Maine Seal

Quarterly Report

HIV/AIDS 1115 Demonstration Project

SFY 2017 Quarter 4

DY 15 Quarter 4

(10/1/17 – 12/31/17)

Department of Health and Human Services
Maine People Living
Safe, Healthy and Productive Lives

Paul R. LePage, Governor Ricker Hamilton, Commissioner

Department of Health and Human Services
MaineCare Services
Nurse Coordinator
11 State House Station
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Tel.: (207) 624-4008; Fax: (207) 287-8601
Toll Free (866) 796-2463; TTY Users: Dial 711 (Maine

Maine Seal

February 28, 2018

Emmett Ruff
Division of State Demonstrations and Waivers
Center for Medicaid and CHIP Services, CMS
Mail Stop S2-01-26
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Mr. Ruff,

Please find enclosed, the quarterly report for the Maine HIV/AIDS Section 1115 Demonstration Waiver for the quarter ending 12/31/2017. Please contact Emily Bean at (207) 624-4005 or emily.bean@maine.gov if further information is needed.

Sincerely,

[redacted]

Stefanie Nadeau, Director
Office of MaineCare Services
11 State House Station, Augusta, ME 04333-0011
Phone: 207-287-2093

Maine HIV/AIDS Demonstration

Section 1115 Quarterly Report

Demonstration Year: 15 (01/01/2017 - 12/31/2017)

Demonstration Quarter: 4 (10/01/2017 - 12/31/2017)

Maine Fiscal Quarter: 1/2018 (10/01/2017 – 12/31/2017)

Federal Fiscal Year (FFY) 18: (10/01/17 – 09/30/18)

Introduction

The MaineCare HIV/AIDS 1115 Demonstration project has completed the fourth quarter of its fifteenth year. This demonstration was implemented on July 1, 2002 and has been approved through December 31, 2018. The demonstration's goal is to provide critical services to people living with HIV/AIDS to delay, prevent, or reverse the progress of their disease.

Enrollment Information

During the fourth quarter of the fifteenth year, there were 789 MaineCare and demonstration members enrolled in the demonstration project.

Enrollment Counts

There were 468 demonstration enrollees included in the quarter. These members qualified by having a diagnosis of HIV/AIDS and income at, or below, 250% of the Federal Poverty Level (FPL). There were 330 Medicaid members included in the quarter. Medicaid members are identified as either the original cohort of members who are receiving MaineCare, or MaineCare members where 25% or more of their Medicaid claims are HIV-related.

Demonstration Populations (as hard coded in the CMS-64)	Count of members enrolled at Start of Quarter	Count of members enrolled During the Quarter	Number of Persons Disenrolled during Quarter for non-payment of premiums*	Number of Persons Disenrolled during the Quarter**	Number of Members who Changed FPL	Members who Switched Rate Codes	Count of members enrolled at End of Quarter
Enrollees at or below 100% FPL - Demonstration Enrollees	162	32	N/A	31	34	7	163
Enrollees above 100% FPL - Demonstration Enrollees	287	23	0	31	32	1	279
Members HIV Positive and MaineCare Eligible	311	28	N/A	24	N/A	2	315
Totals	760	229	0	86	66	10	757

Note: The numbers in the above chart come from different data sources; therefore, they may not reflect accurate enrollment counts, as they are based on FPL.

*Enrollees who fail to pay premiums within the 60-day grace period could lose coverage until premiums are paid. If the coverage is reinstated with no lapse, they will not be considered "disenrolled." (Example: a member has unpaid premiums and their coverage is closed on July 31st. On August 8th, the balance is received and the member is reopened with an August 1st start date. Since the coverage was retroactively opened, they would not be counted as disenrolled).

**Reasons an individual disenrolls could include: moving out of state, going over income, becoming deceased.

Outreach/Innovative Activities

Outreach is ongoing. Methods used for outreach during this period included:

- The Nurse Coordinator making calls to members who had not been contacted in six (6) months or more (see enclosure 5).

- Referring more members to Consumers for Affordable Health Care to help with their unmet healthcare needs/coverage.

- Sending an FDA medication alert to primary care providers regarding Genvoya, Odefsey, Epivir, Norvir, and Descovy. Letters were sent via mail and email, depending on provider preference (see Attachment A: Outreach). Alerts were sent to approximately 360 providers.

- Sending a follow up clinical data collection letter to seven (7) providers who didn't respond to the first mailing. This mailing goes to the providers with members for whom MaineCare Services needs CD4 and viral load data (because we were unable to get recent results from the CDC).

- The Program Manager and Nurse attending the Annual Infectious Disease conference. The first keynote speaker was William Wolfgang from the New York State Department of Health and his topic title was "Whole Genome Sequencing – How It's Changing Clinical Practice." Maroya Walters PhD, ScM, topic of discussion was "Emerging Pathogens." Here were three breakout sessions and the first one was titled "Advancements in HIV Testing Technologies & Interpretation of Lab Reports," by Philip Chan, MD. The second breakout session's topic was "HIV Preexposure Prophylaxis and Treatment as Prevention." The last session was titled "Tick-Borne Disease" by Paige Armstrong, MD, MHS, LCDR.

- The Nurse Coordinator attending a three-part webinar titled "Improving Opioid Prescribing and Patient Safety" with keynote speakers Elisabeth Fowlie Mock, MD and Noah Nesin, MD. Speakers discussed different ways providers can improve with opioid prescribing. This includes supporting prevention efforts, appropriately

diagnosing addiction, establishing goals for pain and function, and careful assessment of the risks and benefits of opioid use. The speakers discussed the Center for Disease Control and Prevention's opioid prescribing guidelines and addressed Chapter 488 Public Law: An Act to Prevent Opiate Abuse by Strengthening the Controlled Substances Prescription Monitoring Program.

- Sending the program's poster and brochures to 154 high schools and universities.

- Sending an educational letter and materials to providers who indicated on their annual provider survey that they had specific areas of unfamiliarity (see attachment A: Outreach). This mailing went to 80 providers who are currently treating our enrolled members.

Operational/Policy Development/Issues

Co-payments and premiums (for waiver enrollees)

Waiver enrollees pay all of the regular Medicaid co-payments except for:

- Physician visit: co-pay is $10.00
- Prescription drugs: co-pay is $10.00/30-day supply for generic medications

- The Maine ADAP pays deductibles, premiums, and co-pays (for medications on the ADAP's formulary). This coverage wraps around MaineCare, Medicare Part D, and private insurance. The ADAP covers medications to treat: HIV, mental illness, high blood pressure, high cholesterol, hepatitis, diabetes, thyroid disease, heartburn, nausea, diarrhea, antibiotics, contraceptives, estrogen, and vaccines. The full ADAP formulary can be found at: http://www.maine.gov/dhhs/mecdc/infectious-disease/hiv-std/provider/documents/adap-quarterly-formulary.pdf.
- The ADAP assists with co-pays in the following way:

- The ADAP pays 100% of the co-pay (for formulary medications) for members with MaineCare (up to $10 per 30-day supply).
- The ADAP pays 100% of the co-pay (for formulary medications) for members with MaineCare and Medicare Part D (up to $5 per 30-day supply as this is the maximum co-pay amount).

