

<b>EFAVIRENZ (EFV) (Updated April 2010)</b>	
<b>Trade Name</b>	Sustiva
<b>Classification</b>	Non-nucleoside Reverse Transcriptase Inhibitor
<b>Form</b>	50-, 200-mg capsules; 600-mg tablets Each Atripla tablet contains EFV 600 mg, FTC 200 mg, and TDF 300 mg
<b>Dosing Recommendations</b>	600 mg once daily, preferably at bedtime on an empty stomach <i>or</i> with FTC and TDF as Atripla, 1 once daily
<b>Hepatic Impairment Dosing</b>	Monitor serum liver enzymes before and during treatment in patients with underlying hepatic disease, including hepatitis B or C co-infection, marked transaminase elevations, or who are taking medications associated with liver toxicity
<b>Food Effect</b>	Take on an empty stomach. Avoid meals with >40-60 g fat. Fatty meal ↑ EFV AUC 28%. Most experts recommended taking on an empty stomach during the first 2 weeks to minimize CNS side effects, but co-administration with food after 2 weeks is acceptable.
<b>Oral Bioavailability</b>	Data not available
<b>Serum Half-life</b>	40-55 hours
<b>Elimination</b>	Metabolized by cytochrome P450 2B6>3A4 (3A4 mixed inducer/inhibitor <i>in vitro</i> , but 3A4 inducer <i>in vivo</i> ); 14%-34% excreted in urine (glucuronidated metabolites, <1% unchanged), 16%-61% in feces
<b>Adverse Events</b>	Rash, <sup>a</sup> central nervous system symptoms (dizziness, somnolence, insomnia, abnormal dreams, confusion, impaired concentration, amnesia), <sup>b</sup> psychiatric symptoms (agitation, depression, depersonalization, hallucinations, euphoria, suicidal ideation)  Increased transaminase levels  False-positive cannabinoid test
<b>FDA Pregnancy Category</b>	D (reported cases of neural tube defect in human fetuses). Birth defects occurred in 14 of 501 live births (first trimester exposure) and 2 of 55 live births (second/third-trimester exposure)
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed
<b>Animal Teratogen Studies</b>	Positive (cynomolgus monkey-anencephaly, anophthalmia, microphthalmia)
<b>Black Box Warnings</b>	None
<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Unboosted atazanavir (for therapy-experienced patients) Fosamprenavir without ritonavir Any other NNRTIs (e.g., DLV, ETR, NVP)  Astemizole, bepridil, cisapride, ergot derivatives, garlic supplements, midazolam, <sup>c</sup> pimozone, rifapentine, St. John's wort, terfenadine, triazolam

<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<p><b>Atazanavir:</b> For therapy-naïve patients – Use ATV 400 mg + RTV 100 mg once daily with food</p> <p><b>Darunavir:</b> DRV C<sub>min</sub> ↓ 31%; EFV AUC and C<sub>min</sub> ↑ 21% and 17%, respectively – Studied dose lower than FDA approved dose. Consider using DRV/r 600/100 mg twice daily with EFV 600 mg qhs <i>or</i> DRV/r 900/100 mg once daily with EFV 600 mg qhs (based on PK data)</p> <p><b>Fosamprenavir:</b> FPV C<sub>min</sub> ↓ 36% when dosed at FPV 1400 mg + RTV 200 mg once daily – Use FPV 700 mg + RTV 100 mg twice daily, or FPV 1400 mg + RTV 300 mg once daily</p> <p><b>Indinavir:</b> IDV ↓ 31% – ↑ IDV dose to 1000 mg q8h, or consider IDV 800 mg + RTV 200 mg q12h</p> <p><b>Lopinavir/ritonavir:</b> LPV AUC ↓ 40% – ↑ LPV/r dose to 500/125 mg twice daily with food</p> <p><b>Maraviroc:</b> ↓ MVC AUC – ↑ MVC dose to 600 mg twice daily (if not co-administered with a PI)</p> <p><b>Saquinavir:</b> SQV ↓ 62%; EFV ↓ 12% – Use SQV 1000 mg + RTV 100 mg q12h</p> <p><b>Tipranavir/ritonavir:</b> Use TPV 500 mg + RTV 200 mg twice daily</p>
<b>Anticoagulants</b>	<b>Warfarin:</b> Potential ↑ or ↓ warfarin levels – Monitor warfarin levels
<b>Anticonvulsants</b>	<b>Carbamazepine, phenobarbital, phenytoin:</b> Unknown – Avoid co-administration. If no alternatives available, use with close monitoring of anticonvulsant levels
<b>Antifungals</b>	<p><b>Itraconazole, ketoconazole:</b> ↓ itra/keto – Consider alternative antifungal</p> <p><b>Voriconazole:</b> ↑ voriconazole to 400 mg q12h plus EFV 300 mg qhs. EFV should not be co-administered with voriconazole at the standard doses. In severe cases of invasive aspergillosis, consider voriconazole therapeutic drug monitoring</p> <p><b>Posaconazole</b> – avoid concomitant use unless benefit outweighs risk. Monitor posaconazole serum concentrations with co-administration</p>
<b>Antimycobacterials</b>	<p><b>Clarithromycin:</b> CL ↓ 39% – Monitor for efficacy; or, if possible, use alternative agent, such as azithromycin</p> <p><b>Rifabutin:</b> RFB ↓ 35% – ↑ RFB dose to 450-600 mg once daily or 600 mg 3x/wk</p> <p><b>Rifampin:</b> EFV ↓ 22% – Consider ↑ EFV dose to 800 mg once daily in persons &gt;60 kg</p>
<b>Calcium Channel Blocker</b>	<b>Diltiazem:</b> ↓ diltiazem – Diltiazem dose adjustment should be guided by clinical response
<b>Oral Contraceptives</b>	<b>Ethinyl estradiol:</b> EE ↑ 37% – Use alternative barrier form or additional method of contraception. Monitor for contraceptive adverse drug reactions

<b>Selective Serotonin Reuptake Inhibitors (SSRIs)</b>	<b>Sertraline:</b> ↓ sertraline – Sertraline dose adjustment should be guided by clinical response
<b>Synthetic Narcotics</b>	<b>Methadone:</b> ↓ methadone levels significantly – Monitor and titrate dose to effect

<sup>a</sup> In clinical trials, EFV was discontinued because of rash in 1.7% of patients. Rare cases of Stevens-Johnson syndrome have been reported.

<sup>b</sup> Symptoms usually subside spontaneously after 2-4 weeks.

<sup>c</sup> Patients experiencing serious psychiatric symptoms should be evaluated to assess whether symptoms may be related to EFV. If so, the clinician should discontinue use of EFV if the risks outweigh the benefits.