC/TD F (STR: $46.39)	$46.39	EVG/COBI/FTC/TA F (STR: $46.39)	$46.39	$0
RAL + FTC/TDF	RAL ($27.00) + FTC/TDF ($29.08)	$56.08	RAL ($27.00) + FTC/TAF 200 mg/ 25 mg ($28.57)	$55.57	–$0.51
DRV/r + FTC/TDF	DRV ($21.72) + ritonavir ($1.47) + FTC/TDF ($29.08)	$52.27	DRV ($21.72) + ritonavir ($1.47) + FTC/TAF 200 mg/ 10 mg ($28.57)	$51.76	–$0.51

Regimen	Unit Costs (with FTC/TDF Backbone Where Applicable)	Total Daily Regimen Cost	Unit Costs (with FTC/TAF Backbone Where Applicable)	Total Daily Regimen Cost	Incremental Cost of FTC/TAF-Based Regimens Versus FTC/TDF-Based Regimen
Alternative Regimens[a]					
EFV/FTC/TDF	EFV/FTC/TDF (STR: $43.78)	$43.78	NA	NA	NA
RPV/FTC/TDF	RPV/FTC/TDF (STR: $43.34)	$43.34	NA	NA	NA
ATV/r + FTC/TDF	ATV ($22.71) + ritonavir ($1.47) + FTC/TDF ($29.08)	$53.26	ATV ($22.71) + ritonavir ($1.47) + FTC/TAF 200 mg/ 10 mg ($28.57)	$52.75	–$0.51
DRV/r + ABC/3TC	DRV ($21.72) + ritonavir ($1.47) + ABC/3TC ($23.95)	$47.14	NA	NA	NA

3TC = lamivudine; ABC = abacavir; ATV = atazanavir; ATV/r = ritonavir-boosted atazanavir; COBI = cobicistat; DHHS = US Department of Health and Human Services; DRV = darunavir; DRV/c = cobicistat-boosted darunavir; DRV/r = ritonavir-boosted darunavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; NA = not available; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide fumarate; TDF = tenofovir disoproxil fumarate.
Note: Adapted from the manufacturer's pharmacoeconomic submission.[2]
[a] The manufacturer indicated in its submission that although DRV/c is listed as an alternative regimen in the DHHS guidelines, it was not included in the analysis, as it is not reimbursed by any public drug plans.

CADTH Common Drug Review Results

CDR conducted a comparison of FTC/TAF-based regimens with all US Department of Health and Human Services (DHSS)–recommended and alternative regimens. As the price of FTC/TAF submitted to CDR is slightly lower than the current list price of FTC/TDF on the ODB formulary, there may be modest cost savings associated with the use of FTC/TAF over FTC/TDF. However, as reported in Table 5, TDF- or TAF-containing regimens are not the lowest-cost regimens available. Of the recommended regimens, DTG/ABC/3TC is the least costly ($41.38 daily), while RAL + FTC/TDF or (RAL + FTC/TAF) is the most expensive regimen ($56.89 daily). Of the alternative regimens, the single-tablet regimen RPV/FTC/TDF is the least costly ($43.34 daily), while ATV/r + FTC/TDF (or ATV/r + FTC/TAF) is the most expensive option ($53.03 daily).

TABLE 5: CADTH COMMON DRUG REVIEW COMPARISON OF DHHS-RECOMMENDED AND ALTERNATIVE REGIMENS

Regimen	Strength	Recommended Use	Daily Cost ($)[4]
Recommended Regimens			
Dolutegravir/abacavir/ Lamivudine (Triumeq)	50 mg/600 mg/300 mg	1 tablet daily	41.38
Dolutegravir (Tivicay) + Emtricitabine/tenofovir disoproxil (Truvada)	50 mg 200 mg/300 mg	50 mg daily 1 tablet daily	47.75

