

# Agenerase (amprenavir)



*The 150-mg soft, gelatin capsule of Agenerase (shown) was large, cream-white, oblong, and imprinted with "GX CC2" on one side. However, beginning in 2005, the drug is only available in 50-mg capsules and as a flavored solution (mainly for pediatric uses). The newer form of this drug, "Lexiva," was approved in 2003 and requires fewer pills of a smaller size (see Lexiva fact sheet).*



**Also known as:** APV, AMP, 141W94

**Background and description.** Agenerase received approval from the US Food and Drug Administration (FDA) in April 1999. The drug was discovered and initially developed by Vertex Pharmaceuticals and is now manufactured and distributed by GlaxoSmithKline. Agenerase is a protease inhibitor recommended for use in combination with other antiretrovirals for the treatment of HIV infection.

**Dose.** The recommended adult dose of Agenerase is 1200 mg twice a day. Alternatively, 1200 mg Agenerase with 200 mg of Norvir (as a booster) once daily or 600 mg Agenerase with 100 mg Norvir twice daily may be used. **A newer formulation known as Lexiva was approved in October 2003, and requires fewer pills of a reduced size (see Lexiva fact sheet).**

**Food restrictions.** Agenerase may be taken with or without food, although a high-fat meal decreases the drug's absorption and should be avoided. Patients taking Agenerase should not take supplemental vitamin E, since the drug's vitamin E content exceeds the recommended daily allowance; however, continued use of multivitamins is safe.

**Storage.** Capsules and solution should be stored at a room temperature.

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

**Side effects and toxicity.** The side effects most frequently associated with Agenerase therapy are gastrointestinal intolerance (nausea, vomiting, diarrhea), rash, perioral paresthesia (numbness around the mouth) and hyperglycemia. Hemophiliacs may experience increased bleeding. Additionally, Stevens-Johnson syndrome, a life-threatening skin reaction, may occur in 1% of treated patients. Agenerase therapy should be discontinued in patients with this syndrome and those with moderate rashes accompanied by systemic symptoms. Agenerase

should only be used during pregnancy if potential benefit outweighs risk. Data are incomplete and animal studies show adverse effects on the fetus. Metabolic (lipid and glucose) and morphologic (fat accumulation and fat atrophy) abnormalities have been associated with protease inhibitors in general.

**Drug interactions.** Agenerase should not be given concurrently with bepridil (Vascor), cisapride (Propulsid), dihydroergotamine (DHE 45), ergotamine (Ergostat), midazolam (Versed), triazolam (Halcion), rifampin (Rifadin, Rimactane) and the lipid-lowering agents simvastatin (Zocor) and lovastatin (Mevacor). Lipid-lowering drugs such as atorvastatin (Lipitor), pravastatin (Pravachol) or fluvastatin (Lescol) should be used with caution. When administered concomitantly with Agenerase, the dose of rifabutin (Mycobutin) should be halved. Levels of Sildenafil (Viagra), Cialis (tadalafil), and Levitra (vardenafil) may be significantly raised in the presence of Agenerase and dose reductions are recommended. Agenerase should not be taken with oral contraceptives since they decrease concentrations of Agenerase. Coadministration of Agenerase and methadone (Dolophine) results in lower levels of both drugs and is generally not recommended. Also, St. John's Wort (*Hypericum perforatum*) is likely to decrease Agenerase levels in the body and therefore should be avoided when taking Agenerase.

The interactions between Agenerase and Viramune or Agenerase and Rescriptor are not yet known. The amount of Agenerase in the blood may be reduced by up to 36% in the presence of Sustiva. When combined with Sustiva, an adjusted 1200 mg dose 3 times a day is recommended. Alternatively a dose of 1200 mg of Agenerase with 200 mg Norvir twice a day may be used. Because of potential problems with drug absorption, Agenerase should be taken at least 1 hour before or after an antacid or original-formulation Videx. Finally, co-administration of Kaletra and Agenerase results in substantial reductions in levels of both drugs and is not recommended.

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## Additional info:

**Resistance and cross-resistance.** Resistance to Agenerase is associated with mutations at positions 50, 54, 82, and 84. The mutation at position 50 is associated with high-level resistance.

**Clinical data.** PROAB3001 is a double-blind, placebo-controlled study in which investigators randomized 232 treatment-naïve patients to a regimen of Agenerase/Retrovir/Epivir or to Retrovir/Epivir. At week 24, using the conservative intent-to-treat method of analysis, almost half (47%) of the subjects in the Agenerase-containing arm had withdrawn from study for toxicity or other reasons or for virologic failure. Data at week 24 show that 53% had viral loads less than 400 copies/mL versus 11% in the Retrovir/Epivir arm.

PROA3006 is a randomized, open-label study in which investigators assigned 504 treatment-experienced patients to a regimen of Agenerase/NRTIs or Crixivan/NRTIs. These patients were NNRTI-experienced, but naïve to protease inhibitors. After 24 weeks of therapy, 43% of subjects in the Agenerase-containing arm had achieved viral loads less than 400 copies/mL. Among patients in the Crixivan-containing arm, 53% achieved the same result.



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