



**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology**

Date: August 21, 2007

To: M. Dianne Murphy, M.D.  
Director, Office of Pediatric Therapeutics (OPT), OIASI  
Office of the Commissioner

CDR Lisa L. Mathis, USPHS M.D.,  
OND Associate Director  
Pediatric and Maternal Health Team

Hari C. Sachs, M.D., FAAP  
Medical Officer  
Pediatric and Maternal Health Team  
Office of New Drugs

Thru: Solomon Iyasu, M.D., M.P.H., Director  
Division of Surveillance, Research and Communication  
Support, HFD-410  
Office of Surveillance and Epidemiology

From: Kendra Worthy, Pharm.D., Drug Use Data Specialist  
Sigal Kaplan, Ph.D., B.Pharm., Pharmacoepidemiologist  
Division of Surveillance, Research and Communication  
Support, HFD-410  
Office of Surveillance and Epidemiology

Subject: One Year Post-Pediatric Exclusivity Post-marketing Adverse  
Event Review:  
Drug Utilization Analysis  
Pediatric Exclusivity Grant Date: May 24, 2006

Drug Name(s): Emtriva® (emtricitabine) Capsules  
Emtriva® (emtricitabine) Oral Solution

Submission Number: S-007  
S-001

Application Type/Number: NDA 21-500  
NDA 21-896

Applicant/sponsor:                   Gilead Sciences

OSE RCM #:                             2007-1092

**\*\*This document contains proprietary drug use data obtained by FDA under contract. The drug use data/information cannot be released to the public/non-FDA personnel without contractor approval obtained through the FDA/CDER Office of Surveillance and Epidemiology.\*\***

## **EXECUTIVE SUMMARY**

This review examines the drug utilization patterns for emtricitabine (Emtriva<sup>®</sup>), a nucleoside reverse transcriptase inhibitor, two years before and one year following the granting of Pediatric Exclusivity on May 24, 2006, with a primary focus on the use in the pediatric population, ages 0 through 16 years. Outpatient drug use patterns for emtricitabine, emtricitabine combinations and nucleoside reverse transcriptase inhibitors (NRTIs) used for the treatment of HIV were examined for the three 12-month periods from June 1, 2004 through May 31, 2007, using proprietary drug use databases licensed by FDA.

The total number of retail prescriptions dispensed for NRTIs, as well as Truvada<sup>®</sup> (emtricitabine/tenofovir) and Atripla<sup>®</sup> (efavirenz/emtricitabine/tenofovir), increased 4% from 2.9 million in the 12-month period of June 2005 – May 2006 to approximately 3.1 million in the 12-month period ending May 2007. Prescriptions for emtricitabine products (excluding emtricitabine combinations) accounted for approximately 1.2% of nucleoside reverse transcriptase inhibitors dispensed during the post-exclusivity period, June 2006 – May 2007.

Emtricitabine is primarily used in adult patients. Patients aged 0-16 years comprise less than 1.5% of all patients that filled a prescription for Emtricitabine during the pre-exclusivity and post-exclusivity periods. Infectious Disease was the most common prescribing specialty for emtricitabine, and pediatricians accounted for less than 1% of all dispensed prescriptions. Data from office-based physician practices in the U.S. indicates no recorded use of emtricitabine within the pediatric population during the post-exclusivity period. However, during the pre-exclusivity period and the year prior, Enlargement of Lymph Nodes and HIV & Specific Infection was reported among the 11-16 year and adult (age 17 year and older) age group.

The small proportion of prescriptions dispensed for pediatric population is consistent with the basic statistics available on HIV in that population. The recommended initial antiretroviral therapy for immunodeficiency virus infection in children is a highly active combination antiretroviral regimen. While a combination therapy has led to better clinical outcomes than monotherapy, the increased survival of HIV-infected children has generated challenges in selecting successive new antiretroviral drug regimens. The use of antiretrovirals in pediatric patients is evolving rapidly and guidelines are updated regularly to provide current information.

## **1 BACKGROUND**

### **1.1 INTRODUCTION**

On January 4, 2002, Congress enacted the Best Pharmaceuticals for Children Act (BPCA) to improve the safety and efficacy of pharmaceuticals for children. Section 17 of that Act requires the review of adverse events associated with the use of a drug in children during the one year following the date on which the drug received marketing exclusivity. In support of this mandate, the FDA is required to provide a report to the Pediatric Advisory Committee on the drug utilization patterns and adverse events associated with the use of the drug soon after the one-year anniversary of granting exclusivity. This review is in addition to the routine post-marketing safety surveillance activities the FDA performs for all marketed drugs.

### **1.2 REGULATORY HISTORY**

Emtricitabine is a nucleoside reverse transcriptase inhibitor. Emtriva<sup>®</sup> (emtricitabine) Capsule, NDA 21-500, was approved on July 2, 2003 for the treatment of HIV infection in adults.

Emtriva® (emtricitabine) Oral Solution, NDA 21-896, in combination with other antiretroviral agents, was approved on September 28, 2005, for the treatment of HIV infection in patients over three months of age.

