

This label may not be the latest approved by FDA.
For current labeling information, please visit <https://www.fda.gov/drugs>

Each film-coated tablet contains:
Efavirenz, USP 600 mg

Usual Dosage: See accompanying
prescribing information.

**Keep this and all medication out of
the reach of children.**

**Store at 20° to 25°C (68° to 77°F).
[See USP Controlled Room
Temperature.]**

Manufactured for:
Mylan Pharmaceuticals Inc.
Morgantown, WV 26505 U.S.A.
Made in India

 **Mylan®** | Mylan.com

RMX22 33H2

NDC 0378-2233-93

Efavirenz
Tablets, USP

600 mg

**ALERT: Find out about medicines that should
NOT be taken with Efavirenz Tablets, USP.**

Note to Pharmacist: Do not cover ALERT box with
pharmacy label.

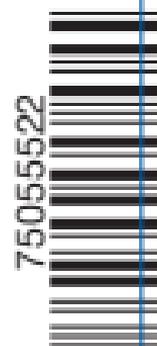
 **Mylan®**

Rx only

30 Tablets



Dispense in original container with
attached prescribing information that
contains the Patient Information Leaflet.
Keep container tightly closed.
Code No.: MH/DRUGS/25/NKD/89



*(36 x 15 mm)
Varnish Free area for
Variable Data Coding*



HIGHLIGHTS OF PRESCRIBING INFORMATION

The following information is not intended to be used as a guide to therapy. The information is intended to be used in conjunction with the full prescribing information for EFV/NRZ TABLETS.

EFV/NRZ TABLETS USP, for oral use

Initial U.S. Approval: 1998

RECENT MAJOR CHANGES

Contraindications, Contraindicated Drugs (4.2) Revised 5/2014

Warnings and Precautions, Drug Interactions (5.1) Revised 5/2014

INDICATIONS AND USAGE

EFV/NRZ TABLETS USP are a non-nucleoside reverse transcriptase inhibitor indicated in combination with other antiretroviral agents for the treatment of human immunodeficiency virus type 1 infection in adults and in pediatric patients. (1)

DOSE AND ADMINISTRATION

- EFV/NRZ TABLETS USP should be taken orally once daily on an empty stomach, preferably at bedtime. (2)
• Recommended adult dose: 600 mg. (2.1)
• Pediatric dosing is based on weight. (2.2)

DOSE FORMS AND STRENGTHS

- Tablets: 600 mg (3)

CONTRAINDICATIONS

• EFV/NRZ TABLETS USP are contraindicated in patients with previously demonstrated hypersensitivity (e.g., Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to any of the components of this product. (4.1)

WARNINGS AND PRECAUTIONS

- Do not use as a single agent or add on as a sole agent to a failing regimen. Consider potential for cross-resistance when choosing other agents. (5.2)
• Not recommended with ART/PLA which contains efavirenz, entricarbicab, and tenofovir disoproxil fumarate, unless needed for dose adjustment when coadministered with rifampin. (5.3)
• Serious psychiatric symptoms: Immediate medical evaluation is recommended for serious psychiatric symptoms such as severe depression or suicidal ideation. (5.4, 17)
• Nervous system symptoms (NSS): NSS are frequent, and usually begin 1 to 2 days after initiating therapy and resolve in 2 to 4 weeks. Dosing at bedtime may improve tolerability. NSS are not predictive of onset of psychiatric symptoms. (5.5, 6.1, 17)
• Embryo-Fetal Toxicity: Avoid administration in the first trimester of pregnancy as fetal harm may occur. (5.6, 8.1)

- Hepatotoxicity: Monitor liver function tests before and during treatment in patients with underlying hepatic disease, including hepatitis B or C infection, marked transaminase elevations, or who are taking medications associated with liver toxicity. Among reported cases of hepatic failure, a few occurred in patients with no pre-existing hepatic disease. (5.8, 6.1, 8.6)
• Rash: Rash usually begins within 1 to 2 weeks after initiating therapy and resolves within 4 weeks. Discontinue if severe rash develops. (5.7, 6.1, 17)
• Seizures: Use caution in patients with a history of seizures. (5.9)
• Lipids: Total cholesterol and triglyceride elevations. Monitor before therapy and periodically thereafter. (5.10)
• Immune reconstitution syndrome: May necessitate further evaluation and treatment. (5.11)
• Redistribution/accumulation of body fat: Observed in patients receiving antiretroviral therapy. (5.12, 17)

ADVERSE REACTIONS

Most common adverse reactions (> 5%, moderate-severe) are impaired concentration, abnormal dreams, rash, dizziness, nausea, headache, fatigue, insomnia, and vomiting. (5, 6)

