

# Lexiva (fosamprenavir)



*Lexiva tablets are light pink in color with "GXLL7" imprinted on one side.*



.....  
**Also known as:** fos-amprenavir calcium, 908

**Background and description.** Lexiva is a prodrug of Agenerase, a previously approved protease inhibitor used to treat HIV. Lexiva is converted into Agenerase in the body, but Lexiva is easier to take because it requires much fewer pills than Agenerase. It is manufactured by GlaxoSmithKline and Vertex Pharmaceuticals, Inc. The FDA approved Lexiva for use in treating HIV in October 2003.

**Dose.** Lexiva is supplied in tablets of 700 mg. For treatment-naïve patients, the recommended dose of Lexiva is 1,400 mg twice daily (without Norvir), 1,400 mg once daily plus 200 mg of Norvir once daily, or 700 mg twice daily plus 100 mg of Norvir twice daily. For protease inhibitor-experienced patients, the recommended dose of Lexiva is 700 mg twice daily plus 100 mg of Norvir twice daily.

**Once-daily administration of Lexiva plus Norvir is not recommended in protease inhibitor-experienced patients.** Lexiva should be taken in combination with other HIV medications.

**Food restrictions.** Lexiva tablets may be taken with or without food.

**Storage.** Lexiva should be stored at room temperature (77°F). The container should be kept tightly closed.

**Patient assistance.** For those who qualify, GlaxoSmithKline offers a patient assistance program. For more information, call 866.728.4368.

**Side effects and toxicity.** The most common side effects of Lexiva are nausea, vomiting, diarrhea, skin rash, headache, diabetes and high blood sugar (hyperglycemia), worsening of pre-existing diabetes, increased bleeding problems in some patients with hemophilia, worsening of liver disease, changes in blood tests such as liver function tests and blood fat levels, decreases in white blood cells, and changes in body fat (lipodystrophy). Severe and life-threatening

Last updated May 2005.

skin reactions, including Stevens-Johnson syndrome, have occurred in patients treated with amprenavir. This syndrome has also been reported in one patient treated with Lexiva. Acute hemolytic anemia has been reported in a patient treated with Agenerase. When taking Lexiva, caution should be exercised in patients with liver problems, kidney problems, diabetes, hemophilia, and patients who are allergic to sulfa medicines. Metabolic (lipid and glucose) and morphologic (fat accumulation and fat atrophy) abnormalities have been associated with protease inhibitors in general.

**Drug interactions.** Lexiva should not be taken with the following: Halcion (triazolam); ergot derivatives such as Cafegot, Migranal, dihydroergotamine (DHE 45), and Methergine; Propulsid (cisapride); Versed (midazolam); Orap (pimozide); Rescriptor; Rifadin or Rimactane (rifampin); St. John's wort (*Hypericum perforatum*); and cholesterol-lowering drugs such as Mevacor (lovastatin) and Zocor (simvastatin). Do not take Tambocor (flecainide) or Rhythmol (propafenone) if you are taking Lexiva and Norvir together. Agenerase and Lexiva should not be taken in the same regimen.

Also, the following medications may require a dosing change of Lexiva and/or the other medicine, and should be used with caution: HIV medications such as Sustiva, Viramune, Crixivan, Viracept, Kaletra, and Invirase or Fortovase; medicines for abnormal heart rhythm such as Cordarone (amiodarone), lidocaine, quinidine (also known as Cardioquin, Quinidex, and others) and Vasacor (bepridil); Coumadin (warfarin); anticonvulsants; antifungals; rifabutin; benzodiazepines; calcium-channel blockers; the corticosteroid dexamethasone; histamine H<sub>2</sub>-receptor antagonists, proton-pump inhibitors such as Nexium (esomeprazole); Lipitor (atorvastatin); medicines to prevent organ transplant rejection; methadone; oral contraceptives; antacids; and tricyclic antidepressants. Levels of Sildenafil (Viagra), Cialis (tadalafil), and Levitra (vardenafil) may be significantly raised in the presence of Lexiva and dose reductions are recommended.

# Agenerase (amprenavir)

## Additional info:

**Resistance and cross-resistance.** Additional data are needed to determine clinically relevant key mutations associated with Lexiva resistance. However, in patients taking Lexiva with or without Norvir boosting, the following Agenerase resistance-associated mutations were found either alone or in combination at positions 32, 46, 47, 50, 54, and 84. The mutation at position 50 is associated with high-level resistance to Agenerase. Patients with existing resistance to Agenerase will likely not obtain a significant benefit from taking Lexiva.