NDA supplements NDA 21-500/S-007 AND NDA 21-896/S-001, which support the inclusion of pharmacokinetic data for children from birth to three months of age, were approved on June 13, 2005. Pediatric exclusivity was granted on May 24, 2006 under the same NDA supplements.

Truvada® (emtricitabine 200 mg/tenofovir disoproxil fumarate 300mg) Tablets, NDA 21-752, was approved on August 2, 2004 in combination with other antiretroviral agents (such as nonnucleoside reverse transcriptase inhibitors or protease inhibitors) for the treatment of HIV-1 infection in adults.

Atripla® (efavirenz 600mg/emtricitabine 200mg/tenofovir disoproxil fumarate 300mg) Tablets, NDA 21-937, was approved July 12, 2006 for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.

### 1.3 PRODUCT LABELING

#### ***Pediatric Use<sup>1</sup>:***

Safety and effectiveness in pediatric patients below the age of 3 months have not been established. The safety and efficacy of emtricitabine is supported by data from three open-label, non-randomized clinical studies in which emtricitabine was administered to 169 HIV-1 infected treatment naïve and experienced (defined as virologically suppressed on a lamivudine containing regimen for which emtricitabine was substituted for lamivudine) patients between 3 months and 21 years of age. Patients received once-daily EMTRIVA Oral Solution (6 mg/kg to a maximum of 240 mg/day) or EMTRIVA Capsules (a single 200 mg capsule once daily) in combination with at least two other antiretroviral agents. Patients had a mean age of 7.9 years (range 0.3–21), 49% were male, 15% Caucasian, 61% Black and 24% Hispanic. Patients had a median baseline HIV RNA of 4.6 log<sub>10</sub> copies/mL (range 1.7–6.4) and a mean baseline CD4 cell count of 745 cells/mm<sup>3</sup> (range 2 □ 2650). Through 48 weeks of therapy, the overall proportion of patients who achieved and sustained an HIV RNA <400 copies/mL was 86%, and <50 copies/mL was 73%. The mean increase from baseline in CD4 cell count was 232 cells/mm<sup>3</sup> (-945, +1512). The adverse event profile observed during these clinical trials was similar to that of adult patients, with the exception of a higher frequency of hyperpigmentation (**see ADVERSE REACTIONS**).

## 2 METHODS AND MATERIALS

Using the currently available data resources, this review describes the outpatient and inpatient drug use patterns for emtricitabine in the pediatric population as well as in the adult population in the years prior to and subsequent to the granting of pediatric exclusivity on May 24, 2006. Proprietary drug use databases licensed by the Agency were used to conduct this analysis.

### 2.1 DETERMINING SETTINGS OF CARE

IMS Health, IMS National Sales Perspectives™ data were used to determine the settings in which emtricitabine is sold. Sales of this product by extended units (number of capsules and milliliters of oral solution) sold from the manufacturer into the various retail and non-retail channels of distribution were analyzed for the year following the granting of pediatric exclusivity, June 2006 through May 2007. From these data, it was clear that this product is distributed to both outpatient

---

<sup>1</sup> Emtriva Product Labeling, Drugs@FDA. Accessed 8/2007.

and inpatient settings of care. 57% of the emtricitabine extended units were sold to retail sales channels (which include 13% of sales to mail service pharmacies), and approximately 43% were sold to inpatient settings of care (Appendix 2, Table 1). Because of the balanced distribution of drug product sales of emtricitabine extended units during this time period, we examined the utilization patterns for emtricitabine focusing on the outpatient and inpatient settings. We also examined selected nucleoside reverse transcriptase inhibitors as well as two combination products that contain emtricitabine, Truvada® and Atripla®.

Premier's Rx Market Advisor™ was used to measure patient demographics for the two 6-month periods before and after pediatric exclusivity was granted; due to a 45-60 day lag time in the collection of data, full 1 year periods are not available in time for this review.

## **2.2 DATA SOURCES USED**

Outpatient use and patient demographics were measured with two data sources from Verispan, LLC: Vector One®: National (VONA) and Total Patient Tracker (TPT) (see Appendix). From these two sources, nationally projected estimates of the number of prescriptions dispensed by retail pharmacies and the number of patients who received a dispensed prescription for Emtriva® (emtricitabine) were obtained. Indications for use were obtained from the Verispan, Physician Drug and Diagnosis Audit database (see Appendix). Outpatient drug utilization patterns were examined for three twelve-month periods from June 1, 2004 through May 31, 2007. Inpatient use and patient demographics were measured with Premier's Rx Market Advisor™ for two six-month periods from November 1, 2005 through April 30, 2006, and May 1, 2006 through October 31, 2006.

## **2.3 PRODUCTS INCLUDED**

We examined prescriptions dispensed for Emtriva® (emtricitabine), Truvada® (emtricitabine/tenofovir), Atripla® (efavirenz/emtricitabine/tenofovir), as well as products in the nucleoside reverse transcriptase inhibitor (NRTI) class based on discussions with the Pediatric and Maternal Health Staff. The NRTI class was analyzed as comparator products at the molecule level and included: efavirenz, tenofovir, lamivudine, nevirapine, didanosine, abacavir, stavudine, zidovudine, emtricitabine, delavirdine, didanosine, and zalcitabine.