To report SUSPECTED ADVERSE REACTIONS, contact Mylan Pharmaceuticals Inc. at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Coadministration of efavirenz can alter the concentrations of other drugs and other drugs may alter the concentrations of efavirenz. The potential for drug-drug interactions should be considered before and during therapy. (7.1, 12.3)

USE IN SPECIFIC POPULATIONS

- Lactation: Breastfeeding not recommended. (8.2)
• Females and males of reproductive potential: Pregnancy testing and contraception are recommended. (8.3)
• Hepatic impairment: Efavirenz is not recommended for patients with moderate or severe hepatic impairment. Use caution in patients with mild hepatic impairment. (8.6)
• Pediatric patients: The incidence of rash was higher than in adults. (5.7, 6.2, 8.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

REVISED APRIL 2014

MLXEFV.R4

Additional pediatric use information is approved for Bristol-Myers Squibb Company's Sustiva® (efavirenz). However, due to Bristol-Myers Squibb Company's marketing exclusivity rights, this drug product is not labeled with that information.

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* Sections or subsections omitted from the full prescribing information are not listed.

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, the adverse reaction rates reported cannot be directly compared to rates in other clinical studies and may not reflect the rates observed in clinical practice.

Adverse Reactions in Adults: The most common (> 5% in either efavirenz treatment group) adverse reactions of at least moderate severity among patients in Study 006 treated with efavirenz in combination with zidovudine/lamivudine or indinavir were dizziness, nausea, headache, fatigue, insomnia, and vomiting.

Selected clinical adverse reactions of moderate or severe intensity observed in a 2% of efavirenz-treated patients in two controlled clinical trials are presented in Table 2.

Table 2: Selected Treatment-Emergent Adverse Reactions of Moderate or Severe Intensity Reported in a 2% of Efavirenz-Treated Patients in Studies 006 and ACTG 364

Table with 6 columns: Adverse Reaction, Efavirenz + ZDV/LAM (n=412), Efavirenz + Indinavir (n=415), Indinavir + ZDV/LAM (n=401), Efavirenz + NRTIs (n=64), Efavirenz + NRTIs (n=65), Nevirapine + NRTIs (n=66)

Body as a Whole

Table with 2 columns: Adverse Reaction, %

Central and Peripheral Nervous System

Table with 2 columns: Adverse Reaction, %

Gastrointestinal

Table with 2 columns: Adverse Reaction, %

Psychiatric

Table with 2 columns: Adverse Reaction, %

Skin & Appendages

Table with 2 columns: Adverse Reaction, %

Other agents

Table with 2 columns: Adverse Reaction, %

Anticoagulants

Table with 2 columns: Adverse Reaction, %

Anticardiacs

Table with 2 columns: Adverse Reaction, %

Phenylthiohydantoin

Table with 2 columns: Adverse Reaction, %

Antidepressants

Table with 2 columns: Adverse Reaction, %

Other agents

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3 DOSE FORMS AND STRENGTHS

• Tablets: 600 mg tablets are dark yellow, film-coated, capsular-shaped, unscored tablets debossed with MYLAN on one side of the tablet and 233 on the other side.

4 CONTRAINDICATIONS

4.1 Hypersensitivity: Efavirenz is contraindicated in patients with previously demonstrated clinically significant hypersensitivity (e.g., Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to any of the components of this product.

5 WARNINGS AND PRECAUTIONS

5.1 Drug Interactions

Efavirenz plasma concentrations may be altered by substrates, inhibitors, or inducers of CYP3A. Likewise, efavirenz may alter plasma concentrations of drugs metabolized by CYP3A or CYP2B6. The most prominent effect of efavirenz at steady-state is induction of CYP3A and CYP2B6. (See Dosage and Administration (2.2), Drug Interactions (7.1), and Pharmacokinetics (12.3).)

EFV/NRZ TABLETS USP should be taken orally once daily on an empty stomach, preferably at bedtime. Table 1 describes the recommended dose of efavirenz tablets for pediatric patients weighing at least 40 kg (See Clinical Pharmacology (12.3)). The recommended dose of efavirenz tablets for pediatric patients weighing 40 kg or greater is 600 mg once daily.

Table 1: Efavirenz Dosing in Pediatric Patients

Table with 3 columns: Patient Body Weight, Efavirenz Tablets Daily Dose, Number of Tablets and Strength to Administer

* Tablets must not be crushed.

