GlaxoWellcome

21st January 2000

IMPORTANT SAFETY INFORMATION ON HYPERSENSITIVITY REACTIONS, RESPIRATORY SYMPTOMS, AND ZIAGEN™ (ABACAVIR SULFATE)

Dear Doctor,

Glaxo Wellcome would like to highlight some additional information about an important safety issue concerning the hypersensitivity reaction to Ziagen (abacavir sulfate), a nucleoside analogue reverse transcriptase inhibitor indicated for use in combination with other antiretroviral drugs for the treatment of HIV-1 infection.

A hypersensitivity reaction occurs in approximately 3% of the patients exposed to Ziagen. Frequently occurring features of these hypersensitivity reactions are fever, rash, gastrointestinal symptoms (nausea, vomiting, diarrhoea, or abdominal pain), and constitutional symptoms (severe fatigue or malaise). Respiratory symptoms have been recognised as part of the hypersensitivity reaction in approximately 20% of patients, and may include dyspnoea, pharyngitis or cough in the initial presentation. In contrast to some allergic reactions, wheezing or bronchospasm have occurred only infrequently in patients with hypersensitivity reactions to abacavir.

Deaths have been reported among patients initially diagnosed with acute respiratory diseases (pneumonia, bronchitis, or flu-like illness) who were later recognised to have had a hypersensitivity reaction to abacavir. In patients experiencing a fatal outcome, respiratory symptoms have been present in approximately 80% of cases. A delay in diagnosis of hypersensitivity can result in Ziagen being continued or re-introduced, leading to more severe hypersensitivity reactions or death.

The diagnosis of hypersensitivity reaction must always be considered in patients presenting with symptoms of acute respiratory diseases in addition to other symptoms associated with hypersensitivity to abacavir, even if alternative respiratory diagnoses (pneumonia, bronchitis, pharyngitis, or flu-like illness) are possible.

- **Prescribers must ensure that patients are fully informed regarding hypersensitivity reactions. Each patient should be reminded to read the package leaflet and the alert card included in the pack.**
- **Patients developing signs or symptoms, including respiratory symptoms possibly linked with a hypersensitivity reaction (fever, shortness of breath, sore throat or cough, skin rash, nausea or vomiting or diarrhoea or abdominal pain, severe tiredness or achiness or "generally ill feeling") should be informed to contact their doctor immediately.**
- **Patients who are diagnosed with a hypersensitivity reaction must discontinue treatment immediately.**
- **Ziagen must never be restarted in patients who have stopped therapy due to a hypersensitivity reaction.**
- **Restarting Ziagen must be avoided in patients in whom a hypersensitivity reaction cannot be excluded.**

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 changes to the *Summary of Product Characteristics*.

Yours sincerely,

Eithne Rooney

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Ziagen "Dear Doctor" letter for EU

Sincerely,

signatory

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