# **3 RESULTS**

## **3.1 OUTPATIENT USE**

### ***3.1.1 Dispensed Prescriptions***

#### **3.1.1.1 Nucleoside Reverse Transcriptase Inhibitor (NRTI) Market**

The total number of retail prescriptions dispensed in the NRTI market, including emtricitabine/tenofovir and efavirenz/emtricitabine/tenofovir, increased 4% from 2.9 million in the 12-month period of June 2005 – May 2006 to approximately 3.1 million in the 12-month period ending May 2007 (Table 1). Excluding emtricitabine/tenofovir and efavirenz/emtricitabine/tenofovir, the market decreased approximately by 12% from 2.3 million dispensed prescriptions to 2.0 million dispensed prescriptions during the same time period.

Emtricitabine products, excluding emtricitabine/tenofovir and efavirenz/emtricitabine/tenofovir, accounted for approximately 1.2% of the nucleoside reverse transcriptase inhibitor class during the post-exclusivity period, June 2006 – May 2007.

### 3.1.1.2 Emtricitabine

Total prescriptions dispensed for emtricitabine decreased by 22%, from approximately 46,500 prescriptions in the pre-exclusivity period (June 2005 –May 2006) to 36,300 prescriptions in the post-exclusivity period (June 2006 – May 2007) (Table 1 below; Figure 1 Appendix). A 60% decrease occurred from June 2004 –May 2005, when the number of prescriptions dispensed for emtricitabine fell from approximately 115,248 prescriptions to 46,500 prescriptions from June 2005 – May 2006.

**Table 1. Total number of prescriptions dispensed by retail pharmacies\* for emtricitabine containing products (in bold) and Nucleoside Reverse Transcriptase Inhibitors, Moving Annual Totals June 2004 through May 2007**

	June 2004- May 2005		June 2005- May 2006		June 2006- May 2007	
	Retail TRxs	Share	Retail TRxs	Share	Retail TRxs	Share
	N	%	N	%	N	%
<b>TOTAL</b>	<b>3,236,168</b>	<b>100.0%</b>	<b>2,943,331</b>	<b>100.0%</b>	<b>3,065,929</b>	<b>100.0%</b>
<b>emtricitabine/tenofovir</b>	<b>221,477</b>	<b>6.8%</b>	<b>626,721</b>	<b>21.3%</b>	<b>759,469</b>	<b>24.8%</b>
zidovudine/lamivudine	706,021	21.8%	578,979	19.7%	510,452	16.6%
lamivudine	738,352	22.8%	479,338	16.3%	376,463	12.3%
abacavir sulfate/lamivudine	82,569	2.6%	209,596	7.1%	277,256	9.0%
efavrnz/emtrctbin/tenfovr	--	--	--	--	<b>269,530</b>	<b>8.8%</b>
didanosine	374,517	11.6%	279,395	9.5%	223,113	7.3%
zidovudine/lamivudine/abacavir	282,281	8.7%	229,356	7.8%	199,075	6.5%
abacavir sulfate	268,880	8.3%	184,319	6.3%	168,125	5.5%
stavudine	358,783	11.1%	231,569	7.9%	167,845	5.5%
zidovudine	82,264	2.5%	73,428	2.5%	75,803	2.5%
<b>emtricitabine</b>	<b>115,248</b>	<b>3.6%</b>	<b>46,495</b>	<b>1.6%</b>	<b>36,319</b>	<b>1.2%</b>
zalcitabine	5,776	0.2%	4,135	0.1%	2,479	0.1%

Verispan, LLC, Vector One® National (VONA), Data extracted 7-2007. Source File: 2007-1092 7-10-07 Emtriva Class.qry

\*mail order pharmacies not included

### 3.1.2 Patient demographics

#### 3.1.2.1 Emtricitabine –Total Prescriptions and Patients

Emtricitabine is primarily used in adult patients. Adults accounted for greater than 98% of total dispensed prescriptions for emtricitabine during each year of this analysis. Prescriptions dispensed to children aged 0-16 years accounted for less than 1% of total dispensed prescriptions except for during the post-exclusivity period, June 2006 – May 2007 when they made up approx. 1.5% (Appendix 2, Table 3).

Similar to dispensed prescriptions, the number of patients receiving a prescription for emtricitabine from outpatient retail pharmacies decreased by 24%, from approximately 9,373 patients in the pre-exclusivity period (June 2005 –May 2006) to 7,153 patients in the post-exclusivity period (June 2006 – May 2007) (Appendix 2, Table 4). Patients aged 0-16 years make up approximately 1% of all patients that filled a prescription for Emtricitabine during the pre-exclusivity period and 1.5% during the post-exclusivity period.