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Drug	Dose	Efavirenz Dose	Number of Subjects	Efavirenz (mean % change)		
				C _{max} (90% CI)	AUC (90% CI)	C _{min} (90% CI)
Lamivudine	150 mg q12h x 14 days	600 mg qd x 14 days	9	↔	↔	↑ 265% (37% to 873%)
Tenofovir [†]	300 mg qd	600 mg qd x 14 days	29	↔	↔	↔
Zidovudine	300 mg q12h x 14 days	600 mg qd x 14 days	9	↔	↔	↑ 225% (43% to 640%)
Maraviroc	100 mg bid	600 mg qd	12	↓ 51% (37% to 62%)	↓ 45% (38% to 51%)	↓ 45% (28% to 57%)
Raltegravir	400 mg single dose	600 mg qd	9	↓ 36% (2% to 59%)	↓ 36% (20% to 48%)	↓ 21% (↓ 51% to 128%)
Boceprevir	800 mg tid x 6 days	600 mg qd x 16 days	NA	↔	↔	↓ 44% (26% to 58%)
Simeprevir	150 mg qd x 14 days	600 mg qd x 14 days	23	↓ 51% (↓ 22% to 1 8%)	↓ 19% (11% to 25%)	↓ 91% (↓ 88% to 1 92%)
Azithromycin	600 mg single dose	400 mg qd x 7 days	14	↑ 22% (4% to 42%)	↔	NA
Clarithromycin 14-OH metabolite	500 mg q12h x 7 days	400 mg qd x 7 days	11	↓ 26% (15% to 35%)	↓ 39% (30% to 46%)	↓ 53% (42% to 63%)
Fluconazole	200 mg x 7 days	400 mg qd x 7 days	10	↔	↔	↔
Itraconazole Hydroxy-itraconazole	200 mg q12h x 28 days	600 mg qd x 14 days	18	↓ 37% (20% to 53%)	↓ 39% (21% to 53%)	↓ 44% (27% to 58%)
Posaconazole	400 mg (oral suspension) bid x 10 and 20 days	400 mg qd x 10 and 20 days	11	↓ 45% (34% to 53%)	↓ 50% (40% to 57%)	NA
Rifabutin	300 mg qd x 14 days	600 mg qd x 14 days	9	↓ 32% (15% to 46%)	↓ 38% (28% to 47%)	↓ 45% (31% to 56%)
Voriconazole	400 mg po q12h x 1 day, then 200 mg po q12h x 8 days	400 mg qd x 9 days	NA	↓ 61%*	↓ 77%*	NA
Artemether/lumefantrine	Artemether 20 mg/lumefantrine 120 mg tablets (six 4-tablet doses over 3 days)	600 mg qd x 26 days	12	↓ 21%	↓ 51%	NA
Artemether dihydro-artemisinin-lumefantrine	Artemether dihydro-artemisinin-lumefantrine	600 mg qd x 26 days	12	↓ 38%	↓ 46%	NA
Atorvastatin	10 mg qd x 4 days	600 mg qd x 15 days	14	↓ 14% (1% to 26%)	↓ 43% (34% to 50%)	↓ 69% (49% to 81%)
Total active (including metabolites)				↓ 15% (2% to 28%)	↓ 32% (21% to 41%)	↓ 48% (23% to 64%)
Pravastatin	40 mg qd x 4 days	600 mg qd x 15 days	13	↓ 32% (↓ 59% to 1 12%)	↓ 44% (26% to 57%)	↓ 19% (0% to 35%)
Simvastatin	40 mg qd x 4 days	600 mg qd x 15 days	14	↓ 72% (63% to 79%)	↓ 68% (62% to 73%)	↓ 45% (20% to 62%)
Total active (including metabolites)				↓ 68% (55% to 78%)	↓ 60% (52% to 68%)	NA
Carbamazepine	200 mg qd x 3 days, 200 mg bid x 3 days, then 400 mg qd x 29 days	600 mg qd x 14 days	12	↓ 20% (15% to 24%)	↓ 27% (20% to 33%)	↓ 35% (24% to 44%)
Epoxide metabolite				↔	↔	↓ 13% (↓ 30% to 1 7%)
Cetirizine	10 mg single dose	600 mg qd x 10 days	11	↓ 24% (18% to 30%)	↔	NA
Diltiazem	240 mg x 21 days	600 mg qd x 14 days	13	↓ 60% (50% to 68%)	↓ 69% (55% to 79%)	↓ 63% (44% to 75%)
Desacetyl diltiazem				↓ 64% (57% to 69%)	↓ 75% (59% to 84%)	↓ 62% (44% to 75%)
N-meso-desethyl-diltiazem				↓ 28% (7% to 44%)	↓ 37% (17% to 52%)	↓ 37% (17% to 52%)
Ethinyl estradiol/Norgestimate	0.035 mg/0.25 mg x 14 days	600 mg qd x 14 days	21	↔	↔	↔
Ethinyl estradiol/Norgestrel			21	↓ 46% (39% to 52%)	↓ 64% (62% to 67%)	↓ 82% (79% to 85%)
Lovastatin			6	↓ 80% (77% to 83%)	↓ 83% (79% to 87%)	↓ 86% (80% to 90%)
Lorazepam	2 mg single dose	600 mg qd x 10 days	12	↑ 16% (2% to 32%)	↔	NA
Methadone	Stable maintenance 35 mg po 100 mg daily	600 mg qd x 14 to 21 days	11	↓ 45% (25% to 59%)	↓ 52% (33% to 66%)	NA
Bupropion	150 mg single dose (sustained-release)	600 mg qd x 14 days	13	↓ 34% (21% to 47%)	↓ 55% (48% to 62%)	NA
Hydroxy-bupropion				↑ 50% (20% to 80%)	↔	NA
Paroxetine	20 mg qd x 14 days	600 mg qd x 14 days	16	↔	↔	↔
Sertraline	50 mg qd x 14 days	600 mg qd x 14 days	13	↓ 29% (15% to 40%)	↓ 39% (27% to 50%)	↓ 46% (31% to 58%)