Regimen	Strength	Recommended Use	Daily Cost ($)[4]
Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil (Stribild)	150 mg/150 mg/ 200 mg/300 mg	1 tablet daily	46.39
Raltegravir (Isentress) + Emtricitabine/tenofovir disoproxil (Truvada)	400 mg 200 mg/300 mg	400 mg twice daily 1 tablet daily	56.89
Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide (Genvoya)	150 mg/150 mg/ 200 mg/10 mg	1 tablet daily	46.39
Darunavir (Prezista) with ritonavir (Norvir) + Emtricitabine/tenofovir disoproxil (Truvada)	800 mg 100 mg 200 mg/300 mg	800 mg daily 100 mg 1 tablet daily	52.32
Alternative Regimens			
Efavirenz/tenofovir disoproxil/emtricitabine (Atripla)	600 mg/200 mg/300 mg	1 tablet daily	43.78
Emtricitabine/rilpivirine/tenofovir disoproxil (Complera)	200 mg/25 mg/300 mg	1 tablet daily	43.34
Atazanavir (Reyataz) with ritonavir (Norvir) + Emtricitabine/tenofovir disoproxil (Truvada)	300 mg 100 mg 200 mg/300 mg	300 mg daily 100 mg 1 tablet daily	53.03
Darunavir/cobicistat (Prezcobix) + Abacavir/lamivudine (Kivexa)	800 mg/150 mg 600 mg/300 mg	1 tablet daily 1 tablet daily	47.12
Darunavir (with ritonavir) + Abacavir/lamivudine (Kivexa)	800 mg (100 mg) 600 mg/300 mg	800 mg daily 100 mg 1 tablet daily	47.18
Darunavir/cobicistat (Prezcobix) + Emtricitabine/tenofovir disoproxil (Truvada)	800 mg/150 mg 200 mg/300 mg	1 tablet daily 1 tablet daily	52.25

DHHS = US Department of Health and Human Services.

CDR also conducted an analysis using a lower price for FTC/TDF, determined from the Saskatchewan Drug Benefit formulary ($27.7030 per tablet).[14] As reported in Table 6, when a lower price for FTC/TDF is used, FTC/TAF-based regimens are $0.87 more costly than FTC/TDF-based regimens.

TABLE 6: CADTH COMMON DRUG REVIEW REANALYSIS OF MANUFACTURER'S ANALYSIS, USING A LOWER PRICE FOR FTC/TDF

Regimen	Unit Costs (with FTC/TDF Backbone Where Applicable)	Total Daily Regimen Cost	Unit Costs (with FTC/TAF Backbone Where Applicable)	Total Daily Regimen Cost	Incremental Cost of FTC/TAF-Based Regimens Versus FTC/TDF-Based Regimen
Recommended Regimens					
DTG/ABC/3TC	DTG/ABC/3TC (STR: $41.38)	$41.38	NA	NA	NA
DTG + FTC/TDF	DTG ($18.67) + FTC/TDF ($27.70)	$46.37	DTG ($18.67) + FTC/TAF 200 mg/ 25 mg ($28.57)	$47.24	$0.87
EVG/COBI/FTC/ TDF	EVG/COBI/FTC/TD F (STR: $46.39)	$46.39	EVG/COBI/FTC/TAF (STR: $46.39)	$46.39	$0
RAL + FTC/TDF	RAL ($27.81) + FTC/TDF ($27.70)	$55.51	RAL ($27.81) + FTC/TAF 200 mg/ 25 mg ($28.57)	$56.38	$0.87
DRV/r + FTC/TDF	DRV ($21.72) + ritonavir ($1.52) + FTC/TDF ($27.70)	$50.93	DRV ($21.72) + ritonavir ($1.52) + FTC/TAF 200 mg/ 10 mg ($28.57)	$51.81	$0.87
Alternative Regimens					
EFV/FTC/TDF	EFV/FTC/TDF (STR: $43.78)	$43.78	NA	NA	NA
RPV/FTC/TDF	RPV/FTC/TDF (STR: $43.34)	$43.34	N/A	N/A	NA
ATV/r + FTC/TDF	ATV ($22.43) + ritonavir ($1.52) + FTC/TDF ($27.70)	$51.65	ATV ($22.43) + ritonavir ($1.52) + FTC/TAF 200 mg/ 10 mg ($28.57)	$52.52	$0.87
DRV/r + ABC/3TC	DRV ($21.72) + ritonavir ($1.52) + ABC/3TC ($23.95)	$47.18	NA	NA	NA
DRV/c + FTC/TDF	DRV/c ($23.17) + FTC/TDF ($27.70)	$50.87	DRV/c ($23.17) + FTC/TDF ($28.57)	$51.74	$0.87

3TC = lamivudine; ABC = abacavir; ATV = atazanavir; ATV/r = ritonavir-boosted atazanavir; COBI = cobicistat; DRV = darunavir; DRV/r = ritonavir-boosted darunavir; DRV/c = cobicistat-boosted darunavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; NA = not available; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide fumarate; TDF = tenofovir disoproxil fumarate.

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