### 3.1.2.2 Combination emtricitabine products – Total Prescriptions and Patients

Examination of the combination emtricitabine products, Truvada®(emtricitabine/tenofovir) and Atripla®(efavirenz/emtricitabine/tenofovir), revealed that more prescriptions for pediatric patients aged 0-16 years filled a prescription for Truvada®(emtricitabine/tenofovir) compared to the other emtricitabine products; however, the number of prescriptions dispensed to pediatric patients aged 0-16 years still only accounts for less than 1% of the total number of prescriptions dispensed for Truvada®(emtricitabine/tenofovir) during the post-exclusivity period (Appendix 2, Table 3). Atripla®(efavirenz/emtricitabine/tenofovir) accounted for approximately 25% of dispensed prescriptions (approximately 269, 531 prescriptions) for emtricitabine products during the post-exclusivity period; however, pediatric prescriptions only accounted for 0.2% of those prescriptions. The single ingredient emtricitabine product accounted for approximately 36,321 dispensed prescriptions during the post-exclusivity period (3.4% of the market).

Approximately 143,247 patients filled a prescription for Truvada®(emtricitabine/tenofovir) and 61,344 patients filled a prescription for Atripla®(efavirenz/emtricitabine/tenofovir) during the post-exclusivity period (June 2006 – May 2007) (Appendix 2, Table 4). Trends for patient data were similar to that of prescription data, with pediatric patients comprising less than 1% of total patients for both of the combination products containing emtricitabine.

## 3.2 PRESCRIBER SPECIALTY

Infectious Disease was the most common prescribing specialty for emtricitabine, accounting for approximately a third of the dispensed prescriptions during each year of the study period (Table 5). Internal Medicine was the second most common prescribing specialty with approximately a quarter of the dispensed prescriptions. Prescriptions by pediatricians accounted for less than 1% of all dispensed prescriptions for emtricitabine during each year of this analysis.

**Table 5: Total number of prescriptions dispensed for emtricitabine by top 11 prescriber specialties, Moving Annual Total June 2004 through May 2007 (mail order pharmacies not included)**

	June 2004- May 2005		June 2005- May 2006		June 2006- May 2007	
	Retail TRxs	Share	Retail TRxs	Share	Retail TRxs	Share
	N	%	N	%	N	%
<b>Emtriva®</b>	115,255	100.0%	46,502	100.0%	36,314	100.0%
<b>Infectious Disease</b>	33,872	29.4%	15,360	33.0%	12,379	34.1%
<b>Internal Medicine</b>	31,031	26.9%	12,490	26.9%	10,064	27.7%
<b>GP/FM/DO§</b>	11,269	9.8%	5,567	12.0%	4,294	11.8%
<b>Unspecified</b>	23,811	20.7%	6,601	14.2%	3,407	9.4%
<b>Nurse Pract.</b>	3,432	3.0%	1,126	2.4%	1,132	3.1%
<b>Hospital</b>	2,767	2.4%	1,442	3.1%	1,117	3.1%
<b>Physician Assist.</b>	1,134	1.0%	603	1.3%	569	1.6%
<b>Other</b>	1,095	1.0%	695	1.5%	545	1.5%
<b>PUD</b>	516	0.4%	271	0.6%	449	1.2%
<b>Allergy/Immunology</b>	940	0.8%	455	1.0%	376	1.0%
<b>Pediatrics</b>	<b>558</b>	<b>0.5%</b>	<b>237</b>	<b>0.5%</b>	<b>310</b>	<b>0.9%</b>
<b>All Others</b>	4,830	4.2%	1,655	3.6%	1,672	4.6%

\*Verispan, LLC, Vector One® National (VONA), Data extracted 7-2007. Source File: 2007-1092 emtriva MD Spec 7-9-07.qry

§ General Practice, Family Medicine, Osteopathic Medicine

### 3.3 INDICATIONS FOR USE

According to Verispan’s office-based physician practice survey database, no mentions of emtricitabine in association with a pediatric patient was recorded for the pediatric population during the post-exclusivity period, June 2006 – May 2007 (data not shown). The following diagnoses associated with the use of emtricitabine in the 11-16 year age group were recorded during the pre-exclusivity period: “enlargement lymph nodes” (ICD-9 785.6) and “HIV and specific infection” (ICD-9 042.0). For adults (ages 17 years and above), the only diagnosis associated with the use of emtricitabine during the pre- and post-exclusivity periods was “HIV and specific infection” (ICD-9 042.0).

### 3.4 INPATIENT UTILIZATION

Total inpatient hospital discharges in which emtricitabine containing products were billed increased by 34% from the six-month period prior to the granting of exclusivity to the following six-month period (Table 6). Trends are similar to outpatient data, with very low pediatric usage (data not shown).

**Table 6: Total number of projected inpatient hospital discharges in which emtricitabine products were billed, November 2005-April 2006 and May 2006-October 2006**

	November 2005 - April 2006	May 2006 - October 2006	Total
	Projected Discharges	Projected Discharges	Projected Discharges
<b>Total, Emtricitabine*</b>	<b>7,119</b>	<b>9,547</b>	<b>16,666</b>

Premier RxMarket Advisor™, Data extracted 7-2007.

\*Includes all products containing emtricitabine

## 4 DISCUSSION

Based on the databases employed for this analysis, prescriptions dispensed for Emtriva® in the pediatric population accounted for only small proportion of the total prescriptions for emtricitabine and for emtricitabine combinations during the pre- and post-exclusivity periods. The small proportion of prescriptions dispensed for pediatric population is consistent with the basic statistics available on HIV in that population. In 2005, the estimated number of diagnoses of AIDS in the U.S. was 40,607, of which 601 cases were estimated to be for patients under the age of 20.<sup>2</sup> The cumulative estimated number of diagnoses of AIDS through 2005 in the U.S. was 952,629, of which 15,466 cases were estimated in those under the age of 20.