† Indicates increase. ↓ Indicates decrease. ↔ Indicates no change or a mean increase or decrease of < 10%.
* Compared with zidovudine 400 mg qd alone.
† Comparator dose of indinavir was 800 mg q8h x 10 days.
* Parallel-group design; n for efavirenz + lopinavir/ritonavir, n for lopinavir/ritonavir alone.
† Values are for lopinavir; the pharmacokinetics of ritonavir in this study were unaffected by concurrent efavirenz.
* 90% CI.
† Soft Gelatin Capsule.
* Tenofovir disoproxil fumarate.
* 90% CI not available.
† Relative to steady-state administration of voriconazole 400 mg for 1 day, then 200 mg po q12h for 2 days.
† Not available because of insufficient data.
NA = not available.

Table 8: Effect of Coadministered Drug on Efavirenz Plasma C_{max}, AUC, and C_{min}

12.4 Microbiology
Mechanism of Action: Efavirenz is an NNRTI of HIV-1. Efavirenz activity is mediated predominantly by noncompetitive inhibition of HIV-1 reverse transcriptase. HIV-2 reverse transcriptase and human cellular DNA polymerases α, β, γ, and δ are not inhibited by efavirenz.
Antiviral Activity in Cell Culture: The concentration of efavirenz inhibiting replication of wild-type laboratory adapted strains and clinical isolates in cell culture by 90% to 95% (EC₅₀) ranged from 1.7 to 25 nM in lymphoblastoid cell lines, peripheral blood mononuclear cells (PBMCs), and macrophage/microglia cells. Efavirenz demonstrated antiviral activity against clade B and most non-clade B isolates (subtypes A, AE, AG, C, D, F, G, I, N), but had reduced antiviral activity against group O viruses. Efavirenz demonstrated additive antiviral activity without cytotoxicity against HIV-1 in cell culture when combined with the NNRTIs delamanvir and nevirapine, NRTIs (abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir, zalcitabine, zidovudine), PIs (amprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir), and the fusion inhibitor enfuvirtide. Efavirenz demonstrated additive to antagonistic antiviral activity in cell culture with atazanavir. Efavirenz was not antagonistic with abeditero, used for the treatment of hepatitis B virus infection, or ribavirin, used in combination with interferon for the treatment of hepatitis C virus infection.
Resistance: In Cell Culture: In cell culture, HIV-1 isolates with reduced susceptibility to efavirenz (> 380-fold increase in EC₅₀ values) emerged rapidly in the presence of drug. Genotypic characterization of these viruses identified single amino acid substitutions L100I or W179D, double substitutions L100V/I108L, and triple substitutions L100V/W179D/V181C in reverse transcriptase.
Clinical Studies: Clinical studies with reduced susceptibility in cell culture to efavirenz have been obtained. One or more substitutions at amino acid positions 98, 100, 101, 103, 106, 108, 188, 190, 225, and 227 in reverse transcriptase were observed in patients failing treatment with efavirenz in combination with indinavir, or with zidovudine plus lamivudine. The K103N substitution was the most frequently observed. Long-term resistance surveillance (average 52 weeks, range 4 to 106 weeks) analyzed 28 matching baseline and virologic failure isolates. Sixty-one percent (17/28) of these failure isolates had decreased efavirenz susceptibility in cell culture with a median 88-fold change in efavirenz susceptibility (EC₅₀ values) from reference. The most frequent NNRTI substitution to develop in these patient isolates was K103N (54%). Other NNRTI substitutions that developed included L100I (7%), K101E/Q/R (14%), V108I (11%), G190S/T/A (7%), P225H (18%), and M230V (11%).
Cross-Resistance: Cross-resistance among NNRTIs has been observed. Clinical isolates previously characterized as efavirenz-resistant were also phenotypically resistant in cell culture to delamanvir and nevirapine compared to baseline. Delamanvir and/or nevirapine-resistant clinical virus isolates with NNRTI resistance-associated substitutions (A98G, L100I, K101E/P, K103N/S, V106A, Y181X, Y188X, Y192H, F227I, or M230L) showed reduced susceptibility to efavirenz in cell culture. Greater than 90% of NNRTI-resistant clinical isolates tested in cell culture retained susceptibility to efavirenz.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: Long-term carcinogenicity studies in mice and rats were carried out with efavirenz. Mice were dosed with 0, 25, 75, 150, or 300 mg/kg/day for 2 years. Incidences of hepatocellular adenomas and carcinomas and pulmonary alveolar/bronchiolar adenomas were increased above background in females. No increases in tumor incidence above background were seen in males. There was no NOAEL in females established for this study because tumor findings occurred at all doses. AUC at the NOAEL (150 mg/kg) in the males was approximately 0.9 times that in humans at the recommended clinical dose. In the rat study, no increases in tumor incidence were observed up to 100 mg/kg/day, for which AUCs were 0.1 (males) or 0.2 (females) times those in humans at the recommended clinical dose.
Mutagenesis: Efavirenz tested negative in a battery of *in vitro* and *in vivo* genotoxicity assays. These included bacterial mutagenicity assays in *S. typhimurium* and *E. coli*, mammalian mutagenicity assays in Chinese hamster ovary cells, chromosome aberration assays in human peripheral blood lymphocytes or Chinese hamster ovary cells, and an *in vivo* mouse bone marrow micronucleus assay.
Impairment of Fertility: Efavirenz did not impair mating or fertility of male or female rats, and did not affect sperm of treated male rats. The reproductive performance of offspring born to female rats given efavirenz was not affected. The AUCs at the NOAEL values in male (200 mg/kg) and female (100 mg/kg) rats were approximately ≤ 0.15 times that in humans at the recommended clinical dose.