- Enrollees with an individual income of 150% of the FPL or higher are required to pay a monthly premium to receive services under the waiver. If a member submits their premium bill to the ADAP, the program will assist them with these payments. The premium amounts are as follows:

INCOME LEVEL	MONTHLY PREMIUM
Equal to, or less than, 150% of Federal Poverty Level	0
150.1% - 200% of Federal Poverty Level	$34.22
200.01% - 250% of Federal Poverty Level	$68.43

*Note: premiums are inflated by five percent (5%) annually

Financial/Budget Neutrality Development/Issues

Member numbers are based on distinct member paid claims of actual participation (refer to enclosure 3), as compared to the enrollment data that is based on member eligibility. Consequently, the number of members calculated in the financial shell does not match exactly to the number of members enrolled.

The figures reported in enclosures 1 and 2 (“Budget Neutrality” and “Overall Service Costs by Demonstration Year,” respectively) come from the Medicaid Program Budget and Expenditure System (MBES): “CMS 64 Schedule C Report for 1115 Waivers.” The data from previous quarters is updated in each enclosure with approved adjustments. ADAP funds spent on MaineCare clients for this quarter can be seen in enclosure 4.

Member Month Reporting

Eligibility Group by Month	October 2017	November 2017	December 2017	Total for Quarter Ending 12/2017
Enrollees	449	445	442	1,336
Members	311	311	314	936

Eligibility Group by Disease Stage	1 - ASX (asymptomatic)	2 - SX (symptomatic)	3 – AIDS	Total for Quarter Ending 12/17
Enrollees	986	270	80	1,336
Members	599	251	86	936

Consumer Issues

The MaineCare Member Services help desk is the first point of contact for all MaineCare members, including those living with HIV/AIDS. Based on our monthly reports from Member Services, there were no complaints this quarter.

There were three complaints received directly by the MaineCare Program Manager and/or Nurse Coordinator.

Type	Contact Note	Resolution
Incoming	Member called to report that he is unhappy with one of the State's transportation brokers because, on separate occasions, the drivers have arrived very early to pick him up, or have been late for the ride home.	Nurse Coordinator sent the member complaint to the transportation unit at MaineCare. This unit outreached directly with the broker and discovered the broker had already addressed and responded to the issue. It was determined the broker was within their pickup windows.

Incoming	Member reported not being happy with his case manager (CM). He stated that it seemed like his case manager didn't want to help him. Member needed an eye exam and frames. He got mixed messages about possible assistance for these services. Member felt as though case manager was putting up roadblocks.	Nurse Coordinator recommended that member ask for a different case manager. Member said he may do this if the time comes that he needs CM services again.
Outgoing	Member got a new CM and she wasn't happy with her because she didn't have all her information and couldn't find it. Member's therapist ended up contacting Frannie Peabody Center (FPC) and finally the on-call CM found her info. Member doesn't feel she wants to go back to FPC.	Nurse Coordinator suggested to member that when she is ready, she can look elsewhere for CM services. Nurse Coordinator to follow up with member in a few months.

Quality Assurance/Monitoring Activity

- Quality indicators continue to be monitored through claims data. These indicators include cost data, number and appropriateness of anti-retroviral medications, hospitalization, physician and ED utilization rates, death rates, compliance with guidelines on prophylactic medications for opportunistic infections, ophthalmology exams, and pap smear exams, including visits to provider offices.

- One of the waiver's primary roles is to establish a close link with provider offices in order to obtain disease progression data, including CD4 and viral load results that will allow tracking of disease state progression and targeted interventions.

- An adherence report was designed based on our members' prescription pick-up dates. A link has been established between CD4 data and the adherence report to help target interventions. Based on this report, daily calls are made to members to remind them about their prescription pick-up dates. We project that this proactive

approach will improve our members' compliance with their anti-retroviral medication. There were 291 adherence calls during the quarter (refer to enclosure 5).

- Member compliance with anti-retroviral medication continues to be tracked via their prescription refills. A link has been established between CD4 data and the compliance report to help target interventions. There are three phases of calls. The first phase is of the greatest concern, where calls are made to members whose CD4 counts are below 200 and they are late picking up their medications. In the second phase, calls are made to members whose CD4 counts are between 200 and 350 and they are late picking up their medications. In the third phase, calls are made to members whose CD4 counts are above 350 and they are late picking up their medications. There were 57 compliance calls during the quarter (refer to enclosure 5).

- Frequent address changes and disconnected phones for this population continue to make it difficult to contact members for adherence and compliance interventions. Ongoing efforts continue by contacting the regional Offices for Family Independence (OFI), case managers, pharmacies, and providers for members' most updated addresses and phone numbers.

- A contact tracking system which includes calls, letters, emails, faxes, complaints, and grievances has been underway since February 6, 2003, with daily data entry by the Nurse Coordinator and Program Coordinator. This system allows us to note the number of calls per day, week, month, and year, and gives us a detailed map of calls by contact entity and reason.

- A total of 1,567 contacts were made in this quarter. Calls were the most common mode of communication, accounting for 89% of incoming contacts and 80% of outgoing contacts. Emails were the next most common; 10% and 15%, respectively

(refer to enclosure 6).

- Eligibility was the most common reason for contacts being made, accounting for 17% of incoming contacts and 20% of outgoing contacts (refer to enclosure 5).