<sup>2</sup> CDC HIV/AIDS Surveillance Report: HIV Infection and AIDS in the United States and Dependent Areas, 2005. HIV/AIDS Surveillance Report, Volume 17, Revised Edition, June 2007. Available at <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2005report/pdf/2005SurveillanceReport.pdf> Accessed (July 31, 2007)

According to the current Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection (2006), the recommended antiretroviral regimens for initial therapy for immunodeficiency virus infection in children is a highly active combination antiretroviral regimen that generally contains at least 3 drugs: a 2-drug NRTI backbone with 1 Non-NRTI or 1 protease inhibitor (PI) combined.<sup>3</sup> The preferred 2-drug NRTI backbone are: Zidovudine *plus* (lamivudine *or* didanosine *or* emtricitabine) *or* Didanosine *plus* (lamivudine *or* emtricitabine). Similar recommendations are available for adults and adolescents.<sup>4</sup>

While a combination therapy (initially dual NRTI treatment) has led to better clinical, immunologic, and virologic outcomes than monotherapy, the increased survival of HIV-infected children is associated with challenges in selecting successive new antiretroviral drug regimens.<sup>3</sup> Additionally, therapy is associated with short- and long-term toxicities, some of which have only recently been recognized in children.<sup>3</sup> In addition, antiretroviral drug-resistant virus can develop in both multi-drug experienced children and children who received initial regimens containing 1 or 2 drugs that incompletely suppressed viral replication. It is within this context that it is noteworthy, that the use of antiretrovirals in pediatric patients is evolving rapidly and guidelines are updated regularly to provide current information.

Findings from this review should be interpreted in the context of the known limitations of the databases used. We estimated that emtricitabine products are distributed primarily in outpatient and inpatient settings based on the IMS Health, IMS National Sales Perspectives™. These data do not provide a direct estimate of use but do provide a national estimate of units sold from the manufacturer into the various channels of distribution. The amount of product purchased by these retail and non-retail channels of distribution may be a possible surrogate for use, if we assume the facilities purchase drugs in quantities reflective of actual patient use.

While we conducted a comprehensive analysis of the use of this product in the outpatient and inpatient settings, in which the majority of use occurred, a significant proportion of wholesale sales of emtricitabine products were to mail order pharmacies and clinics. Verispan's mail order data begins January 2005, and was therefore not included in this analysis. The FDA currently does not have access to a data source which can characterize the use within clinics.

Verispan's Physician Drug & Diagnosis Audit (PDDA) data provide estimates of patient demographics and indications for use of medicinal products in the U.S. Due to the sampling and data collection methodologies, the small sample size can make these data unstable, particularly if use is not common in the pediatric population. Verispan recommends caution interpreting projected annual uses or mentions below 100,000 as the sample size is very small with correspondingly large confidence intervals and trending variability. For instance, the diagnoses associated with the use of emtricitabine should be viewed without regard to extent of use.

## 5 CONCLUSIONS

---

<sup>3</sup> Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. October 26, 2006 1-126. Available at <http://aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf>. Accessed (July 31, 2007)

<sup>4</sup> Panel on Antiretroviral Guidelines for Adult and Adolescents. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Department of Health and Human Services. October 10, 2006; 1-113. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentsGL.pdf>. Accessed (July 31, 2007)

Emtricitabine is being used in a small number of pediatric patients. In the most recent 12-months of this analysis, Infectious Disease was the most common prescribing specialty for emtricitabine at 33%, followed by Internal Medicine at 25%. Prescriptions by pediatricians accounted for less than 1% of all dispensed prescriptions for emtricitabine during each year of this analysis. Examining product usage by diagnosis, emtricitabine was the most commonly mentioned drug product associated with the indication “HIV and specific infection” in the pediatric and adult population during the entire study period.

## **APPENDICES**

### ***APPENDIX 1: Database Descriptions***

---

#### ***Verispan, LLC: Vector One: National (VONA)***

Verispan’s VONA measures retail dispensing of prescriptions or the frequency with which drugs move out of retail pharmacies into the hands of consumers via formal prescriptions. Information on the physician specialty, the patient’s age and gender, and estimates for the numbers of patients that are continuing or new to therapy are available.

The Vector One database integrates prescription activity from a variety of sources including national retail chains, mass merchandisers, mail order pharmacies, pharmacy benefits managers and their data systems, and provider groups. Vector One receives over 2 billion prescription claims, representing over 160 million unique patients.

Prescriptions are captured from a sample of approximately 54,000 pharmacies throughout the US. The pharmacies in the data base account for nearly all retail pharmacies and represent approximately 50% of retail prescriptions dispensed nationwide. Verispan receives all prescriptions from approximately one-third of the stores and a significant sample of prescriptions from the remaining stores.