13.2 Animal Toxicology
Nonfatal convulsions were observed in 6 of 20 monkeys receiving efavirenz doses yielding plasma AUC values 4- to 13-fold greater than those in humans given the recommended dose (see **Warnings and Precautions** (5.9)).
14 CLINICAL STUDIES
14.1 Adults
Study 006: A randomized, open-label trial, compared efavirenz (600 mg once daily) + zidovudine (ZDV, 300 mg q12h) + lamivudine (LAM, 150 mg q12h) or efavirenz (600 mg once daily) + indinavir (IDV, 1000 mg q8h) with indinavir (800 mg q8h) + zidovudine (300 mg q12h) + lamivudine (150 mg q12h). Twelve hundred sixty-six patients (mean age 36.5 years [range 18 to 81], 50% female) were randomized to either efavirenz, lamivudine, indinavir, NNRTI-, and PI-based study entry. The median baseline CD4+ cell count was 320 cells/mm³ and the median baseline HIV-1 RNA level was 4.8 log₁₀ copies/mL. Treatment outcomes with standard assay (assay limit 400 copies/mL) through 48 and 168 weeks are shown in Table 9. Plasma HIV RNA levels were quantified with standard (assay limit 400 copies/mL) and ultrasensitive (assay limit 50 copies/mL) versions of the AMPLICOR HIV-1 MONITOR assay. During the study, version 1.5 of the assay was introduced in Europe to enhance detection of non-clade B virus.

Outcome	Efavirenz + ZDV + LAM (n = 422)		Efavirenz + IDV (n = 429)		IDV + ZDV + LAM (n = 415)	
	Week 48	Week 168	Week 48	Week 168	Week 48	Week 168
Responder ^a	69%	48%	57%	40%	50%	29%
Virologic failure ^b	6%	12%	15%	20%	13%	19%
Discontinued for adverse events	7%	8%	6%	8%	16%	20%
Discontinued for other reasons ^c	17%	31%	22%	32%	21%	32%
CD4+ cell count (cells/mm ³)						
Observed subjects (n)	(279)	(205)	(256)	(158)	(228)	(129)
Mean change from baseline	190	329	191	319	180	329

^a Patients achieved and maintained confirmed HIV-1 RNA < 400 copies/mL through Week 48 or Week 168.
^b Includes patients who rebounded, patients who were on study at Week 48 and failed to achieve confirmed HIV-1 RNA < 400 copies/mL at time of discontinuation, and patients who discontinued due to lack of efficacy.
^c Includes consent withdrawn, lost to follow-up, noncompliance, never treated, missing data, protocol violation, death, and other reasons. Patients with HIV RNA < 400 copies/mL who chose not to continue in the voluntary extension phases of the study were censored at date of last dose of study medication.

