# Common Drug Review
## *Pharmacoeconomic Review Report*

**November 2016**

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|---|---|
| **Drug** | Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF) (Genvoya®) fixed-dose combination, oral tablet) |
| **Indication** | As a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and pediatric patients 12 years of age and older (and weighing ≥ 35 kg) and with no known mutations associated with resistance to the individual components of Genvoya |
| **Reimbursement request** | For treatment-naive and virologically suppressed HIV-1 infected adult and pediatric patients 12 years of age and older with no known mutations associated with resistance to the individual components of EVG/COBI/FTC/TAF |
| **Dosage form(s)** | EVG 150 mg/COBI 150 mg/FTC 200 mg/TAF 10 mg |
| **NOC date** | November 27, 2015 |
| **Manufacturer** | Gilead Sciences Canada, Inc. |

This review report was prepared by the Canadian Agency for Drugs and Technologies in Health (CADTH). In addition to CADTH staff, the review team included a clinical expert in the treatment of HIV infection who provided input on the conduct of the review and the interpretation of findings.

Through the CADTH Common Drug Review (CDR) process, CADTH undertakes reviews of drug submissions, resubmissions, and requests for advice, and provides formulary reimbursement recommendations to all Canadian publicly funded federal, provincial, and territorial drug plans, with the exception of Quebec.

The report contains an evidence-based clinical and/or pharmacoeconomic drug review, based on published and unpublished material, including manufacturer submissions; studies identified through independent, systematic literature searches; and patient-group submissions. In accordance with *CDR Update — Issue 87*, manufacturers may request that confidential information be redacted from the CDR Clinical and Pharmacoeconomic Review Reports.

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# ABBREVIATIONS

| | |
|---|---|
| **3TC** | lamivudine |
| **ABC** | abacavir |
| **ART** | antiretroviral therapy |
| **ARV** | antiretroviral |
| **CDR** | CADTH Common Drug Review |
| **COBI** | cobicistat |
| **DHHS** | Department of Health and Human Services |
| **DTG** | dolutegravir |
| **EVG** | elvitegravir |
| **FDC** | fixed-dose combination |
| **FTC** | emtricitabine |
| **HIV-1** | human immunodeficiency virus type 1 |
| **STR** | single-tablet regimen |
| **TAF** | tenofovir alafenamide fumarate |
| **TDF** | tenofovir disoproxil fumarate |

# SUMMARY

## Background

Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide fumarate (EVG/COBI/FTC/TAF) (Genvoya) is a fixed-dose combination (FDC) of integrase strand transfer inhibitor (INSTI) EVG 150 mg, cytochrome P450 inhibitor COBI 150 mg, nucleoside reverse transcriptase inhibitor (NRTI) FTC 200 mg, and NRTI TAF 10 mg. It is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and pediatric patients 12 years of age and older (weighing 35 kg or more), with no known mutations associated with resistance to the individual components.[1] It is available as a film-coated tablet at the recommended dose of one tablet daily.[1] At the manufacturer-submitted confidential price of $[redacted] per tablet,[2] the daily cost of treatment is $[redacted]. The manufacturer's reimbursement request is in line with the indication.

## Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost analysis comparing the drug cost of EVG/COBI/FTC/TAF with recommended antiretroviral (ARV) regimens for treatment-naive patients 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*:[3] dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) (50/600/300 mg daily); DTG (50 mg daily) + tenofovir disoproxil fumarate (TDF)/FTC (200/300 mg daily); EVG/COBI/FTC/TDF FDC (150/150/200/300 mg daily); raltegravir (RAL) (400 mg twice daily) + TDF/FTC (200/300 mg daily); and darunavir (DRV) (800 mg daily) boosted with 100 mg ritonavir + TDF/FTC (200/300 mg daily). Only drug costs were considered, as the manufacturer assumed that other resource use components were equivalent among all ARV regimens. Drug costs were obtained from the Ontario Drug Benefit (ODB) formulary.[4] All prices excluded mark-up and dispensing fees.