#### ***Verispan, LLC: Vector One: Total Patient Tracker (TPT)***

Verispan’s Total Patient Tracker is a national-level projected audit designed to estimate the total number of unique patients across all drugs and therapeutic classes in the retail outpatient setting. TPT derives its data from the Vector One database which integrates prescription activity from a variety of sources including national retail chains, mail order pharmacies, mass merchandisers, pharmacy benefits managers and their data systems. Vector one receives over 2 billion prescription claims per year, which represents over 160 million patients tracked across time.

#### ***Verispan, LLC: (Physician Drug & Diagnosis Audit) PDDA***

Verispan’s Physician Drug & Diagnosis Audit (PDDA) is a monthly survey designed to provide descriptive information on the patterns and treatment of diseases encountered in office-based physician practices in the U.S. The survey consists of data collected from approximately 3,100 office-based physicians representing 29 specialties across the United States that report on all patient activity during one typical workday per month. These data may include profiles and trends of diagnoses, patients, drug products mentioned during the office visit and treatment patterns. The data are then projected nationally by physician specialty and region to reflect national prescribing patterns.

Verispan uses the term "drug uses" to refer to mentions of a drug in association with a diagnosis during an office-based patient visit. This term may be duplicated by the number of diagnosis for which the drug is mentioned. It is important to note that a "drug use" does not necessarily result in prescription being generated. Rather, the term indicates that a given drug was mentioned during an office visit.

***Premier***

Premier's database is a large hospital drug utilization and financial database. Information is available from over 450 acute care and pediatric facilities and includes approximately 16 million inpatient records. On an annual basis, this constitutes roughly one out of every seven inpatient discharges in the United States. Data are available from January 2000 through the present, but have a lag time of approximately six months. Premier's primary mission is to assist health care institutions improve clinical and operating performance in three strategic areas: group purchasing, supply chain and healthcare informatics. To that end, the Premier Informatics group developed this database in part to analyze utilization of resources to improve clinical efficiency.

The hospitals that contribute information to this database are a select sample of both Premier and U.S. institutions, and do not necessarily represent all hospitals in the U.S. Data are collected from this sample of participating hospitals with diverse characteristics based upon geographic location, bed size, population served, payers and teaching status. The data collected include demographic and pharmacy-billing information, as well as all diagnoses and procedures for every patient discharge. Preliminary comparisons between participating Premier hospital and patient characteristics and those of the probability sample of hospitals and patients selected for the National Hospital Discharge Survey (NHDS) proved to be very similar with regard to patient age, gender, length of stay, mortality, primary discharge diagnosis and primary procedure groups. Based upon these analyses, FDA believes that most estimates of national inpatient drug use based on Premier data appear to be reasonable, but strongly recommends making this determination on a drug-specific basis.

***IMS Health: IMS, National Sales Perspectives Retail, Non-Retail or Combined (NSP)***

The IMS Health, IMS National Sales Perspective measures the volume of drug products (both prescription and over-the-counter) and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, food stores, and mail service. Outlets within the non-retail market include clinics, non-federal hospitals, federal facilities, HMOs, long-term care facilities, home health care, and other miscellaneous settings. IMS National Sales Perspectives™ measures the volume of drug products moving from manufacturer into retail and non-retail settings in terms of sales dollars, eaches, extended units, and share of market. These data are based on national projections.

APPENDIX 2: Tables and Figures

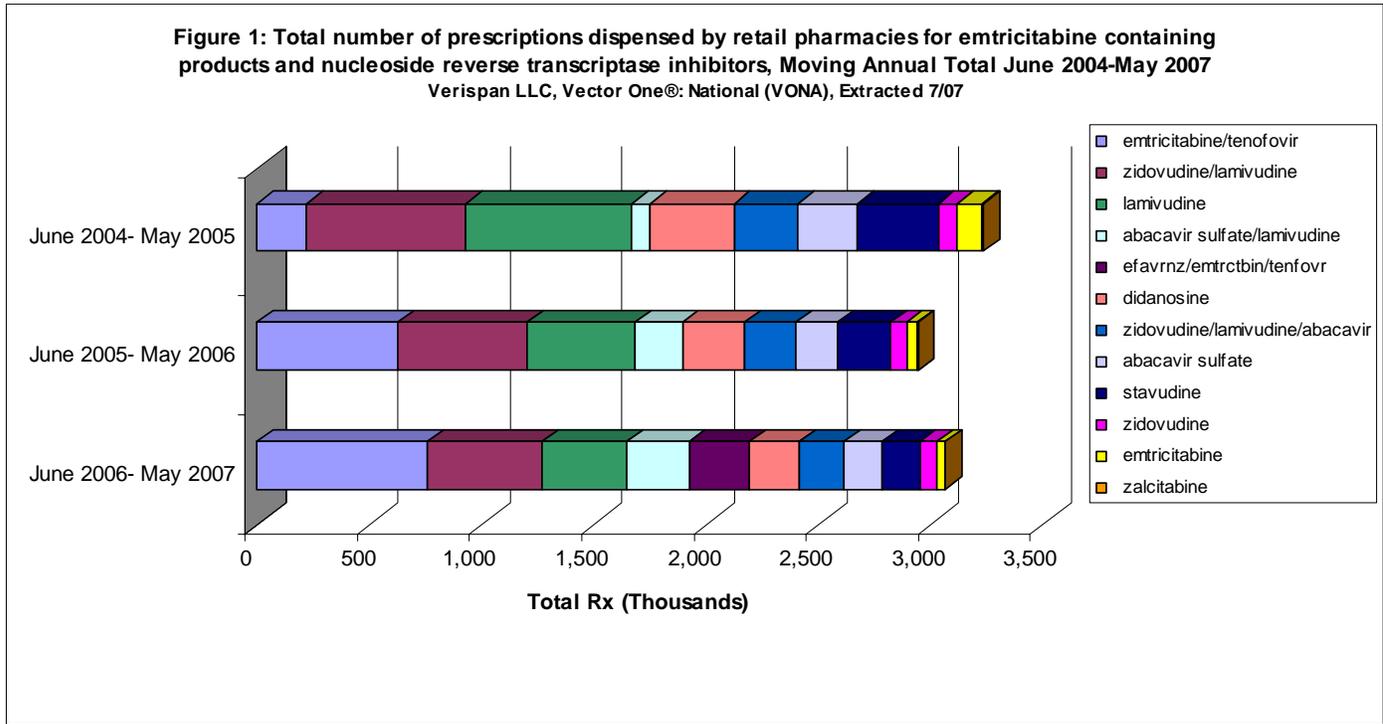
**Table 2: Projected number of total extended units\* of emtricitabine (in thousands) sold to specific channels<sup>§</sup> in the U.S., moving annual totals June 2004 through May 2007**