For patients treated with efavirenz + zidovudine + lamivudine, efavirenz + indinavir, or indinavir + zidovudine + lamivudine, the percentage of responders with HIV-1 RNA < 50 copies/mL was 65%, 50%, and 45%, respectively, through 48 weeks, and 43%, 31%, and 23%, respectively, through 168 weeks. A Kaplan-Meier analysis of time to loss of virologic response (HIV RNA < 400 copies/mL) suggests that both the trends of virologic response and differences in response continue through 4 years.
ACTG 384 is a randomized, double-blind, placebo-controlled, 48-week study in NRTI-experienced patients who had completed two prior ART studies. One-hundred ninety-six patients (mean age 41 years [range 19 to 76], 74% Caucasian, 85% male) received NRTIs in combination with efavirenz (600 mg once daily), or nevirapine (NFV, 750 mg three times daily), or efavirenz (600 mg once daily) + nevirapine in a randomized, double-blinded manner. The mean baseline CD4+ cell count was 395 cells/mm³ and mean baseline HIV-1 RNA level was 8.130 copies/mL. Upon entry into the study, all patients were assigned to an open-label NRTI regimen, which was dependent on their previous NRTI treatment experience. There was no significant difference in the mean CD4+ cell count among treatment groups; the overall mean change was approximately 100 cells at 48 weeks among patients who continued on study regimens. Treatment outcomes are shown in Table 10. Plasma HIV RNA levels were quantified with the AMPLICOR HIV-1 MONITOR assay using a lower limit of quantification of 500 copies/mL.

Outcome	Efavirenz + NFV + NRTIs (n = 65)	Efavirenz + NRTIs (n = 65)	NFV + NRTIs (n = 66)
	HIV-1 RNA < 500 copies/mL ^b	71%	63%
HIV-1 RNA ≥ 500 copies/mL ^b	17%	34%	54%
CDC Category C Event	2%	0%	0%
Discontinuations for adverse events ^c	3%	3%	5%
Discontinuations for other reasons ^d	8%	0%	0%

^a For some patients, Week 56 data were used to confirm the status at Week 48.
^b Subjects achieved virologic response (two consecutive viral loads < 500 copies/mL) and maintained it through Week 48.
^c Includes viral rebound and failure to achieve confirmed < 500 copies/mL by Week 48.
^d See **Adverse Reactions** (6.1) for a safety profile of these regimens.
^e Includes loss to follow-up, consent withdrawn, noncompliance.

A Kaplan-Meier analysis of time to treatment failure through 72 weeks demonstrates a longer duration of virologic suppression (HIV RNA < 500 copies/mL) in the efavirenz-containing treatment arms.

14.2 Pediatric Patients
Additional pediatric use information is approved for Bristol-Myers Squibb Company's Sustiva[®] (efavirenz). However, due to Bristol-Myers Squibb Company's marketing exclusivity rights, this drug product is not labeled with that information.

16 HOW SUPPLIED/STORAGE AND HANDLING
16.2 Tablets
Efavirenz Tablets, USP are available containing 600 mg of efavirenz, USP. The 600 mg tablets are dark yellow, film-coated, cap-sular-shaped, unscored tablets debossed with MYLAN on one side of the tablet and 233 on the other side. They are available as follows:
NDC 0378-2233-93
bottles of 30 tablets

16.3 Storage
Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]
Dispense in original container with attached prescribing information that contains the Patient Information Leaflet.

