Ziagen (abacavir)

Abacavir tablets are yellow, capsule-shaped, film-coated and imprinted with "GX623" on one side. The drug is also available in an oral solution.

Also known as: ABV, 1592, abacavir sulfate

Background and description. Ziagen is a nucleoside reverse transcriptase inhibitor (NRTI). This drug is the most powerful in its class and one of the most potent antiretrovirals available. The US Food and Drug Administration (FDA) approved abacavir in December 1998. The drug is manufactured by GlaxoSmithKline. Ziagen is indicated in combination with other antiretrovirals for the treatment of HIV infection.

Coformulations. Ziagen is included in the combination drug Trizivir (Retrovir, Epivir, and Ziagen), which is taken twice a day. Epzicom (a fixed-dose, once-daily, co-formulation of Ziagen with the HIV drug Epivir) was approved by the FDA in August 2004. (This is known as "Kivexa" in Europe).

Dose. The approved dose of Ziagen for adults is 600 mg daily, either as 300 mg (1 tablet) twice a day or 600 mg (2 tablets) once a day.

Food restrictions. None.

Storage. The tablets should be stored at a room temperature of 68° to 77°F; the solution should be kept at room temperature or refrigerated, but not frozen.

Patient assistance. GlaxoSmithKline provides a patient assistance program. For more information, call 866.728.4368.

Side effects and toxicity. The side effects most commonly associated with Ziagen therapy include nausea, vomiting, fatigue, headache, diarrhea, and loss of appetite. As a class, NRTIs have been implicated in damage to mitochondrial DNA and may therefore play a role in the development of metabolic and morphologic changes.

The most serious side effect, however, is a **hypersensitivity reaction** that occurs in approximately 5% of those receiving Ziagen. Symptoms of hypersensitivity usually appear **within the first 6 weeks of treatment** and include a skin rash and 2 or more of the following sets of symptoms: fever, nausea, vomiting, diarrhea, abdominal pain, severe tiredness, achiness, or a general sense of ill-health. A review of cases revealed that respiratory symptoms including cough, dyspnea (shortness of breath), and pharyngitis (sore throat) occurred in approximately 20% of patients having hypersensitivity reactions. Deaths have been reported in patients receiving Ziagen who were initially diagnosed with an acute respiratory disease, but were later recognized to have had hypersensitivity reactions. Patients who believe they are experiencing Ziagen hypersensitivity should stop taking the drug and call their physician immediately. Those who experience hypersensitivity to Ziagen must never take the drug again. Any effort to restart the drug can produce life-threatening symptoms.

Drug interactions. Ziagen is not known to have clinically significant interactions with other drugs.

Additional info:

Resistance and cross-resistance. Patients who have used and developed resistance to multiple NRTIs are unlikely to reduce their viral load with the use of Ziagen. On the other hand, patients who have used and developed resistance to only 2 NRTIs may see significant reductions in viral load when Ziagen is combined with other drugs. In a Glaxo-sponsored expanded access program, which provided the drug to patients with advanced disease and few treatment options, Ziagen produced a 0.5 log reduction in viral load for only 1 in 4 patients.

Clinical data. In a pivotal study of abacavir, a team of Glaxo investigators randomized 86 patients to a regimen of Retrovir/Epivir and another 87 to a combination of Ziagen/Retrovir/Epivir. Participants were required to be naïve to antiretroviral therapy. The median baseline viral load among the subjects was approximately 38,000 copies/mL, while the median baseline CD4 T cell count was approximately 450 cells/mm^3. At the end of the first 16 weeks, which were double-blind, approximately 80% of the subjects in the 3-drug arm had undetectable viral loads (less than 400 copies/mL). Unsurprisingly, less than 40% of the subjects in the double-NRTI comparison arm had undetectable plasma viremia. By week 48, approximately 60% of the triple-therapy subjects still had undetectable viral loads; however, participants with a baseline viral load of greater than 100,000 copies/mL were much less likely than other subjects to achieve undetectable viremia with the use of Ziagen. Glaxo reported that only 6% of the subjects assigned to the 3-drug group withdrew from study for adverse events.

For those who have been heavily treated with other NRTIs, Ziagen may have limited utility because of pre-existing resistance. However, for patients with limited or no NRTI experience, this nucleoside offers a potent, convenient, and generally well-tolerated choice.

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

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