	June 2004- May 2005		June 2005- May 2006		June 2006- May 2007	
	Extended Units	Share	Extended Units	Share	Extended Units	Share
	N (000)	%	N (000)	%	N (000)	%
<b>Emtricitabine</b>	<b>5,666</b>	<b>100.0%</b>	<b>2,454</b>	<b>100.0%</b>	<b>2,253</b>	<b>100.0%</b>
<b>Retail</b>	<b>3,876</b>	<b>100.0%</b>	<b>626,721</b>	<b>66.2%</b>	<b>1,288</b>	<b>57.1%</b>
<b>Capsules</b>	<b>3,876</b>	<b>100.0%</b>	<b>1,623</b>	<b>99.0%</b>	<b>1,209</b>	<b>93.9%</b>
<b>Oral Solution</b>	<b>--</b>	<b>--</b>	<b>1,606</b>	<b>1.0%</b>	<b>77</b>	<b>6.4%</b>
<b>Non-Retail</b>	<b>1,791</b>	<b>31.6%</b>	<b>830</b>	<b>33.7%</b>	<b>966</b>	<b>42.8%</b>
<b>Capsules</b>	<b>1,791</b>	<b>100.0%</b>	<b>815</b>	<b>98.2%</b>	<b>922</b>	<b>95.4%</b>
<b>Oral Solution</b>	<b>--</b>	<b>--</b>	<b>15</b>	<b>1.8%</b>	<b>44</b>	<b>4.6%</b>
<b>Mail Service</b>	<b>753</b>	<b>13.3%</b>	<b>371</b>	<b>15.1%</b>	<b>300</b>	<b>13.3%</b>
<b>Capsules</b>	<b>753</b>	<b>100.0%</b>	<b>363</b>	<b>97.9%</b>	<b>288</b>	<b>96.1%</b>
<b>Oral Solution</b>	<b>--</b>	<b>--</b>	<b>8</b>	<b>2.1%</b>	<b>12</b>	<b>3.9%</b>

IMS HEALTH, IMS National Sales Perspective™, June 2004 - May 2007, Data extracted 6-2007. Source File: NSPC 2007-1092 emtriva 6-29-07 0706emtr.dvr

\*Extended Units are the number of individual tablets, capsules, etc. for solids; number of grams or milliliters for other forms.

§Retail Channels: Food Stores, Chain Pharmacies, Independent Pharmacies, Mail Order Pharmacies. Non-Retail Channels: Long Term Care Facilities, Clinics, Non-Federal Hospitals, Prisons, Federal Facilities, Home Health Care, HMOs, Universities.



**Table 3. Total number of prescriptions dispensed by retail pharmacies for Emtriva by patient age, Moving Annual Total June 2004 through May 2007 (mail order pharmacies not included)**