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA approved patient labeling (*Patient Information and Instructions for Use*).
Drug Interactions: A statement to patients and healthcare providers is included on the product's bottle labels.
ALERT: Find out about medicines that should NOT be taken with Efavirenz Tablets, USP.
Efavirenz tablets may interact with some drugs; therefore, patients should be advised to report to their doctor the use of any other prescription or nonprescription medication.
General Information: Patients should be informed that efavirenz tablets are not a cure for HIV-1 infection and patients may continue to experience illnesses associated with HIV-1 infection, including opportunistic infections. Patients should remain under the care of a physician while taking efavirenz tablets.
Patients should be advised to avoid doing things that can spread HIV-1 infection to others.
• Do not share or reuse needles or other injection equipment.
• Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.
• Do not have any kind of sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.
• Do not breastfeed. Mothers with HIV-1 should not breastfeed because HIV-1 can be passed to the baby in breast milk.
Dosing Instructions: Patients should be advised to take efavirenz tablets every day as prescribed. If a patient forgets to take efavirenz, tell the patient to take the missed dose right away, unless it is almost time for the next dose. Advise the patient not to take two doses at one time and to take the next dose at the regularly scheduled time. Advise the patient to see a healthcare provider if he/she needs advice in planning the best times to take his/her medicines.
Efavirenz tablets must always be used in combination with other antiretroviral drugs. Patients should be advised to take efavirenz tablets on an empty stomach, preferably at bedtime. Taking efavirenz tablets with food increases efavirenz concentrations and may increase the frequency of adverse reactions. Dosing at bedtime may improve the tolerability of nervous system symptoms [see **Dosage and Administration** (2) and **Adverse Reactions** (6.1)]. Healthcare providers should assist patients or caregivers in determining the best efavirenz dosing schedule.
Patients should call their healthcare provider or pharmacist if they have any questions.
Additional pediatric use information is approved for Bristol-Myers Squibb Company's Sustiva[®] (efavirenz). However, due to Bristol-Myers Squibb Company's marketing exclusivity rights, this drug product is not labeled with that information.

Nervous System Symptoms: Patients should be informed that central nervous system symptoms (NSS) including dizziness, insomnia, impaired concentration, drowsiness, and abnormal dreams are commonly reported during the first weeks of therapy with efavirenz tablets [see **Warnings and Precautions** (5.5)]. Dosing at bedtime may improve the tolerability of these symptoms which are likely to improve with continued therapy. Patients should be alerted to the potential for additive effects when efavirenz tablets are used concomitantly with alcohol or psychoactive drugs. Patients should be instructed that if they experience NSS they should avoid potentially hazardous tasks such as driving or operating machinery.
Psychiatric Symptoms: Patients should be informed that serious psychiatric symptoms including severe depression, suicide attempts, aggressive behavior, delusions, paranoia, and psychosis-like symptoms have been reported in patients receiving efavirenz [see **Warnings and Precautions** (5.4)]. If they experience severe psychiatric adverse experiences they should seek immediate medical evaluation. Patients should be advised to inform their physician of any history of mental illness or substance abuse.
Rash: Patients should be informed that a common side effect is rash [see **Warnings and Precautions** (5.7)]. Rashes usually go away without any change in treatment. However, since rash may be serious, patients should be advised to contact their physician promptly if rash occurs.

Females of Reproductive Potential: Advise females of reproductive potential to use effective contraception as well as a barrier method during treatment with efavirenz tablets and for 12 weeks after discontinuing efavirenz tablets. Advise patients to contact their healthcare provider if they plan to become pregnant, become pregnant, or if pregnancy is suspected during treatment with efavirenz tablets [see **Warnings and Precautions** (5.6) and **Use in Specific Populations** (8.1, 8.3)].
Pregnancy Exposure Registry: Advise patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to efavirenz during pregnancy [see **Use in Specific Populations** (8.1)].
Fat Redistribution: Patients should be informed that redistribution or accumulation of body fat may occur in patients receiving antiretroviral therapy and that the cause and long-term health effects of these conditions are not known [see **Warnings and Precautions** (5.12)].

PATIENT INFORMATION EFAVIRENZ TABLETS, USP (ef[®] v[®] ir[®] enz) 600 mg

Important: Ask your doctor or pharmacist about medicines that should not be taken with efavirenz tablets. For more information, see the section **“What should I tell my doctor before taking efavirenz tablets?”**

Read this Patient Information before you start taking efavirenz tablets and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or treatment.

What is efavirenz?
Efavirenz is a prescription HIV-1 (Human Immunodeficiency Virus type 1) medicine used with other antiretroviral medicines to treat HIV-1 infection in adults and in children who are at least 3 months old and who weigh at least 7 pounds 12 ounces (3.5 kg). HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

It is not known if efavirenz is safe and effective in children younger than 3 months of age or who weigh less than 7 pounds 12 ounces (3.5 kg).
When used with other antiretroviral medicines to treat HIV-1 infection, efavirenz may help:

- reduce the amount of HIV-1 in your blood. This is called viral load.
- increase the number of a type of CD4+ (T) cells in your blood that help fight off other infections.

Reducing the amount of HIV-1 and increasing the CD4+ (T) cells in your blood may help improve your immune system. This may reduce your risk of death or getting infections that can happen when your immune system is weak (opportunistic infections).