The manufacturer's assumption of similar efficacy and safety of EVG/COBI/FTC/TAF and other ARV regimens was based on clinical evidence from five phase 3 clinical trials. The conclusion of non-inferiority for the primary outcome of virological success, defined by the proportion of patients with plasma HIV-1 ribonucleic acid (RNA) of < 50 copies/mL at 48 weeks, was based on 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] and an open-label, active-controlled, non-inferiority trial that compared patients who switched to EVG/COBI/FTC/TAF from a pre-existing regimen (TDF/FTC + a third drug) with those who remained on their pre-existing regimen, in virologically suppressed adults (i.e., treatment-experienced patients) (Study 109).[7] Additional information on efficacy and safety in specific subgroups of patients, including 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.[8,9] Based on the evidence presented, the manufacturer assumed similar efficacy and safety of EVG/COBI/FTC/TAF and other DHHS-recommended ARV regimens.[2]

## Key Limitations

- **Lack of comparative clinical information for EVG/COBI/FTC/TAF versus other ARV regimens in adolescent patients:** There are no head-to-head comparative trials for EVG/COBI/FTC/TAF compared with other ARV regimens, and the manufacturer did not conduct an indirect comparison for adolescent patients. 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 years 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 CADTH Common Drug Review (CDR) clinical expert, 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 EVG/COBI/FTC/TAF in a treatment-experienced adolescent population.

- **Lack of comparative clinical information for EVG/COBI/FTC/TAF versus recommended ARV regimens for initial therapy other than EVG/COBI/FTC/TDF in adult patients:** Three phase 3 non-inferiority trials compared EVG/COBI/FTC/TAF with EVG/COBI/FTC/TDF, two in treatment-naive patients (Studies 104 and 111),[5,6] and one in treatment-experienced patients (Study 109).[7] In Studies 104 and 111, EVG/COBI/FTC/TAF was statistically similar to EVG/COBI/FTC/TDF for the primary outcome of virological success at 48 weeks. In Study 109, patients receiving EVG/COBI/FTC/TAF were shown to have statistically higher rates of virological success at 48 weeks (97.2% of patients) compared with patients that continued therapy on their existing regimen (93.1% of patients). From this evidence, the manufacturer assumed EVG/COBI/FTC/TAF to be clinically equivalent to other recommended ARV regimens included in its analysis. The comparative clinical effectiveness and safety of EVG/COBI/FTC/TAF and DHHS-recommended ARV regimens for initial therapy other than EVG/COBI/FTC/TDF in adult patients, and thus, comparative cost-effectiveness, is unknown. This includes the single-tablet regimen (STR) DTG/ABC/3TC.
- **Analysis for the adolescent population:** The manufacturer did not conduct a separate cost analysis for adolescent patients (12 years to 18 years), but only adult (18 years of age and older) patients. Some differences exist between the regimens used to treat adolescents and adults. As noted by the CDR clinical expert, adolescents are often treated with select STRs such as DTG/ABC/3TC (Triumeq), efavirenz (EFV)/TDF/FTC (Atripla), and FTC/RPV/TDF (Complera). CDR compared the costs of EVG/COBI/FTC/TAF versus these regimens (Table 7).

## Issues for Consideration

- EVG/COBI/FTC/TAF is the first STR to be indicated for an adolescent population in Canada. However, as noted earlier, select STRs are often used off-label. The choice of antiretroviral therapy (ART) depends on a number of factors, including the age and weight of the patient.
- There is variability in the price of ARTs across CDR-participating drug plans. This affects the cost differential versus EVG/COBI/FTC/TAF and may result in EVG/COBI/FTC/TAF being more expensive.
- Of note, FDC FTC/TAF is currently under review at Health Canada and likely to be available in 2016.
- While the availability of regimens in co-formulated FDCs offers benefits to patients in terms of convenience and potentially adherence, it presents challenges to generic entrants as individual drug patents expire.
- EVG/COBI/FTC/TAF will be added as one of the recommended initial regimens for ART-naive adults and adolescents in a subsequent update of the DHHS guidelines.[10]
- 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, information on comparative harms was provided only for EVG/COBI/FTC/TAF and EVG/COBI/FTC/TDF; how EVG/COBI/FTC/TAF compares with other ARV regimens was not considered. As EVG/COBI/FTC/TAF is an STR, adherence is likely to be similar to other STRs.