Demonstration Evaluation

The HIV/AIDS project is fully operational. Analysis of quality and cost data is continually underway. Enrollment is ongoing with 756 members included in the demonstration project at the end of the fourth quarter of the fifteenth year. Reports to CMS have been provided as specified in the Special Terms and Conditions

Enclosures/Attachments

Attachment A: Outreach

Financial

Enclosure 1: Budget Neutrality Assessment
Enclosure 2: Overall Service Costs by Demonstration Year
Enclosure 3: Actual Participation by Demonstration Quarter
Enclosure 4: ADAP Funds Spent on MaineCare Clients

Communications

Enclosure 5: Contact Tracking by Reason
Enclosure 6: Contact Tracking by Method Used

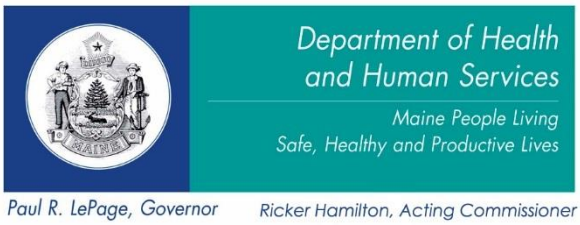
State Contact

Emily Bean, Program Manager
Office of MaineCare Services
11 State House Station, Augusta, ME 04330

emily.bean@maine.gov
207-624-4005

Date submitted to CMS: February 28, 2018

Attachment A: Outreach



Department of Health and Human Services
MaineCare Services
Nurse Coordinator
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Augusta, Maine 04333-0011
Tel.: (207) 624-4008; Fax: (207) 287-8601
Toll Free (866) 796-2463; TTY Users: Dial 711 (Maine Relay)

Authorization to Release Information

We are committed to the privacy of your health information. Please read this form carefully.

☒ Office of Maine Care Services	❒ Substance Abuse and Mental Health Services
❒ Office for Family Independence	❒ Office of Child and Family Services
❒ Maine Centers for Disease Control and Prevention	❒ Office of Aging and Disability Services
❒ Dorothea Dix Psychiatric Center	❒ Other:
❒ Riverview Psychiatric Center	

Your Name:	Your Date of Birth: Your Social Security Number:

Your Address:

Street Town/City State Zip Code

Records to be released, including written, electronic and verbal communication:

☒ All Healthcare, including treatment, services, supplies and medicines

☒ Billing, payment, income, banking, tax, asset, and/or other information regarding financial eligibility for DHHS program benefits such as MaineCare

❒Other:_____

❒ Limit to the following date(s) or type(s) of information:
(e.g. “lab test dated June 2, 2013” or “hospital records from 1/1/12- 1/15/12”)

I authorize the DHHS office(s) checked above to:
☒ Release my information to: ☒Obtain my information from:

Ryan White or named Case Management Agency: _____

Address:

_____

Street Town/City State Zip Code **Infectious Disease Specialist:**_____

Address:

_____

Street Town/City State Zip Code

If requesting that electronic information be transmitted by email, please clearly print the email address below:

_____

☒ I understand that DHHS systems may not be able to send my information securely through email. I understand that email and the internet have risks that DHHS cannot control and that the information potentially could be read by a third party. I accept those risks and still request that DHHS send my information by email. Initials _____

Please allow the office(s) named above to disclose my information for the following purpose(s):

❒ Legal ☒Insurance ☒Coordination of Care ❒ Personal Request ❒ Other:

By initialing below, I wish for my release to include the following types of records:

_____ **Mental health treatment provider or program**
(initials)

_____ **Substance/Alcohol/drug abuse treatment provider or program**
(initials)

_____ **HIV infection status or test results:** Maine law requires us to tell you that releasing this information
(initials) may have implications. Positive implications may include giving you more complete care, and negative implications may include discrimination if the data is misused. **DHHS will protect your HIV data, and all your records, as the law requires.**

I (individual/personal representative of individual named above,) give permission to the DHHS office(s) listed above to release and/or share my records as written on this form. This form will remain in effect for one year from the date below. Other releases of my information are permitted during that time unless I revoke this form.

I further understand and agree that:

- DHHS will not condition my treatment, payment for services, or benefits on whether I sign this form, unless I need to sign this form so that the right offices of DHHS can make eligibility or enrollment decisions.

- I have the right to make a written request to access and copy my healthcare or billing information, and a copy fee will be charged as permitted by law.

- If I want a review of my mental health program or provider records before they are released, I can check here. ❒ I understand that the review will be supervised.

- I may take back my permission to share the records listed on this form at any time by contacting the Privacy Officer of the specific DHHS office: Beth Glidden 207-624-6913

- I understand that taking back my permission does not apply to the information that was already shared, as a result of my signing this form. If I revoke my permission, it may be the basis for denial of health benefits or other insurance coverage.

- I may refuse to disclose all or some health care information, but that refusal may result in improper diagnosis or treatment, denial of coverage or a claim for health benefits or other insurance, or other adverse consequences.

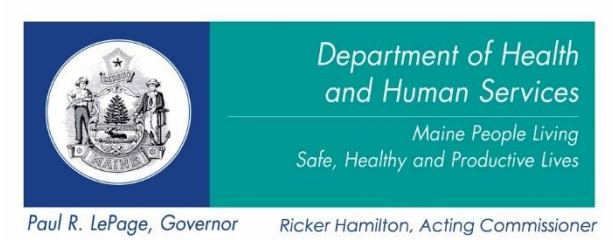
- DHHS offices will keep my information confidential as required by law. If I give my permission to share my records with people who are not required by law to keep them private, they may no longer be protected by confidentiality laws.

- If alcohol or drug provider or program records are included in this release, DHHS will tell the person receiving the records that they may not be shared with others who are not on this form without my written permission, unless required or permitted by law.

- I am signing this form voluntarily, and I have the right to a signed copy of this form if I request one.

Date: _____ Signature_____

Personal Representative's authority to sign: _____



Department of Health and Human Services
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October 16, 2017

Dear MaineCare Provider:

You are receiving this informational letter because you have been identified as a provider for one or more MaineCare members living with HIV. The Department of Health and Human Services has developed quality initiatives to improve care for these MaineCare members. One of these quality initiatives is to provide timely, important information to providers on certain aspects of HIV care. The Department finds it important to provide information to you, as a Primary Care Provider (PCP), because not all PCPs who see MaineCare members living with HIV are experienced in the use of anti-retroviral medication.

Enclosed, please find information from the FDA regarding HIV medication changes and alerts. For more information, please refer to the FDA's website.

Please contact Sherry Boochko, RN at 207-624-4008 if you currently have no patients with HIV.

If you have any questions, you may contact me by sending an email to beth.ketch@maine.gov or the Nurse Coordinator, Sherry Boochko, RN at sherry.boochko@maine.gov.