Efavirenz tablets do not cure HIV-1 infection or AIDS. You should keep taking HIV-1 medicines to control HIV-1 infection and decrease HIV-related illnesses.

Avoid doing things that can spread HIV-1 infection to others:

- Do not share or reuse needles or other injection equipment.
- Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor blades.
- Do not have any kind of sex without protection. Always practice safer sex by using a latex or polyurethane condom to lower the chance of sexual contact with any body fluids such as semen, vaginal secretions, or blood.

Ask your doctor if you have any questions about how to prevent passing HIV to other people.

Who should not take efavirenz tablets?

Do not take efavirenz tablets if you are allergic to efavirenz or any of the ingredients in efavirenz tablets. See the end of this leaflet for a complete list of ingredients in efavirenz tablets.

What should I tell my doctor before taking efavirenz tablets?

Before taking efavirenz tablets, tell your doctor if you have any medical conditions and in particular, if you:

- have ever had a mental health problem
- have ever used street drugs or large amounts of alcohol
- have liver problems, including hepatitis B or C virus infection
- have a history of seizures
- are pregnant or plan to become pregnant. Efavirenz may harm your unborn baby. If you are able to become pregnant your healthcare provider should do a pregnancy test before you start efavirenz tablets. You should not become pregnant while taking efavirenz tablets and for 12 weeks after stopping treatment with efavirenz tablets.

Females who are able to become pregnant should use two effective forms of birth control during treatment and for 12 weeks after stopping treatment with efavirenz tablets. A barrier form of birth control should always be used along with another type of birth control.

- Barrier forms of birth control may include latex or polyurethane condom, contraceptive sponge, diaphragm with spermicide, and cervical cap.
- Hormonal forms of birth control, such as birth control pills, injections, vaginal rings, or implants may not work during treatment with efavirenz tablets.

- Talk to your doctor about forms of birth control that may be used during treatment with efavirenz tablets.

Pregnancy Registry. There is a pregnancy registry for women who take antiretroviral medicines during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your doctor about how you can take part in this registry.

- Do not breastfeed if you take efavirenz tablets.
- You should not breastfeed if you have HIV because of the risk of passing HIV to your baby.

Tell your doctor and pharmacist about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Efavirenz tablets may affect the way other medicines work, and other medicines may affect how efavirenz tablets work, and may cause serious side effects. If you take certain medicines with efavirenz tablets, the amount of efavirenz in your body may be too low and it may not work to help control your HIV infection. The HIV virus in your body may become resistant to efavirenz or other HIV medicines that are like it.
You should not take efavirenz tablets if you take ATRIPLA (efavirenz, emtricitabine, tenofovir disoproxil fumarate) unless your doctor tells you to.
Tell your doctor and pharmacist about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with efavirenz tablets.
Keep a list of your medicines to show your doctor and pharmacist.

- You can ask your doctor or pharmacist for a list of medicines that interact with efavirenz tablets.
- Do not start taking a new medicine without telling your doctor. Your doctor can tell you if it is safe to take efavirenz tablets with other medicines.

How should I take efavirenz tablets?

- Take efavirenz tablets exactly as your doctor tells you to.
- Do not change your dose or stop taking efavirenz tablets unless your doctor tells you to.
- Stay under the care of your doctor during treatment with efavirenz tablets.
- Efavirenz tablets must be used with other antiretroviral medicines.
- Take efavirenz tablets one time each day.
- Efavirenz comes as tablets.
- Efavirenz tablets must not be broken.
- Swallow efavirenz tablets whole with liquid.

How and when to take efavirenz tablets:

- You should take efavirenz on an empty stomach at bedtime. Taking efavirenz with food increases the amount of medicine in your body. Some side effects may bother you less if you take efavirenz on an empty stomach and at bedtime.
- Your child's doctor will prescribe the right dose of efavirenz based on your child's weight.
- If you have difficulty swallowing tablets, tell your doctor.
- Do not miss a dose of efavirenz tablets. If you forget to take efavirenz, take the missed dose right away, unless it is almost time for your next dose. Do not take two doses at one time. Just take your next dose at your regularly scheduled time. If you need help in planning the best times to take your medicine, ask your doctor or pharmacist.
- If you take too much efavirenz, call your doctor or go to the nearest hospital emergency room right away.
- When your efavirenz supply starts to run low, get more from your doctor or pharmacy. It is important not to run out of efavirenz tablets. The amount of HIV-1 in your blood may increase if the medicine is stopped for even a short time. The virus may become resistant to efavirenz and harder to treat.

What are the possible side effects of efavirenz tablets?

Efavirenz tablets may cause serious side effects, including