## Results and Conclusions

With the exception of EVG/COBI/FTC/TDF in the adult population, the comparative cost-effectiveness of EVG/COBI/FTC/TAF versus ARV regimens cannot be assessed due to the lack of comparative clinical studies or a well-conducted indirect comparison, in both the adolescent and adult patient populations (in the initial therapy setting).

At a confidential daily cost of $[redacted], EVG/COBI/FTC/TAF is similar in costs or less expensive than other ARV regimens most often used in the treatment of HIV-1 infection in adolescent patients (daily cost ranging from $41.38 to $43.78 for other STRs) and adult patients (daily cost ranging from $41.38 to $55.57 for DHHS-recommended regimens).

# APPENDIX 1: COST COMPARISON

The comparators presented in the following tables are based on the recommended and alternative regimen options for treatment-naive patients in the US Department of Health and Human Services (DHHS) guidelines for the use of antiretroviral (ARV) drugs in human immunodeficiency virus type 1 (HIV-1)-infected adolescents and adults (2015),[3] and have been confirmed by the clinical expert. The guidelines do not make specific recommendations for treatment-experienced patients; however, as noted by the clinical expert, these drugs are most often used in treatment-experienced patients as well.

Costs in Table 1, Table 2, and Table 3 are manufacturer list prices, unless otherwise specified. Existing product listing agreements are not reflected in the table and as such may not represent the actual costs to public drug plans.

**TABLE 1: COST COMPARISON TABLE FOR HIV ANTIRETROVIRAL DRUGS IN TREATMENT-NAIVE ADULT PATIENTS — RECOMMENDED REGIMENS**

| Drug/Comparator | Strength | Dosage Form | Price ($) | Recommended Use | Daily Cost ($) | Freq. of Use (/day) | No. of Pills (/day) |
|---|---|---|---|---|---|---|---|
| **Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya)[a]** | **150/150/200/10 mg** | **Tab** | [redacted][b] | **1 tablet daily** | [redacted] | **1** | **1** |
| **Recommended Antiretroviral Regimen Options** | | | | | | | |
| **INSTI-based** | | | | | | | |
| Dolutegravir/abacavir/ lamivudine (Triumeq) | 50/600/300 mg | Tab | 41.3834 | 1 tablet daily | 41.38 | 1 | 1 |
| Dolutegravir (Tivicay)<br>+<br>Emtricitabine/tenofovir disoproxil (Truvada) | 50 mg<br><br>200/300 mg | Tab | 18.6665<br><br>28.5710 | 50 mg daily<br><br>1 tablet daily | 47.24 | 1 | 2 |
| Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil (Stribild) | 150/150/200/300 mg | Tab | 46.3894 | 1 tablet daily | 46.39 | 1 | 1 |
| Raltegravir (Isentress)<br>+<br>Emtricitabine/tenofovir disoproxil (Truvada) | 400 mg<br><br>200/300 mg | Tab | 13.5000<br><br>28.5710 | 400 mg twice daily<br>1 tablet daily | 55.57 | 2 | 3 |

| Drug/Comparator | Strength | Dosage Form | Price ($) | Recommended Use | Daily Cost ($) | Freq. of Use (/day) | No. of Pills (/day) |
|---|---|---|---|---|---|---|---|
| **Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya)[a]** | **150/150/200/10 mg** | **Tab** | [redacted][b] | **1 tablet daily** | [redacted] | **1** | **1** |
| **PI-based** | | | | | | | |
| Darunavir (Prezista)<br>with ritonavir (Norvir)<br>+<br>Emtricitabine/tenofovir disoproxil (Truvada) | 800 mg<br>100 mg<br><br>200/300 mg | Tab | 21.7160<br>1.4671<br><br>28.5710 | 800 mg daily<br>100 mg<br><br>1 tablet daily | 51.75 | 1 | 3 |