**Clinical data.** The approval of Lexiva was based on two studies in antiretroviral naïve patients and one study in protease inhibitor experienced patients. Study APV30001 was a randomized, open-label study comparing treatment with Lexiva (1,400 mg twice daily) versus Viracept (1250 mg twice daily) in 249 antiretroviral-naïve patients. Both treatment groups also received Ziagen (300 mg twice daily) and Epivir (150 mg twice daily). At baseline, the median CD4 cell count was 212 cells/mm<sup>3</sup> (18% of patients had a CD4 cell count of <50 cells/mm<sup>3</sup> and 30% were in the range of 50 to <200 cells/mm<sup>3</sup>). Baseline median HIV-1 RNA was 4.83 log<sub>10</sub> copies/mL (45% of patients had >100,000 copies/mL). The proportion of patients who achieved and maintained confirmed HIV RNA < 400 copies/mL through week 48 was 66% (57% for patients < 50 copies/mL) for the Lexiva group and 52% (42%) for the Viracept group, respectively. Through 48 weeks of therapy, the median increases from baseline in CD4 cell counts were 201 cells/mm<sup>3</sup> in the group receiving Lexiva and 216 cells/mm<sup>3</sup> in the Viracept group.

Study APV30002 was a randomized, open-label study comparing treatment with Lexiva (1,400 mg once daily) plus Norvir (200 mg once daily) versus Viracept (1,250 mg twice daily) in 649 treatment-naïve patients. Both treatment groups also received Ziagen (300 mg twice daily) and Epivir (150 mg twice daily). At baseline, the median CD4 cell count was 170 cells/mm<sup>3</sup> (20% of patients had a CD4 cell count of <50 cells/mm<sup>3</sup> and 35% were in the range of 50 to <200 cells/mm<sup>3</sup>). Baseline median HIV-1 RNA was 4.81 log<sub>10</sub> copies/mL (43% of patients had >100,000 copies/mL). The proportions of patients who achieved and maintained confirmed HIV RNA < 400 copies/mL (< 50 copies/mL) through week 48 was 69% (58%) for the Lexiva group and 68% (55%) for the Viracept group, respectively. Through 48 weeks of therapy, the median increases from baseline in CD4 cell counts were 203 cells/mm<sup>3</sup> in the group receiving Lexiva and 207 cells/mm<sup>3</sup> in the Viracept group.

Study APV30003 was a randomized, open-label, multicenter study comparing two different regimens of Lexiva plus Norvir (Lexiva 700 mg twice daily plus Norvir 100 mg twice daily or Lexiva 1,400 mg once daily plus Norvir 200 mg once daily) versus Kaletra twice daily in 315 patients who had experienced virologic failure to 1 or 2 prior protease inhibitor-containing regimens. The median CD4 cell count at baseline was 263 cells/mm<sup>3</sup>. Baseline median plasma HIV-1 RNA level was 4.14 log<sub>10</sub> copies/mL. The time-averaged changes in plasma HIV-1 RNA from baseline at 48 weeks (the endpoint on which the study was powered) were -1.4 log<sub>10</sub> copies/mL for twice-daily Lexiva/Norvir and -1.67 log<sub>10</sub> copies/mL for the Kaletra group. The proportion of patients who achieved and maintained confirmed HIV-1 RNA <400 copies/mL were 58% with twice-daily Lexiva/Norvir and 61% with Kaletra. The proportions of patients with HIV-1 RNA <50 copies/mL with twice-daily Lexiva/Norvir and with Kaletra were 46% and 50%, respectively. Through 48 weeks of therapy, the median increases from baseline in CD4 cell counts were 81 cells/mm<sup>3</sup> with twice-daily Lexiva/Norvir and 91 cells/mm<sup>3</sup> with Kaletra. However, the protease inhibitor-experienced patient study was not large enough to reach a definitive conclusion that Lexiva/Norvir and Kaletra are clinically equivalent.

.....

To contact The Center for AIDS,  
call **713.527.8219** or toll free  
**888.341.1788.**

P.O. Box 66306  
HOUSTON, TEXAS 77266-6306  
1407 HAWTHORNE STREET  
HOUSTON, TEXAS 77006  
E-mail: [info@centerforaids.org](mailto:info@centerforaids.org)  
Website: [www.centerforaids.org](http://www.centerforaids.org)