Sincerely,

Beth Ketch

Beth Ketch, Director
Policy and Provider Services
Office of MaineCare Services

On August 15, 2017, the FDA approved revisions to the GENVOYA (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) package insert to include 144-week safety, efficacy and resistance data from Studies GS-US-292 0104 and GS-US-292 0111 in antiretroviral treatment-naïve adults. Additionally, drug-drug interaction data were updated. The major revisions include the following:

Section 6 Adverse Reactions was updated as follows with the 144-week safety data

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

- **Clinical Trials in Treatment-Naïve Adults:** The primary safety assessment of GENVOYA was based on Week 144 pooled data from 1,733 subjects in two randomized, double-blind, active-controlled trials, Study 104 and Study 111, in antiretroviral treatment-naïve HIV-1 infected adult subjects. A total of 866 subjects received one tablet of GENVOYA once daily

Table 2 Adverse Reactions[a] (All Grades) Reported in ≥ 5% of HIV-1 Infected Treatment-Naïve Adults Receiving GENVOYA in Studies 104 and 111 (Week 144 analysis)

	GENVOYA N=866	**STRIBILD** N=867
Nausea	11%	13%
Diarrhea	7%	9%
Headache	6%	5%
Fatigue	5%	4%

[a] Frequencies of adverse reactions are based on all adverse events attributed to study drugs by the investigator.

The majority of events presented in Table 2 occurred at severity Grade 1

- **Bone Mineral Density Effects:** Treatment-Naïve Adults: In a pooled analysis of Studies 104 and 111, the effects of GENVOYA compared to STRIBILD on bone mineral density (BMD) change from baseline to Week 144 were assessed by dual-energy X-ray absorptiometry (DXA). The mean percentage change in BMD from baseline to Week 144 was −0.92% with GENVOYA compared to −2.95% with STRIBILD at the lumbar spine

and −0.75% compared to −3.36% at the total hip. BMD declines of 5% or greater at the lumbar spine were experienced by 15% of GENVOYA subjects and 29% of STRIBILD subjects. BMD declines of 7% or greater at the femoral neck were experienced by 15% of GENVOYA subjects and 29% of STRIBILD subjects. The long-term clinical significance of these BMD changes is not known.

- **Laboratory Abnormalities:** The frequency of laboratory abnormalities (Grades 3–4) occurring in at least 2% of subjects receiving GENVOYA in Studies 104 and 111 are presented in Table 3.

Table 3 Laboratory Abnormalities (Grades 3–4) Reported in ≥ 2% of Subjects Receiving GENVOYA in Studies 104 and 111 (Week 144 analysis)

Laboratory Parameter Abnormality[a]	GENVOYA N=866	STRIBILD N=867
Creatine Kinase (≥10.0 x ULN)	11%	10%
LDL-cholesterol (fasted) (>190 mg/dL)	11%	5%
Total cholesterol (fasted) (>300mg/dL)	4%	3%
Amylase	3%	5%
ALT	3%	3%
AST	3%	4%
Urine RBC (Hematuria) (>75 RBC/HPF)	3%	3%

[a] Frequencies are based on treatment-emergent laboratory abnormalities.

- **Serum Lipids:** Subjects receiving GENVOYA experienced greater increases in serum lipids compared to those receiving STRIBILD.

Changes from baseline in total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides and total cholesterol to HDL ratio are presented in Table 4.

Table 4 Lipid Values, Mean Change from Baseline, Reported in Subjects Receiving GENVOYA or STRIBILD in Studies 104 and 111[a]

	GENVOYA N=866		STRIBILD N=867	
	Baseline	**Week 144**	**Baseline**	**Week 144**
	mg/dL	Change[b]	mg/dL	Change[b]
Total Cholesterol (fasted)	162 [N=647]	+31 [N=647]	165 [N=627]	+14 [N=627]
Triglycerides (fasted)	111 [N=647]	+31 [N=647]	115 [N=627]	+17 [N=627]
LDL-cholesterol (fasted)	103 [N=647]	+18 [N=643]	107 [N=628]	+8 [N=628]
HDL-cholesterol (fasted)	47 [N=647]	+7 [N=647]	46 [N=627]	+3 [N=627]
Total Cholesterol to HDL ratio	3.7 [N=647]	0.2 [N=647]	3.8 [N=627]	0.1 [N=627]

[a] Excludes subjects who received lipid lowering agents during the treatment period.
[b] The change from baseline is the mean of within-subject changes from baseline for subjects with both baseline and Week 144 values.

Section 7: DRUG INTERACTIONS was updated with clinical comments for corticosteroids

Section 14: Clinical Studies was updated to include the Week 144 efficacy data as follows

14.2 Clinical Trial Results in HIV-1 Treatment-Naïve Subjects

In both Study 104 and Study 111, subjects were randomized in a 1:1 ratio to receive either GENVOYA (N=866) once daily or STRIBILD (elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg, TDF 300 mg) (N=867) once daily. The mean age was 36 years (range 18–76), 85% were male, 57% were White, 25% were Black, and 10% were Asian. Nineteen percent of subjects identified as Hispanic/Latino. The mean baseline plasma HIV-1 RNA was 4.5 log10 copies per mL (range 1.3–7.0) and 23% of subjects had baseline viral loads greater than 100,000 copies per mL. The mean baseline CD4+ cell count was 427 cells per mm3 (range 0–1360) and 13% had CD4+ cell counts less than 200 cells per mm3.

Pooled treatment outcomes of Studies 104 and 111 through Week 144 are presented in Table 13.

Table 13 Pooled Virologic Outcomes of Randomized Treatment in Studies 104 and 111 at Week 144[a] in Treatment-Naïve Subjects

	GENVOYA (N=866)	STRIBILD (N=867)
HIV-1 RNA < 50 copies/mL[b]	84%	80%
HIV-1 RNA ≥ 50 copies/mL[c]	5%	4%
No Virologic Data at Week 144 Window	11%	16%
Discontinued Study Drug Due to AE or Death[d]	2%	3%
Discontinued Study Drug Due to Other Reasons and Last Available HIV-1 RNA < 50 copies/mL[e]	9%	11%
Missing Data During Window but on Study Drug	1%	1%

[a] Week 144 window was between Day 966 and 1049 (inclusive).
[b] The primary endpoint was assessed at Week 48 and the virologic success rate was 92% in the GENVOYA group and 90% in the STRIBILD group, with a treatment difference of 2.0% (95% CI: -0.7% to 4.7%). The difference at Week 144 was primarily driven by discontinuations due to other reasons with last available HIV-1 RNA <50 copies/mL.
[c] Included subjects who had ≥50 copies/mL in the Week 144 window; subjects who discontinued early due to lack or loss of efficacy; subjects who discontinued for reasons other than an adverse event (AE), death or lack or loss of efficacy and at the time of discontinuation had a viral value of ≥ 50 copies/mL.
[d] Includes subjects who discontinued due to AE or death at any time point from Day 1 through the time window if this resulted in no virologic data on treatment during the specified window.
[e] Includes subjects who discontinued for reasons other than an AE, death or lack or loss of efficacy; e.g., withdrew consent, loss to follow-up, etc.