ART = antiretroviral therapy; ARV = antiretroviral; COBI = cobicistat; DHHS = Department of Health and Human Services; EVG = elvitegravir; Freq. = frequency; FTC = emtricitabine; HIV = human immunodeficiency virus; HIV-1 = human immunodeficiency virus type 1; INSTI = integrase strand transfer inhibitors; ODB = Ontario Drug Benefit; PI = protease inhibitor; Tab = tablet; TAF = tenofovir alafenamide fumarate.

[a] While not currently included, EVG/COBI/FTC/TAF will be added as one of the recommended initial regimens for ART-naive adults and adolescents in a subsequent update of the DHHS guidelines.[10]

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

Note: Based on the US DHHS guidelines for the use of ARV drugs in HIV-1-infected adults and adolescents (2015 update).[3] All prices are from the ODB formulary (accessed January 2016),[4] unless otherwise indicated.

### TABLE 2: COST COMPARISON TABLE FOR HIV ANTIRETROVIRAL DRUGS IN TREATMENT-NAIVE ADULT PATIENTS — ALTERNATIVE REGIMENS

| Drug/Comparator | Strength | Dosage Form | Price ($) | Recommended Use | Daily Cost ($) | Freq. of Use (/day) | No. of Pills (/day) |
|---|---|---|---|---|---|---|---|
| **Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya)[a]** | **150/150/200/10 mg** | **Tab** | [redacted][b] | **1 tablet daily** | [redacted] | **1** | **1** |
| **Alternative Antiretroviral Regimen Options** | | | | | | | |
| *NNRTI-based* | | | | | | | |
| Efavirenz/tenofovir disoproxil/ emtricitabine (Atripla) | 600/200/300 mg | Tab | 43.7833 | 1 tablet daily | 43.78 | 1 | 1 |
| Emtricitabine/rilpivirine/ tenofovir disoproxil (Complera) | 200/25/300 mg | Tab | 43.3428 | 1 tablet daily | 43.34 | 1 | 1 |

| Drug/Comparator | Strength | Dosage Form | Price ($) | Recommended Use | Daily Cost ($) | Freq. of Use (/day) | No. of Pills (/day) |
|---|---|---|---|---|---|---|---|
| **Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya)[a]** | **150/150/200/10 mg** | **Tab** | **[redacted][b]** | **1 tablet daily** | **[redacted]** | **1** | **1** |
| *PI-based* | | | | | | | |
| Atazanavir (Reyataz)<br>with ritonavir (Norvir)<br>+<br>Emtricitabine/tenofovir disoproxil (Truvada) | 300 mg<br>100 mg<br><br>200/300 mg | Cap | 22.4330[c]<br>1.4671<br><br>28.5710 | 300 mg daily<br>100 mg<br><br>1 tablet daily | 52.47 | 1 | 3 |
| Darunavir/cobicistat (Prezcobix)<br>+<br>Abacavir/lamivudine (Kivexa) | 800/150 mg<br><br>600/300 mg | Tab | 23.1720[d]<br><br>23.9498 | 1 tablet daily<br><br>1 tablet daily | 47.12 | 1 | 2 |
| Darunavir<br>(with ritonavir)<br>+<br>Abacavir/lamivudine (Kivexa) | 800 mg<br>(100 mg)<br><br>600/300 mg | Tab | 21.7160<br>1.4671<br><br>23.9498 | 800 mg daily<br>100 mg<br><br>1 tablet daily | 47.13 | 1 | 3 |
| Darunavir/cobicistat (Prezcobix)<br>+<br>Emtricitabine/tenofovir disoproxil (Truvada) | 800/150 mg<br><br>200/300 mg | Tab | 23.1720[d]<br><br>28.5710 | 1 tablet daily<br><br>1 tablet daily | 51.74 | 1 | 2 |

