

# Sustiva (efavirenz)



*The 200-mg capsules of Sustiva are gold-colored, reverse-printed with "SUSTIVA" on the body and imprinted with "200 mg" on the cap. Other dose formulations, including a single 600-mg capsule, are available.*



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**Also known as:** EFV, DMP-266

**Background and description.** Sustiva is a non-nucleoside reverse transcriptase inhibitor (NNRTI) originally developed and manufactured by DuPont Pharmaceuticals Company. The drug was granted approval by the US Food & Drug Administration (FDA) in September 1998 to treat HIV infection and is now owned by Bristol-Myers Squibb. The company is currently working with Gilead Sciences to develop a combination pill of Sustiva, Viread, and Emtriva as a complete, one-pill, once-a-day HIV regimen.

**Dose.** The recommended dose of Sustiva is 600 mg once a day.

**Food restrictions.** Sustiva may be taken with or without food. However, a high fat meal may increase the absorption of Sustiva and should be avoided.

**Storage.** Capsules should be stored at 77°F. Short-term variations from 59° to 86°F are acceptable.

**Patient assistance.** Patients can contact the Sustiva Reimbursement Counseling & Assistance Program at 800.334.4486.

**Side effects and toxicity.** The most common side effects of Sustiva are related to the central nervous system. In clinical trials side effects included dizziness, sleep disturbances, nightmares, hallucinations, problems concentrating, and confusion. These side effects occurred in over 50% of patients with a median duration of 21 days. Serious depression has been seen in a small number of patients, as well as treatment-related psychosis, suicidal thoughts, aggression, paranoia, and mania. Patients with a history of psychiatric problems or recreational drug use should speak with their healthcare provider before taking Sustiva to see if other options may be better. In addition, rash has been reported in approximately 30% of patients. Most rash resolves

when drug is discontinued and does not recur upon resumption. More severe cases of rash have been known to appear in children. Other side effects include nausea and diarrhea, as well as elevated lipid levels, especially when Sustiva is combined with protease inhibitors. Sustiva should not be taken by pregnant women.

**Drug interactions.** Sustiva should not be taken with the following: Hismanal (astemizole), Versed (midazolam), Halcion (triazolam), Propulsid (cisapride), Voriconazole (VFEND), and ergot derivatives such as Wigraine and Cafergot. Levels of Biaxin (clarithromycin), as well as Rifadin and Rimactane (generically known as rifampin), are reduced by Sustiva. The significance of such reduction is unknown. Levels of Mycobutin (rifabutin) are also reduced by Sustiva and a dose increase of 50% of Mycobutin (to 450 mg) should be considered. Sustiva also lowers levels of methadone. A slow increase in methadone dosing may be warranted if signs of withdrawal are seen when given concomitantly with Sustiva. St. John's Wort (*Hypericum perforatum*) is likely to decrease Sustiva levels in the body and therefore should be avoided when taking Sustiva.

Sustiva has several interaction with protease inhibitors (PIs). It should not be combined with Fortovase or Invirase since such co-administration significantly decreases their levels. Crixivan levels are reduced by Sustiva and an increase of Crixivan to 1000 mg every 8 hours should be considered. Agenerase and Sustiva should not be combined without the addition of 200 mg of Norvir or the addition of a full dose of Viracept. Sustiva lowers the levels of Kaletra. A dose increase in Kaletra (to 4 capsules twice a day) is recommended for PI-experienced patients, but not for PI-naïve patients, when combining Kaletra with Sustiva. If Reyataz is combined with Sustiva, the recommended dose is 300mg Reyataz boosted with 100 mg Norvir taken once daily in PI-naïve patients only (this combination has not been studied in PI-experienced patients).

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## Additional info:

**Resistance and cross-resistance.** A mutation at position 103 confers resistance to Sustiva and results in virologic failure. Other common mutations occur at positions 100, 108, 179, 181, and 188.

**Clinical data.** Approval of Sustiva was based on 2 clinical trials in which the response was measured as time to treatment failure. Study 006 is an ongoing, randomized, open-label trial comparing Sustiva/Crixivan against Sustiva/Retrovir/Epivir against Crixivan/Retrovir/Epivir. At 48 weeks the percentage of patients with viral loads below 50 copies/mL was 68% for the Sustiva/Retrovir/Epivir group compared to 55% for the Sustiva/Crixivan group and 49% for the Crixivan/Retrovir/Epivir group. The overall mean increase in CD4 T cells across arms was 200 cells/mm<sup>3</sup>. In August 2004, data out to 168 weeks was added to the Sustiva labeling showing that more than 40% of patients maintained undetectable viral loads when using Sustiva as part of their antiretroviral regimen.

ACTG 364 is a randomized, double-blind, placebo-controlled study in nucleoside reverse transcriptase inhibitor (NRTI)-experienced patients. Patients received Sustiva/NRTIs or Viracept/NRTIs or Sustiva/Viracept/NRTIs. The overall mean increase in CD4 T cell count was approximately 100 cells/mm<sup>3</sup> at 48 weeks among patients who continued their regimens. The percentages of patients with viral loads below 500 copies/mL were as follows: 71% for the Sustiva/Viracept/NRTIs arm; 60% for the Sustiva/NRTIs arm; and 33% for the Viracept/NRTIs arm. Additional studies have shown that Sustiva may successfully achieve and maintain viral suppression without a protease inhibitor, thus sparing protease inhibitors as a class available for subsequent therapy.

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