Treatment outcomes were similar across subgroups by age, sex, race, baseline viral load, and baseline CD4+ cell count.
In Studies 104 and 111, the mean increase from baseline in CD4+ cell count at Week 144 was 326 cells per mm^3 in GENVOYA-treated subjects and 305 cells per mm^3 in STRIBILD-treated subjects.

The updated labels will soon be available on the FDAs website.

Steve Morin
Office of Health and Constituent Affairs
Food and Drug Administration

Kimberly Struble
Division of Antiviral Products
Food and Drug Administration

Richard Klein
Office of Health and Constituent Affairs
Food and Drug Administration

On August 21, 2017, FDA approved changes to the Odefsey (emtricitabine/rilpivirine/tenofovir alafenamide) label to include data from 48 week data from trials in which subjects switched to Odefsey from tenofovir disoproxil fumarate based regimens (Complera (emtricitabine/rilpirivine/tenofovir disoproxil fumarate) or Atripla (efavirenz/emtricitabine/tenofovir disoproxil fumarate)). The major changes to the label are summarized below.

Section 6: Adverse Reactions was updated as follows:

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug (or a drug given in various combinations with other concomitant therapy) cannot be directly compared to rates in the clinical trials of another drug (or drug given in the same or different combination therapy) and may not reflect the rates observed in practice.

Adverse Reactions in Clinical Trials of ODEFSEY in Virologically-Suppressed Adult Subjects with HIV-1 Infection

The safety of ODEFSEY in virologically-suppressed adults is based on Week 48 data from two randomized, double-blinded, active-controlled clinical trials, 1160 and 1216, that enrolled 1505 adult subjects who were virologically-suppressed for at least 6 months. Both trials were designed to compare switching to ODEFSEY to maintaining efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) or emtricitabine/rilpivirine/tenofovir disoproxil fumarate (FTC/RPV/TDF) in Trials 1160 and 1216, respectively. A total of 754 subjects received one tablet of ODEFSEY daily [see Clinical Studies (14.1)].
The most common adverse reactions (all Grades) reported in at least 2% of subjects in the ODEFSEY group across Trials 1216 and 1160 were headache and sleep disturbances (Table 1). Over 98% of the adverse reactions in the ODEFSEY group were of mild to moderate intensity. The proportion of subjects who discontinued treatment with ODEFSEY due to adverse events, regardless of severity, was 2% compared to 1% for FTC/RPV/TDF and 2% for EFV/FTC/TDF.

Renal Laboratory Tests

In Trial 1216, the median baseline eGFR was104 mL per minute for subjects who switched to ODEFSEY from FTC/RPV/TDF (N=316) and the mean serum creatinine decreased by 0.02 mg per dL from baseline to Week 48.

In Trial 1160, the median baseline eGFR was 110 mL per minute for subjects who switched to ODEFSEY from EFV/FTC/TDF (N=438), and the mean serum creatinine increased by 0.1 mg per dL from baseline to Week 48.

Bone Mineral Density Effects

Changes in BMD from baseline to Week 48 were assessed by dual-energy X-ray absorptiometry (DXA) in Trials 1216 and 1160.

In Trial 1216, mean bone mineral density (BMD) increased in subjects who switched to ODEFSEY (1.61% lumbar spine, 1.04% total hip) and remained stable or decreased in subjects who remained on FTC/RPV/TDF (0.08% lumbar spine, −0.25% total hip). BMD declines of 5% or greater at the lumbar spine were experienced by 1.7% of ODEFSEY subjects and 3.0% of FTC/RPV/TDF subjects. BMD declines of 7% or greater at the femoral neck were experienced by 0% of ODEFSEY subjects and 1.2% of FTC/RPV/TDF subjects.

In Trial 1160, mean BMD increased in subjects who switched to ODEFSEY (1.65% lumbar spine, 1.28% total hip) and decreased slightly in subjects who remained on EFV/FTC/TDF (−0.05% lumbar spine, −0.13% total hip). BMD declines of 5% or greater at the lumbar spine were experienced by 2.3% of ODEFSEY subjects and 4.9% of EFV/FTC/TDF subjects. BMD declines of 7% or greater at the femoral neck were experienced by 1.4% of ODEFSEY subjects and 3.3% of EFV/FTC/TDF subjects. The long-term clinical significance of these BMD changes is not known.

Serum Lipids

Changes from baseline in total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, and total cholesterol to HDL ratio for Trials 1216 and 1160 are presented in Table 2.

Table 2 Lipid Values, Mean Change from Baseline Reported in Subjects Receiving ODEFSEY, FTC/RPV/TDF and EFV/FTC/TDF in Trials 1216 and 1160 at 48 Weeks

	Trial 1216		**Trial 1160**	
	ODEFSEY N=316 [n=235]	**FTC/RPV/TDF N=314 [n=245]**	**ODEFSEY N=438 [n=295]**	**EFV/FTC/TDF N=437 [n=308]**

	Baseline	Week 48	Baseline	Week 48	Baseline	Week 48	Baseline	Week 48
	mg/dL	Change [a,b]	mg/dL	Change [a,b]	mg/dL	Change [a,b]	mg/dL	Change [a,b]
Total Cholesterol (fasted)	176	+17	171	0	193	-7	192	-3
HDL-Cholesterol (fasted)	50	+3	48	0	56	-4	55	-2
LDL-Cholesterol (fasted)	111	+13	108	+1	118[c]	-1[c]	119	-1
Triglycerides (fasted)	116	+12	119	-9	139	-12	133	+3
Total Cholesterol to HDL Ratio	3.7	+0.2	3.8	+0.1	3.7	+0.2	3.8	0

[a] The change from baseline is the mean of within-subject changes from baseline for subjects with both baseline and Week 48 values.
[b] Subjects who received lipid-lowering agents during the treatment period were excluded.
[c] [n=296] for ODEFSEY group in Study 1160 for LDL-Cholesterol (fasted)

Section 12.4 Microbiology now includes the following

ODEFSEY: Through Week 48, in subjects who switched to ODEFSEY from FTC/RPV/TDF or EFV/FTC/TDF (Trials 1216 (N=316) and 1160 (N=438), respectively), of seven subjects who developed virologic failure, three subjects had detectable NNRTI and/or NRTI resistance substititions at virologic failure that were pre-existing in the baseline sample by proviral DNA sequencing; one of these subjects resuppressed while maintaining ODEFSEY.

