



QUESTIONS AND ANSWERS ON ABACAVIR AND THE RISK OF HEART ATTACK

What is abacavir?

Abacavir is an antiviral medicine. It is used in combination with other antiviral medicines to treat adults and children who are infected with human immunodeficiency virus (HIV), the virus that causes acquired immune deficiency syndrome (AIDS). It belongs to the class of medicines called 'nucleoside reverse transcriptase inhibitors' (NRTIs).

Abacavir has been authorised by the European Commission since July 1999 as Ziagen. It is also available in combination with lamivudine as Kivexa, and with both lamivudine and zidovudine as Trizivir. These medicines are marketed in most European Union Member States.

What is the issue with abacavir?

Recent results from a large study have shown that the recent use of abacavir may be linked with an increased risk of myocardial infarction (heart attack). 'Data collection of Adverse effects of anti-HIV Drugs' or 'D:A:D' is an 'observational study' that has been running since 1999. It follows more than 33,000 HIV-positive patients being treated in Europe, Australia and the United States of America and collects information on side effects of anti-HIV medicines affecting the heart and blood vessels.

What were the results of the study?

In February 2008, the most recent results of the study showed that the use of abacavir in the last six months may be linked to an increased risk of heart attack. Over 33,000 patients had been followed in the study: 517 of the patients had had a heart attack, 192 of whom had taken abacavir in the six months prior to their heart attack.

This was calculated to represent a 'relative risk' of 1.90. This means that the risk of having a heart attack in these patients was almost double their 'baseline' risk, taking into account other risk factors such as older age, being male, being overweight, smoking, a family history of heart problems, diabetes, high cholesterol and high blood pressure. The risk of heart attack had fallen to normal levels six months after stopping abacavir. The potential risk linked with abacavir is lower than that linked with smoking, which increases the risk of having a heart attack by two- to threefold.

What has the EMEA been doing?

The Committee for Medicinal Products for Human Use (CHMP) and its Pharmacovigilance Working Party (PhVWP) discussed the available information during their March 2008 meetings to determine whether it should have an impact on the way the medicine is used.

In addition to the results from the D:A:D study, the CHMP asked the company that makes abacavir-containing medicines to provide information on the risk of heart attack with abacavir. This included the results of 54 clinical studies that compared abacavir with other anti-HIV medicines, involving almost 10,000 patients taking abacavir. No increased risk of heart attack could be seen in these studies. However, the Committee noted that the studies were not specifically designed to look into the potential for abacavir to affect the heart. In addition, the number of heart attacks seen (27 cases) is considered too low to enable the Committee to draw any firm conclusions.

The Committee also noted that the available information provides no clear evidence of a biological mechanism linking abacavir to damage to the heart.

Overall, the Committee concluded that the available information did not allow a definitive conclusion on the link between the use of abacavir and an increased risk of heart attack to be drawn.

What is happening next?

The CHMP has concluded that no changes to the prescribing information for abacavir-containing medicines are needed for the time being. They will continue to look actively into this issue. There are other observational studies¹ currently ongoing, which are expected to provide information later in the year. The CHMP has requested this information and will assess any possible impact on the use of abacavir-containing medicines as soon as this information has been received.

What is happening with didanosine?

A similar but lower potential risk of heart attack was seen with the use of the NRTI didanosine. The relative risk of didanosine in D.A.D. study has been found to be 1.49. This medicine is approved as Videx for the treatment of HIV infection in combination with other anti-HIV medicines. However, in contrast to abacavir-containing medicines which are authorised by the European Commission, Videx is authorised by regulatory authorities in Member States. Member States will take appropriate action on the use of Videx if necessary.

What is the advice to patients and doctors?

- Patients should not stop taking any anti-HIV medicine unless they are told to do so by their doctor.
- Doctors and patients should bear in mind the ways they can reduce the risk of a heart attack. These include not smoking, controlling diabetes, and lowering blood pressure and cholesterol through diet, exercise or medicines.
- Patients who have any concerns should talk to their doctor or pharmacist.

¹ Studies already identified as able to provide information are the 'French Hospital Database on HIV (FHDH) cohort' and 'Veterans Affairs (VA) study'. Work is currently underway to identify more cohort studies that could also provide relevant information.