GlaxoWellcome

January 2000

IMPORTANT DRUG WARNING

RE: Fatal Hypersensitivity Reactions, Respiratory Symptoms, and Ziagen® (abacavir sulfate)

Dear Health Care Provider:

Glaxo Wellcome Inc. would like to bring to your attention a revised WARNING in the labeling for Ziagen (abacavir sulfate) about fatal hypersensitivity reactions to abacavir in patients presenting with respiratory symptoms. Ziagen is a nucleoside analogue reverse transcriptase inhibitor indicated for use in combination with other antiretroviral drugs for the treatment of HIV-1 infection.

Since its approval in December 1998, the labeling for Ziagen has included a WARNING and description of fatal hypersensitivity reactions to Ziagen. Although presentations vary markedly between patients, frequently occurring features of these hypersensitivity reactions are fever, rash, gastrointestinal symptoms (nausea, vomiting, diarrhea, or abdominal pain), and fatigue or malaise. While respiratory symptoms have been recognized as part of the hypersensitivity reaction in some patients, recent information underscores their importance.

Fatalities in patients treated with Ziagen who developed hypersensitivity reactions in which the initial presentation included respiratory symptoms of dyspnea, cough, or pharyngitis have been reported. Deaths have been reported in patients receiving Ziagen who were initially diagnosed with an acute respiratory disease (pneumonia, bronchitis, or flu-like illness) who were later recognized to have had a hypersensitivity reaction to abacavir that included respiratory symptoms. A delay in diagnosis of hypersensitivity can result in Ziagen being continued or re-introduced, leading to more severe hypersensitivity reactions, including life-threatening hypotension and death.

Review of reports of hypersensitivity in patients receiving Ziagen indicates that respiratory symptoms (including cough, dyspnea, and pharyngitis) have occurred in approximately 20% of patients who have had hypersensitivity reactions. In contrast to some allergic reactions, wheezing or bronchospasm have occurred only infrequently in patients with hypersensitivity reactions to Ziagen.

The diagnosis of hypersensitivity reaction should be carefully considered for patients presenting with symptoms of acute respiratory diseases and other symptoms associated with hypersensitivity to abacavir, even if alternative respiratory diagnoses (pneumonia, bronchitis, pharyngitis, or flu-like illness) are possible. **If the clinical presentation of an acute illness cannot be clearly differentiated from a hypersensitivity reaction, Ziagen must be permanently discontinued.** Ziagen should not be restarted following a hypersensitivity reaction because more severe symptoms will recur within hours and may include life-threatening hypotension and death.

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This updated warning about fatal hypersensitivity reactions to abacavir in patients presenting with respiratory symptoms is now included in the revised labeling for Ziagen. In addition, this revised warning is reflected in the Patient Medication Guide and Warning Card and should be discussed with patients treated with Ziagen.

This information is provided to help you in the management of patients prescribed Ziagen Tablets or Ziagen Oral Solution. Please take the time to read the enclosed revised package insert, including the revised boxed warning shown below (with the revisions underlined), for additional product information and other risks associated with the recommended use of Ziagen.

WARNING:

FATAL HYPERSENSITIVITY REACTIONS HAVE BEEN ASSOCIATED WITH THERAPY WITH ZIAGEN. PATIENTS DEVELOPING SIGNS OR SYMPTOMS OF HYPERSENSITIVITY (WHICH INCLUDE FEVER; SKIN RASH; FATIGUE; GASTROINTESTINAL SYMPTOMS SUCH AS NAUSEA, VOMITING, DIARRHEA, OR ABDOMINAL PAIN; AND RESPIRATORY SYMPTOMS SUCH AS PHARYNGITIS, DYSPNEA, OR COUGH) SHOULD DISCONTINUE ZIAGEN AS SOON AS A HYPERSENSITIVITY REACTION IS SUSPECTED. ZIAGEN SHOULD NOT BE RESTARTED FOLLOWING A HYPERSENSITIVITY REACTION BECAUSE MORE SEVERE SYMPTOMS WILL RECUR WITHIN HOURS AND MAY INCLUDE LIFE-THREATENING HYPOTENSION AND DEATH (see WARNINGS, PRECAUTIONS: Information for Patients, and ADVERSE REACTIONS).

LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS, INCLUDING FATAL CASES, HAVE BEEN REPORTED WITH THE USE OF NUCLEOSIDE ANALOGUES ALONE OR IN COMBINATION, INCLUDING ZIAGEN AND OTHER ANTIRETROVIRALS (SEE WARNINGS).

ZIAGEN in combination with other antiretroviral agents is indicated for the treatment of HIV-1 infection. This indication is based on analyses of surrogate markers in controlled studies of up to 24 weeks in duration. At present, there are no results from controlled trials evaluating long-term suppression of HIV RNA or disease progression with ZIAGEN.

Although hypersensitivity reaction is described in the package insert for Ziagen, you can assist us in continuing to monitor the safety of Ziagen products by reporting all cases of hypersensitivity reaction occurring in patients treated with Ziagen to the Abacavir Hypersensitivity Reaction Registry at Glaxo Wellcome at 1-800-270-0425 or to the FDA MedWatch program by telephone at 1-800-FDA-1088, via fax at 1-800-FDA-0178, or by mail at MedWatch HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20857.

We appreciate the opportunity to provide this information to facilitate the care of your patients. Any questions from health care professionals may be directed to our Drug Information Department at 1-800-334-0089. Thank you.

Sincerely,

Richard S. Kent

Richard S. Kent, M.D.
Vice President, U.S. Medical Operations