GlaxoWellcome

July 2000

IMPORTANT DRUG WARNING

RE: Severe Hypersensitivity Reactions following reintroduction with ZIAGEN® (abacavir sulfate) Products

Dear Health Care Provider,

Glaxo Wellcome Inc. is writing to inform you of important new safety information about hypersensitivity reactions to abacavir, a nucleoside analogue reverse transcriptase inhibitor which, in combination with other antiretroviral agents, is indicated for the treatment of HIV-1 infection. Fatal hypersensitivity reactions are a described risk associated with the use of abacavir (Ziagen); patients who have developed hypersensitivity reactions upon abacavir rechallenge are at an increased risk of a severe hypersensitivity reaction, which may result in death.

Recent reports indicate that **severe or fatal hypersensitivity reactions can occur within hours after ZIAGEN reintroduction in patients who have no identified history or unrecognized symptoms of hypersensitivity to abacavir therapy.** In these reports:

- Hypersensitivity to abacavir was not recognized before abacavir therapy was interrupted.
- Most of these hypersensitivity reactions were indistinguishable from hypersensitivity reactions associated with abacavir rechallenge: short time to onset, increased severity of symptoms, and poor outcome (including death).
- Reasons for discontinuation of abacavir included interruption in drug supply and discontinuation of abacavir while treating other medical conditions.
- Severe or fatal hypersensitivity reactions occurred upon reintroduction when abacavir was discontinued for reasons unrelated to symptoms of hypersensitivity. In some cases, symptoms consistent with hypersensitivity may have been present before abacavir was discontinued, but may have been attributed to other medical conditions (for example, acute onset respiratory diseases, gastroenteritis or reactions to other medications).
- Hypersensitivity reactions occurred days to weeks following abacavir reintroduction in a minority of reports.

If abacavir has been discontinued for reasons other than symptoms of hypersensitivity, and if reinitiation of Ziagen therapy is under consideration:

- The reason for discontinuation should be evaluated to ensure that the patient did not have symptoms of a hypersensitivity reaction. If hypersensitivity is suspected, abacavir should **NOT** be reintroduced.
- If symptoms consistent with hypersensitivity are not identified, reintroduction should be undertaken with caution. Patients should be made aware that a hypersensitivity reaction can occur upon reintroduction of abacavir, and that reintroduction should be undertaken only if medical care can be readily accessed by the patient and others.

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Please read the enclosed package insert for revisions in the **BOXED WARNING, WARNINGS, ADVERSE REACTIONS, PRECAUTIONS: Information for Patients** and patient **Medication Guide**. This information is provided to help you in the management of patients prescribed Ziagen Tablets or Ziagen Oral Solution.

Glaxo Wellcome is committed to providing you with the current product information for the management of your patients being treated with ZIAGEN. You can assist us in monitoring the safety of ZIAGEN by reporting adverse reactions to the Glaxo Wellcome Product Surveillance Department at 1-888-825-5249 or to the FDA MedWatch program by telephone at 1-800-332-1088, by FAX at 1-800-332-0178, via www.FDA.gov/medwatch, or by mail to MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20857.

Please refer to the enclosed revised prescribing information for ZIAGEN. If you have questions about the new information or want additional medical information about ZIAGEN, please contact the Glaxo Wellcome Customer Response Center at 1-888-TALK2GW (1-888-825-5249).

Sincerely,

Marc Rubin, M.D.
Vice President, Therapeutic Development and Product Strategy
HIV, Infectious Diseases, and Hepatitis