	June 2004- May 2005		June 2005- May 2006		June 2006- May 2007	
	Retail TRxs	Share	Retail TRxs	Share	Retail TRxs	Share
	N	%	N	%	N	%
<b>TOTAL MARKET</b>	<b>336,746</b>	<b>100.0%</b>	<b>673,213</b>	<b>100.0%</b>	<b>1,065,326</b>	<b>100.0%</b>
<b>Truvada</b>	221,476	65.8%	626,719	93.1%	759,474	71.3%
<b>0-16</b>	825	0.4%	2,110	0.3%	2,579	0.3%
<b>0-1</b>	53	0.0%	40	0.0%	54	0.0%
<b>2-5</b>	58	0.0%	96	0.0%	31	0.0%
<b>6-10</b>	116	0.1%	198	0.0%	236	0.0%
<b>11-16</b>	598	0.3%	1,776	0.3%	2,258	0.3%
<b>17+</b>	219,187	99.0%	621,224	99.1%	754,808	99.4%
<b>UNSPEC.</b>	1,464	0.7%	3,385	0.5%	2,087	0.3%
<b>Atripla</b>	--	--	--	--	269,531	25.3%
<b>0-16</b>	--	-	--	-	540	0.2%
<b>0-1</b>	--	--	--	--	8	0.0%
<b>2-5</b>	--	--	--	--	2	0.0%
<b>6-10</b>	--	--	--	--	69	0.0%
<b>11-16</b>	--	--	--	--	461	0.2%
<b>17+</b>	--	--	--	--	268,263	99.5%
<b>UNSPEC.</b>	--	--	--	--	728	0.3%
<b>Emtriva</b>	<b>115,270</b>	<b>34.2%</b>	<b>46,494</b>	<b>6.9%</b>	<b>36,321</b>	<b>3.4%</b>
<b>0-16</b>	<b>725</b>	<b>0.6%</b>	<b>353</b>	<b>0.8%</b>	<b>538</b>	<b>1.5%</b>
<b>0-1</b>	<b>1</b>	<b>0.0%</b>	<b>1</b>	<b>0.0%</b>	<b>6</b>	<b>0.0%</b>
<b>2-5</b>	<b>104</b>	<b>0.1%</b>	<b>2</b>	<b>0.0%</b>	<b>20</b>	<b>0.1%</b>
<b>6-10</b>	<b>49</b>	<b>0.0%</b>	<b>41</b>	<b>0.1%</b>	<b>83</b>	<b>0.2%</b>
<b>11-16</b>	<b>571</b>	<b>0.5%</b>	<b>309</b>	<b>0.7%</b>	<b>429</b>	<b>1.2%</b>
<b>17+</b>	<b>113,709</b>	<b>98.6%</b>	<b>45,812</b>	<b>98.5%</b>	<b>35,636</b>	<b>98.1%</b>
<b>UNSPEC.</b>	<b>836</b>	<b>0.7%</b>	<b>329</b>	<b>0.7%</b>	<b>147</b>	<b>0.4%</b>

\*Verispan, LLC, Vector One® National (VONA), Data extracted 7-2007. Source File: 2007-1092 emtriva age 7-9-07.qry

**Table 4: Total number of patients\* receiving a prescription for Emtriva®, Truvada®, and Atripla® in outpatient retail pharmacies by patient age, Moving Annual Total June 2004 through May 2007 (mail order pharmacies not included)**

Custom Age Group	June 2004- May 2005		June 2005- May 2006		June 2006- May 2007	
	Projected Patient Count	Share %	Projected Patient Count	Share %	Projected Patient Count	Share %
<b>EMTRIVA®</b>	<b>26,521</b>	<b>34.91%</b>	<b>9,373</b>	<b>7.41%</b>	<b>7,153</b>	<b>3.85%</b>
0-16	253	0.95%	95	1.01%	106	1.48%
0 - 2	62	0.23%	1	0.02%	12	0.16%
3 - 5	53	0.20%	2	0.02%	4	0.05%
6 - 10	22	0.08%	10	0.11%	16	0.22%
11 - 16	172	0.65%	79	0.85%	88	1.23%
17+	26,071	98.30%	9,221	98.38%	7,024	98.19%
Unknown Age	886	.034%	339	3.62%	148	2.06%
<b>TRUVADA®</b>	<b>59,712</b>	<b>78.61%</b>	<b>119,470</b>	<b>94.49%</b>	<b>143,247</b>	<b>77.10%</b>
0-16	307	0.51%	479	0.40%	695	0.49%
0 - 2	36	0.06%	54	0.05%	25	0.02%
3 - 5	21	0.04%	10	0.01%	10	0.01%
6 - 10	36	0.06%	47	0.04%	57	0.04%
11 - 16	215	0.036%	385	0.32%	610	0.43%
17+	59,018	98.84%	118,349	99.06%	142,174	99.25%
Unknown Age	1,481	2.48%	3,442	2.33%	1,911	1.33%
<b>ATRIPLA®</b>	<b>---</b>	<b>---</b>	<b>---</b>	<b>---</b>	<b>61,344</b>	<b>33.02%</b>
0-16					160	0.26%
0 - 2					5	0.01%
6 - 10					20	0.03%
11 - 16					136	0.22%
17+					61,028	99.48%
Unknown Age					734	1.20%

\*Subtotals may not sum exactly, due to rounding. Due to aging of patients during the study period ("the cohort effect"), patients may be counted more than once in the individual age categories. For this reason, summing across age bands is not advisable and will result in overestimates of patient counts.

Source: Verispan, LLC: Total Patient Tracker, June 2004 -May 2007, Extracted July07. File: TPT Emtriva 2007-1092 7-9-



-----  
**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
-----

/s/

-----  
Kendra Worthy  
8/21/2007 11:28:46 AM  
DRUG SAFETY OFFICE REVIEWER

Solomon Iyasu  
8/22/2007 01:02:05 PM  
MEDICAL OFFICER