The efficacy results from Trials 1216 and 1160 were included in Section 14: Clinical Studies

14 CLINICAL STUDIES

14.1 Clinical Trial Results in HIV-1 Virologically-Suppressed Subjects Who Switched to ODEFSEY

In Trial 1216, the efficacy and safety of switching from emtricitabine/rilpivirine/tenofovir disoproxil fumarate (FTC/RPV/TDF) to ODEFSEY were evaluated in a randomized, double-blind study of virologically-suppressed HIV-1 infected adults. Subjects were suppressed (HIV-1 RNA <50 copies/mL) on their baseline regimen of FTC/RPV/TDF for at least 6 months and have no documented resistance mutations to FTC, TAF, or RPV prior to study entry. Subjects were randomized in a 1:1 ratio to either switch to ODEFSEY (N=316) once daily or stay on FTC/RPV/TDF (N=314) once daily. Subjects had a mean age of 45 years (range: 23−72), 90% were male, 75% were White, and 19% were Black. The mean baseline CD4+ cell count was 709 cells/mm3 (range: 104−2527).

In Trial 1160, the efficacy and safety of switching from efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) to ODEFSEY were evaluated in a randomized, double-blind study of virologically-suppressed HIV-1 infected adults. Subjects must have been stably suppressed (HIV-1 RNA <50 copies/mL) on their baseline regimen of EFV/FTC/TDF for at least 6 months and have no documented resistance mutations to FTC, TAF, or RPV prior to study entry. Subjects were randomized in a 1:1 ratio to either switch to ODEFSEY (N=438) once daily or stay on EFV/FTC/TDF (N=437) once daily. Subjects had a mean age of 48 years (range: 19−76), 87% were male, 67% were White, and 27% were Black. The mean baseline CD4+ cell count was 700 cells/mm3 (range: 140−1862).

In addition, section 2.1 was updated to state, “It is recommended that serum creatinine, serum phosphorus, estimated creatinine clearance, urine glucose, and urine protein should be assessed before initiating ODEFSEY and during therapy in all patients as clinically appropriate.”

Also, velpatasvir was added to list of drugs without clinically significant interactions with Odefsey.

The updated labels will soon be available on the FDAs website.

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The FDA recently approved changes to the EPIVIR package insert. The approved changes are detailed below.

DOSAGE AND ADMINISTRATION was updated to increase the recommended total daily dosage for EPIVIR oral solution from 8 mg/kg/day to 10 mg/kg/day in HIV-1 infected pediatric patients aged 3 months and older. The specific wording in the package insert is as follows:

Oral Solution

The recommended dosage of EPIVIR oral solution in HIV 1-infected pediatric patients aged 3 months and older is 5 mg per kg taken orally twice daily or 10 mg per kg taken orally once daily (up to a maximum of 300 mg daily), administered in combination with other antiretroviral agents. Consider HIV-1 viral load and CD4+ cell count/percentage when selecting the dosing interval for patients initiating treatment with oral solution

The WARNINGS AND PRECAUTIONS, DRUG INTERACTIONS and the CLINICAL PHARMACOLOGY, Pharmacokinetics sections were revised to include drug interaction information with sorbitol-containing solutions based on data from a pharmacokinetic trial conducted in healthy subjects. The following text was added to the package insert.

WARNINGS AND PRECAUTIONS: Lower Virologic Suppression Rates and Increased Risk of Viral Resistance with Oral Solution

Pediatric subjects who received EPIVIR oral solution (at weight band-based doses approximating 8 mg per kg per day) concomitantly with other antiretroviral oral solutions at any time in the ARROW trial had lower rates of virologic suppression, lower plasma lamivudine exposure, and developed viral resistance more frequently than those receiving EPIVIR tablets

EPIVIR scored tablet is the preferred formulation for HIV 1-infected pediatric patients who weigh at least 14 kg and for whom a solid dosage form is appropriate. An all-tablet regimen should be used when possible to avoid a potential interaction with sorbitol. Consider more frequent monitoring of HIV-1 viral load when treating with EPIVIR oral solution.

DRUG INTERACTIONS: Sorbitol

Coadministration of single doses of lamivudine and sorbitol resulted in a sorbitol dose-dependent reduction in lamivudine exposures. When possible, avoid use of sorbitol-containing medicines with lamivudine

CLINICAL PHARMACOLOGY: Pediatric Patients: The pharmacokinetics of lamivudine have been studied after either single or repeat doses of EPIVIR in 210 pediatric subjects. Pediatric subjects receiving lamivudine oral solution (dosed at approximately 8 mg per kg per day) achieved approximately 25% lower plasma concentrations of lamivudine compared with

HIV 1-infected adults. Pediatric subjects receiving lamivudine oral tablets achieved plasma concentrations comparable to or slightly higher than those observed in adults. The absolute bioavailability of both EPIVIR tablets and oral solution are lower in children than adults. The relative bioavailability of EPIVIR oral solution is approximately 40% lower than tablets containing lamivudine in pediatric subjects despite no difference in adults. Lower lamivudine exposures in pediatric patients receiving EPIVIR oral solution is likely due to the interaction between lamivudine and concomitant solutions containing sorbitol (such as ZIAGEN). Modeling of pharmacokinetic data suggests increasing the dosage of EPIVIR oral solution to 5 mg per kg taken orally twice daily or 10 mg per kg taken orally once daily (up to a maximum of 300 mg daily) is needed to achieve sufficient concentrations of lamivudine. There are no clinical data in HIV-1 infected pediatric patients coadministered with sorbitol-containing medicines at this dose.

PATIENT COUNSELING INFORMATION was updated to advise patients that an all-tablet regimen should be used when possible due to an increased rate of treatment failure among pediatric subjects who received EPIVIR oral solution.

The updated labels will soon be available on the FDAs website.

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The FDA approved changes to the GENVOYA (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) to update the package insert with Week 24 safety and efficacy data from Study GS-US-292-0106 (Cohort 2) in HIV-1 positive, virologically suppressed children 6 to < 12 years of age weighing at least 25 kilograms (kg). The specific changes are summarized below.

Section 1: INDICATIONS AND USAGE
GENVOYA is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 25 kg who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of GENVOYA

Section 2: DOSAGE AND ADMINISTRATION
Recommended Dosage

GENVOYA is a four-drug fixed dose combination product containing 150 mg of elvitegravir, 150 mg of cobicistat, 200 mg of emtricitabine, and 10 mg of tenofovir alafenamide (TAF). The recommended dosage of GENVOYA is one tablet taken orally once daily with food in adults and pediatric patients with body weight at least 25 kg and creatinine clearance greater than or equal to 30 mL per minute

Section 6: ADVERSE REACTI

Clinical Trials in Pediatric Subjects:

Safety in Pediatric Patients

The safety of GENVOYA in HIV-1 infected pediatric subjects was evaluated in treatment-naïve subjects between the ages of 12 to less than 18 years and weighing at least 35 kg (N=50) through Week 48 (cohort 1), and in virologically-suppressed subjects between the ages of 6 to less than 12 years and weighing at least 25 kg (N=23) through Week 24 (cohort 2) in an open-label clinical trial (Study 106). With the exception of a decrease in the mean CD4+ cell count observed in cohort 2 of Study 106, the safety profile in pediatric subjects who received treatment with GENVOYA was similar to that in adults. One 13-year-old female subject developed unexplained uveitis while receiving GENVOYA that resolved and did not require discontinuation of GENVOYA.