ART = antiretroviral therapy; ARV = antiretroviral; Cap = capsule; CDR = CADTH Common Drug Review; COBI = cobicistat; DHHS = Department of Health and Human Services; EVG = elvitegravir; Freq. = frequency; FTC = emtricitabine; HIV = human immunodeficiency virus; HIV-1 = human immunodeficiency virus type 1; INSTI = integrase strand transfer inhibitors; NNRTI = non-nucleoside reverse transcriptase inhibitors; ODB = Ontario Drug Benefit; PI = protease inhibitor; Tab = tablet; TAF = tenofovir alafenamide fumarate.

[a] While not currently included, EVG/COBI/FTC/TAF will be added as one of the recommended initial regimens for ART-naive adults and adolescents in a subsequent update of the DHHS guidelines.[10]

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

[c] Saskatchewan Drug Benefit Formulary (accessed January 2016).[11]

[d] Price submitted to CDR, non-confidential.[12] Not available on any public drug plans.

Note: Based on the US DHHS guidelines for the use of ARV drugs in HIV-1-infected adults and adolescents (2015 update).[3] All prices are from the ODB formulary (accessed January 2016),[4] unless otherwise indicated.

The comparators presented in Table 3 are based on the recommended regimens for initial therapy for HIV infection in children in the US DHHS guidelines for the use of ARV drugs in pediatric HIV-1 infection (2015).[13] Patients 12 years to 18 years of age may be prescribed treatment regimens based on the pediatric guidelines included here or the guidelines for adolescents and adult patients[3] (included in the preceding table).

**TABLE 3: COST COMPARISON TABLE FOR HIV ANTIRETROVIRAL DRUGS IN ADOLESCENT PATIENTS (12 YEARS TO 18 YEARS OF AGE)**

| Drug/Comparator | Strength | Dosage Form | Price ($) | Recommended Use | Daily Cost ($) | Freq. of Use (/day) | No. Of Pills (/day) |
|---|---|---|---|---|---|---|---|
| **Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya)[a]** | **150/150/200/10 mg** | **Tab** | [redacted][b] | **1 tablet daily** | [redacted] | **1** | **1** |
| **Preferred Antiretroviral Regimen Options[c]** | | | | | | | |
| Atazanavir (Reyataz)<br>with ritonavir (Norvir)<br>+<br>Abacavir/lamivudine (Kivexa) | 300 mg<br>100 mg<br><br>600/300 mg | Cap<br><br><br>Tab | 22.4330[d]<br>1.4671<br><br>23.9498 | 300 mg daily[e]<br>100 mg daily<br><br>1 tablet daily | 47.85 | 1 | 3 |
| Efavirenz (Generics)<br>+<br>Abacavir/lamivudine (Kivexa) | 600 mg<br><br>600/300 mg | Tab | 3.8030<br><br>23.9498 | 600 mg daily[e]<br><br>1 tablet daily | 27.75 | 1 | 2 |
| Lopinavir<br>(with ritonavir) (Kaletra)<br>+<br>Abacavir/lamivudine (Kivexa) | 100/25 mg<br>200/50 mg<br><br><br>600/300 mg | Tab | 2.7598<br>5.5197<br><br><br>23.9498 | 4 tablets (100/25 mg)<br>or 2 tablets (200/50 mg) twice daily<br>1 tablet daily | 46.03 | 2 | 5-9 |
| **Alternative Antiretroviral Regimen Options[c]** | | | | | | | |
| Dolutegravir (Tivicay)<br>+<br>Abacavir/lamivudine | 50 mg<br><br>600/300 mg | Tab | 18.6665<br><br>23.9498 | 50 mg daily[e]<br><br>1 tablet daily | 42.62 | 1 | 2 |

| Drug/Comparator | Strength | Dosage Form | Price ($) | Recommended Use | Daily Cost ($) | Freq. of Use (/day) | No. Of Pills (/day) |
|---|---|---|---|---|---|---|---|
| (Kivexa) | | | | | | | |