Bone Mineral Density Effects

Cohort 1: Treatment-naïve adolescents (12 to less than 18 years; at least 35 kg)

- Among the subjects in cohort 1 receiving GENVOYA, mean BMD increased from baseline to Week 48, + 4.2% at the lumbar spine and + 1.3% for the total body less head (TBLH). Mean changes from baseline BMD Z-scores were −0.07 for lumbar spine and −0.20 for TBLH at Week 48. One GENVOYA subject had significant (at least 4%) lumbar spine BMD loss at Week 48.

Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)

- Among the subjects in cohort 2 receiving GENVOYA, mean BMD increased from baseline to Week 24, +2.9% at the lumbar spine and +1.7% for TBLH. Mean changes from baseline BMD Z-scores were -0.06 for lumbar spine and -0.18 for TBLH at Week 24. Two GENVOYA subjects had significant (at least 4%) lumbar spine BMD loss at Week 24.
- Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)

Change from Baseline in CD4+ cell counts

- Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)
- Cohort 2 of Study 106 evaluated pediatric subjects (N=23) who were virologically-suppressed and who switched from their antiretroviral regimen to GENVOYA. Although all subjects had HIV-1 RNA < 50 copies/mL, there was a decrease from baseline in CD4+ cell count at Week 24. The mean baseline and mean change from baseline in CD4+ cell count and in CD4% from Week 2 to Week 24 are

presented in Table 5. All subjects maintained their CD4+ cell counts above 400 cells/mm^3.

Table 5:

Mean Change in CD4+ Count and Percentage from Baseline to Week 24 Virologically -Suppressed Pediatric Patients from 6 to <12 Years Who Switched to GENVOYA

	Baseline	Mean Change from Baseline			
		Week 2	Week 4	Week 12	Week 24
CD4+ Cell Count (cells/mm^3)	966 (201.7)[a]	-162	-125	-162	-150
CD4%	40 (5.3)[a]	+0.5%	-0.1%	-0.8%	-1.5%

a. Mean (SD)

Section 8.4 Pediatric Use

The safety and effectiveness of GENVOYA for the treatment of HIV-1 infection was established in pediatric patients with body weight greater than or equal to 25 kg.

Use of GENVOYA in pediatric patients between the ages of 12 to less than 18 years and weighing at least 35 kg is supported by studies in adults and by a study in antiretroviral treatment-naïve HIV-1 infected pediatric subjects ages 12 to less than 18 years and weighing at least 35 kg (cohort 1 of Study 106, N=50). The safety and efficacy of GENVOYA in these pediatric subjects was similar to that in adults.

Use of GENVOYA in pediatric patients weighing at least 25 kg is supported by studies in adults and by an open-label trial in virologically-suppressed pediatric subjects ages 6 to less than 12 years and weighing at least 25 kg, in which subjects were switched from their antiretroviral regimen to GENVOYA (cohort 2 of Study 106, N=23). The safety in these subjects through 24 weeks was similar to that in antiretroviral treatment-naïve adults with the exception of a decrease in mean change from baseline in CD4+ cell count.

Safety and effectiveness of GENVOYA in pediatric patients less than 25 kg have not been established.

14.5 Clinical Trial Results in HIV-1 Infected Pediatric Subjects Between the Ages of 6 to Less than 18

In Study 106, an open-label, single arm trial the efficacy, safety, and pharmacokinetics of GENVOYA in HIV-1 infected pediatric subjects were evaluated in treatment-naïve adolescents between the ages of 12 to less than 18 years weighing at least 35 kg (N=50) and in virologically-suppressed children between the ages of 6 to less than 12 years weighing at least 25 kg (N=23).

Cohort 1: Treatment-naïve adolescents (12 to less than 18 years; at least 35 kg)

Subjects in cohort 1 treated with GENVOYA once daily had a mean age of 15 years (range 12-17); 44% were male, 12% were Asian, and 88% were Black. At baseline, mean plasma HIV-1 RNA was 4.6 $\log_{10}$ copies per mL (22% had baseline plasma HIV-1 RNA greater than 100,000 copies per mL), median CD4+ cell count was 456 cells per mm^3 (range: 95 to 1110), and median CD4+ percentage was 23% (range: 7% to 45%).

In subjects in cohort 1 treated with GENVOYA, 92% (46/50) achieved HIV-1 RNA less than 50 copies per mL at Week 48. The mean increase from baseline in CD4+ cell count at Week 48 was 224 cells per mm^3. Three of 50 subjects had virologic failure at Week 48; no emergent resistance to GENVOYA was detected through Week 48.

Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)

Subjects in cohort 2 treated with GENVOYA once daily had a mean age of 10 years (range: 8-11), a mean baseline weight of 31.6 kg, 39% were male, 13% were Asian, and 78% were Black. At baseline, median CD4+ cell count was 969 cells/mm3 (range: 603 to 1421), and median CD4% was 39% (range: 30% to 51%).

After switching to GENVOYA, 100% (23/23) of subjects in cohort 2 remained suppressed (HIV-1 RNA < 50 copies/mL) at Week 24. From a mean (SD) baseline CD4+ cell count of 966 (201.7), the mean change from baseline in CD4+ cell count was 150 cells/mm^3 and the mean (SD) change in CD4% was -1.5% (3.7%) at Week 24. All subjects maintained CD4+ cell counts above 400 cells/mm^3

The updated labels will soon be available on the FDAs website.

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The NORVIR (ritonavir) Oral Solution package insert was recently updated with the types of feeding tubes that are compatible for use.

The DOSAGE AND ADMISTRATION section was updated as follows:

Administering Oral Solution by Feeding Tube

Because NORVIR oral solution contains ethanol and propylene glycol, it is not recommended for use with polyurethane feeding tubes due to potential incompatibility. Feeding tubes that are compatible with ethanol and propylene glycol, such as silicone and polyvinyl chloride (PVC) feeding tubes, can be used for administration of NORVIR oral solution. Follow instructions for use of the feeding tube to administer the medicine.

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The DESCOVY (emtricitabine/tenofovir alafenamide) package insert was recently updated to include the Week 24 safety and efficacy data from Study GS-US-292-0106 (cohort 2) in HIV-1 positive, virologically suppressed children 6 to less than 12 years of age weighing at least 25 kg. The following revisions were made to the package insert.

Section 1: INDICATIONS AND USAGE was updated as follows:
DESCOVY is indicated, in combination with other antiretroviral agents, for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 35 kg.

DESCOVY is also indicated, in combination with other antiretroviral agents other than protease inhibitors that require a CYP3A inhibitor, for the treatment of HIV-1 infection in pediatric patients weighing at least 25 kg and less than 35 kg.

Section 2: DOSAGE AND ADMINISTRATION was updated to state:

Recommended Dosage

DESCOVY is a two-drug fixed dose combination product containing 200 mg of emtricitabine (FTC) and 25 mg of tenofovir alafenamide (TAF). The recommended dosage of DESCOVY is one tablet taken orally once daily with or without food in adults and pediatric patients with body weight at least 25 kg and creatinine clearance greater than or equal to 30 mL per minute.

For specific dosing recommendations for coadministered third agents, refer to their respective prescribing information. The safety and effectiveness of DESCOVY coadminstered with an HIV-1 protease inhibitor that is administered with either ritonavir or cobicistat have not been established in pediatric subjects weighing less than 35 kg.

Section 5 WARNINGS AND PRECAUTIONS subsection 5.5 Bone Loss and Mineralization Defects was deleted from the package insert. The bone mineral density effects are included in Section 6: ADVERSE REACTIONS along with other changes as follows:

<u>Adverse Reactions in Clinical Trials in Pediatric Subjects with HIV-1 Infection</u>
In an open-label trial of antiretroviral treatment-naïve HIV-1 infected pediatric subjects between the ages of 12 to less than 18 years weighing at least 35 kg through 48 weeks (N=50; cohort 1) and virologically-suppressed subjects between the ages of 6 to less than 12 years weighing at least 25 kg (N=23; cohort 2) who received FTC+TAF with EVG+COBI through 24 weeks, with the exception of a decrease in the mean CD4+ cell count observed in cohort 2, the safety of this

combination was similar to that of adults.

Bone Mineral Density Effects

- *Cohort 1: Treatment-naïve adolescents (12 to less than 18 years; at least 35 kg)*

Among the subjects in cohort 1 receiving FTC+TAF with EVG+COBI, mean BMD increased from baseline to Week 48, +4.2% at the lumbar spine and +1.3% for the total body less head (TBLH). Mean changes from baseline BMD Z-scores were −0.07 for lumbar spine and −0.20 for TBLH at Week 48. One subject had significant (at least 4%) lumbar spine BMD loss at Week 48.

- *Cohort 2: Virologically-suppressed children (6 to less than 12 years; at least 25 kg)*

Cohort 2 evaluated pediatric subjects (N=23) who were virologically-suppressed and who switched from their antiretroviral regimen to FTC+TAF with EVG+COBI. Although all subjects had HIV-1 RNA < 50 copies/mL, there was a decrease from baseline in CD4+ cell count at Week 24. The mean baseline and mean change from baseline in CD4+ cell count and in CD4% from Week 2 to Week 24 are presented in Table 1. All subjects maintained their CD4+ cell counts above 400 cells/mm^3.

Section 8.4 Pediatric Use was updated as follows:

The safety and effectiveness of DESCOVY, in combination with other antiretroviral agents, for the treatment of HIV-1 infection was established in pediatric patients with body weight greater than or equal to 25 kg.

Use of DESCOVY in pediatric patients between the ages of 12 to less than 18 years weighing at least 35 kg is supported by adequate and well controlled studies of FTC+TAF with EVG+COBI in adults and by an open-label trial in antiretroviral treatment-naïve HIV-1 infected pediatric subjects ages 12 to less than 18 years and weighing at least 35 kg (N=50; cohort 1). The safety and efficacy of FTC+TAF with EVG+COBI in these pediatric subjects was similar to that of HIV-1 infected adults on this regimen.

Use of DESCOVY in pediatric patients weighing at least 25 kg is supported by adequate and well controlled studies of FTC+TAF with EVG+COBI in adults and by an open-label trial in virologically-suppressed pediatric subjects between the ages of 6 to less than 12 years weighing at least 25 kg, in which subjects were switched from their antiretroviral regimen to FTC+TAF with EVG+COBI (N=23; cohort 2). The safety in these subjects through 24 weeks of FTC+TAF with EVG+COBI was similar to that of HIV-1 infected adults on this regimen, with the exception of a decrease in mean change from baseline in CD4+ cell count.

Safety and effectiveness of DESCOVY coadminstered with an HIV-1 protease inhibitor that is administered with either ritonavir or cobicistat have not been established in pediatric subjects weighing less than 35 kg.

Safety and effectiveness of DESCOVY in pediatric patients less than 25 kg have not been

established.

Section 12 CLINICAL PHARMACOLOGY and Section 14 CLINICAL STUDIES was updated as follows

Pediatric Patients

Mean exposures of TAF in 24 pediatric subjects aged 12 to less than 18 years who received FTC+TAF with EVG+COBI were decreased (23% for AUC) and FTC exposures were similar compared to exposures achieved in treatment-naïve adults following administration of this dosage regimen. The TAF exposure differences are not thought to be clinically significant based on exposure-response relationships (Table 6).

Exposures of FTC and TAF achieved in 23 pediatric subjects between the ages of 6 to less than 12 years and weighing at least 25 kg (55 lbs) who received FTC+TAF with EVG+COBI were higher (20 to 80% for AUC) than exposures achieved in adults following the administration of this dosage regimen; however, the increase was not considered clinically significant (Table 7) *[see Use in Specific Populations (8.4)]*.

The updated labels will soon be available on the FDAs website.

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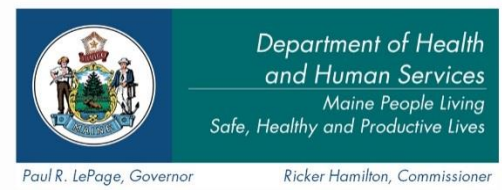

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February 21, 2018

Dear (*insert provider name*):

Thank you for responding to our survey!

You indicated on your MaineCare HIV/AIDS Provider Survey that you had some level of unfamiliarity with programs and resources that are available for people living with HIV/AIDS.

The area(s) you indicated were:

- Maine AIDS Education and Training Center
- MaineCare's Special Benefit Waiver
- The Ryan White/AIDS Drug Assistance Program (ADAP)
- HIV/AIDS treatment guidelines and recommendations

Please find enclosed materials that address the area(s) of unfamiliarity. If you have any questions, or if you would like specific information about the survey results, please contact me at 207-624-4005 or emily.bean@maine.gov.

Thank you,

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