ART = antiretroviral therapy; ARV = antiretroviral; CDR = CADTH Common Drug Review; COBI = cobicistat; DHHS = Department of Health and Human Services; EVG = elvitegravir; Freq. = frequency; FTC = emtricitabine; HIV = human immunodeficiency virus; INSTI = integrase strand transfer inhibitors; NRTIs = nucleoside reverse transcriptase inhibitors; ODB = Ontario Drug Benefit; TAF = tenofovir alafenamide fumarate.

[a] While not currently included, EVG/COBI/FTC/TAF will be added as one of the recommended initial regimens for ART-naive adults and adolescents in a subsequent update of the DHHS guidelines.[10]

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

[c] US DHHS guidelines for the use of ARV drugs in pediatric HIV infection recommend the use of 2 NRTIs + a third drug. As noted in the CDR clinical review report, among children aged 12 years and older, this would likely be abacavir + lamivudine or abacavir + emtricitabine; however, emtricitabine is not indicated for patients under the age of 18 years.

[d] Saskatchewan Drug Benefit Formulary (accessed January 2016).[11]

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

Note: Based on the US DHHS guidelines for the use of ARV drugs in pediatric HIV infection (2015 update).[13] All prices are from the ODB formulary (accessed January 2016),[4] unless otherwise indicated.

# APPENDIX 2: REVIEWER WORKSHEETS

**TABLE 4: SUMMARY OF MANUFACTURER'S SUBMISSION**

| | |
|---|---|
| **Drug Product** | Genvoya (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/tenofovir alafenamide fumarate 10 mg, FDC product) |
| **Treatment** | EVG/COBI/FTC/TAF 150/150/200/10 mg taken once daily with food |
| **Comparators** | Recommended regimens based on US DHHS.[3]<br>INSTI-based regimens:<br>• DTG/ABC/3TC 50/600/300 mg (Triumeq) daily<br>• DTG 50 mg daily + TDF/FTC 200/300 mg daily<br>• EVG/COBI/FTC/TDF 150/150/200/300 mg (Stribild) daily<br>• RAL 400 mg twice daily + TDF/FTC 200/300 mg daily<br>PI-based regimens:<br>• DRV 800 mg daily boosted with ritonavir 100 mg + TDF/FTC 200/300 mg daily |
| **Study Question** | "To conduct a cost-minimization analysis of EVG/COBI/FTC/TAF 150 mg/150 mg/200 mg/10 mg versus appropriate comparators, over a one-day horizon and from a government perspective, in patients with HIV-1 infection." |
| **Type of Economic Evaluation** | Cost comparison (drugs costs only) |
| **Target Population** | Patients with HIV-1 infection |
| **Perspective** | Health care system |
| **Outcomes Considered** | Virological success, defined by the proportion of patient with plasma HIV-1 RNA < 50 copies/mL at 24 and 48 weeks |
| **Key Data Sources** | |
| **Cost** | • Cost of EVG/COBI/FTC/TAF from the manufacturer<br>• Cost of other ARTs obtained from the Ontario Drug Benefit[4]<br>• Health care resource use and those associated with adverse events were not included<br>• All costs excluded mark-up and dispensing fees |
| **Clinical Efficacy** | Based on five phase 3 clinical trials:<br>• Three active-controlled (two double-blind, one open-label) non-inferiority trials[5-7]<br>• Two open-label cohort studies[8,9] |
| **Harms** | Based on same studies noted earlier |
| **Time Horizon** | Daily |
| **Results for Base Case** | The daily cost of EVG/COBI/FTC/TAF ($[redacted]) was calculated to be [redacted] to the daily cost of DTG/ABC/3TC ($41.38) and less costly than the other recommended regimens, including EVG/COBI/FTC/TDF, with cost savings ranging from $[redacted] to $[redacted] daily. |
| **Results from the Sensitivity Analysis** | The manufacturer conducted an alternate analysis where they considered comparators deemed alternative regimens in the US DHHS guidelines. These included:<br>• EFV/TDF/FTC 600/300/200 mg q.d. (Atripla)<br>• FTC/RPV/TDF 200/25/300 mg q.d. (Complera)<br>• ATV 300 mg boosted with ritonavir 100 mg + TDF/FTC 200/300 mg q.d.<br>• DRV 800 mg boosted with ritonavir 100 mg + ABC/3TC 600/300 mg q.d. |

| | |
|---|---|
| [redacted] | The daily cost of EVG/COBI/FTC/TAF is less costly than all alternative regimens, with cost savings ranging from $[redacted] to $[redacted] daily. |

3TC = lamivudine; ABC = abacavir; ARTs = antiretroviral therapies; ATV = atazanavir; COBI = cobicistat; DHHS = Department of Health and Human Services; DRV = darunavir; DTG = dolutegravir; EVF = efavirenz; EVG = elvitegravir; FDC = fixed-dose combination; FTC = emtricitabine; HIV-1 = human immunodeficiency virus type 1; INSTI = integrase strand transfer inhibitor; PI = protease inhibitor; q.d. = once daily; RAL = raltegravir; RNA = ribonucleic acid; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide fumarate; TDF = tenofovir disoproxil fumarate.

[a] TDF/FTC + a third drug included the following: EVG/COBI/FTC/TDF, EFV/FTC/TDF, ATV/co + FTC/TDF and ATV/r + TDF.

## Manufacturer's Results

The manufacturer conducted a cost comparison analysis for the full population (i.e., adolescent and adult patients). As reported in Table 5, the daily cost of EVG/COBI/FTC/TAF ($[redacted]) is [redacted] to the daily cost of DTG/ABC/3TC. Moreover, it is less costly than similar ARV regimen, STR EVG/COBI/FTC/TDF, with cost savings of $[redacted] per day, as well as other recommended ARV regimens (DTG + FTC/TDF; RAL + FTC/TDF; and DRV + FTC/TDF), with cost savings ranging from $[redacted] to $[redacted] per day.

**TABLE 5: MANUFACTURER'S BASE-CASE ANALYSIS RESULTS**

| Regimen | Strength | Price ($) | Recommended Use | Daily Cost ($) | Incremental Costs ($) |
|---|---|---|---|---|---|
| Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya) | 150/150/200/10 mg | [redacted] | 1 tablet daily | [redacted] | Reference |
| **Recommended Antiretroviral Regimens** | | | | | |
| Dolutegravir/abacavir/ lamivudine | 50 mg/600/300 mg | 41.38 | 1 tablet daily | 41.38 | [redacted] |
| Dolutegravir<br>+<br>Emtricitabine/tenofovir disoproxil | 50 mg<br><br>200/300 mg | 18.67<br><br>28.57 | 50 mg daily<br><br>1 tablet daily | 47.24 | [redacted] |
| Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil | 150/150/200/300 mg | 46.39 | 1 tablet daily | 46.39 | [redacted] |
| Raltegravir<br>+<br>Emtricitabine/tenofovir disoproxil | 400 mg<br><br>200/300 mg | 13.50<br><br>28.57 | 400 mg twice daily<br><br>1 tablet daily | 55.57 | [redacted] |
| Darunavir<br>with ritonavir<br>+<br>Emtricitabine/tenofovir disoproxil | 800 mg once<br>100 mg<br><br>200/300 mg | 21.72<br>1.47<br><br>28.57 | 800 mg daily<br>100 mg<br><br>1 tablet daily | 51.76 | [redacted] |

Note: Adapted from the manufacturer's pharmacoeconomic submission.[2]

As reported in Table 6, the daily cost of EVG/COBI/FTC/TAF ($[redacted]) is less costly than alternative ARV regimens (costs savings ranging from $[redacted]-$[redacted]).

**TABLE 6: MANUFACTURER'S SENSITIVITY (ALTERNATE) ANALYSIS RESULTS**

| Regimen | Strength | Price ($) | Recommended Use | Daily Cost ($) | Incremental Costs ($) for Comparator |
|---|---|---|---|---|---|
| Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya) | 150/150/200/10 mg | [redacted] | 1 tablet daily | [redacted] | Reference |
| **Alternative Antiretroviral Regimens** | | | | | |
| Efavirenz/tenofovir disoproxil/ emtricitabine | 600/300/200 mg | 43.78 | 1 tablet daily | 43.78 | [redacted] |
| Emtricitabine/rilpivirine/ tenofovir disoproxil | 200/25/300 mg | 43.34 | 1 tablet daily | 43.34 | [redacted] |
| Atazanavir<br>with ritonavir<br>+<br>Emtricitabine/tenofovir disoproxil | 300 mg<br>100 mg<br><br>200/300 mg | 22.71<br>1.47<br><br>28.57 | 300 mg daily<br>100 mg<br><br>1 tablet daily | 52.75 | [redacted] |
| Darunavir<br>with ritonavir<br>+<br>Abacavir/lamivudine | 800 mg<br>100 mg<br><br>600/300 mg | 21.72<br>1.47<br><br>23.95 | 800 mg daily<br>100 mg<br><br>1 tablet daily | 47.13 | [redacted] |

Adapted from the manufacturer's pharmacoeconomic submission.[2]

## CADTH Common Drug Review Assessment and Results

CADTH Common Drug Review (CDR) identified no concerns with the manufacturer's base-case cost comparison for the adult population.

CDR considered the adolescent population separately given potential differences in the ARV regimens used. CDR compared EVG/COBI/FTC/TAF to other ARV regimens, reported as daily cost per patient (Table 7). Patients aged 12 years to 18 years may be prescribed ARV regimens based on the pediatric guidelines,[13] or may be treated with STRs. The three STRs included here are used most often in adolescent patients in clinical practice, based on clinical expert opinion. The daily cost of STR EVG/COBI/FTC/TAF is [redacted] to the daily cost of STR DTG/ABC/3TC and is less costly than STRs EFV/TDF/FTC and FTC/RPV/TDF, with cost savings ranging from $[redacted] to $[redacted] per day.

**TABLE 7: CADTH COMMON DRUG REVIEW COST COMPARISON ANALYSIS IN ADOLESCENT PATIENTS**

| Regimen | Strength | Recommended Use | Daily Cost ($) | Incremental Cost ($) for Comparator |
|---|---|---|---|---|
| **Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide fumarate (Genvoya)** | **150/150/200/10 mg** | **1 tablet daily** | [redacted] | **Reference** |
| **Other ARV regimens**[a] | | | | |
| Dolutegravir/abacavir/ lamivudine (Triumeq) | 50/600/300 mg | 1 tablet daily | 41.38 | [redacted] |
| Efavirenz/tenofovir disoproxil/ emtricitabine (Atripla) | 600/200/300 mg | 1 tablet daily | 43.78 | [redacted] |
| Emtricitabine/rilpivirine/tenofovir disoproxil (Complera) | 200/25/300 mg | 1 tablet daily | 43.34 | [redacted] |

ARV = antiretroviral.

[a] None of these drugs are indicated for use in patients under the age of 18 years. However, as noted in the issues for consideration, these drugs are used in adolescent patients in clinical practice (off-label).

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