The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

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CPMP PUBLIC STATEMENT
Metabolic and cardiovascular complications of antiretroviral combination therapy in HIV-infected patients

Combination antiretroviral therapy (CART) has dramatically improved survival in HIV-infected patients. Treatment-associated metabolic side effects have been observed. Some of these are known to be risk factors for cardiovascular disease, including dyslipidemia, insulin resistance and diabetes mellitus. Together with reports of cardiovascular and cerebrovascular disease in association with this chronic treatment as well as with HIV infection itself, these observations have raised concern about adverse effects of long-term CART and questions regarding the management of patients.

Following the first observations of lipodystrophy in 1998, the Committee for proprietary medicinal products (CPMP) requested all concerned marketing authorisation holders (MAHs) of HIV protease inhibitors to collectively answer questions concerning the prevalence and especially the incidence of long-term cardiovascular complications and the relationship to body composition changes and metabolic abnormalities associated with CART. A group of MAHs for both protease inhibitors and other antiretroviral products committed jointly to support a number of scientific studies on these issues. An Oversight Committee was established in 1999 with members from the MAHs, academia, patient organisations and the regulatory agencies in Europe (EMEA-CPMP) - and the US (FDA).

In February 2003 currently available results from these studies (mainly the D.A.D.[1] and VA[2] cohort studies) were presented to the CPMP by the principal investigators of the studies and by the MAHs. Results and different methodological issues were assessed by the CPMP and were further discussed between EU experts and the Oversight Committee in the February meeting.

The CPMP concluded that

- The available results from the studies clearly demonstrate that the benefit/risk balance of antiretroviral treatment remains strongly positive.
- The long-term cardiovascular effect of combination antiretroviral therapy in HIV-infected patients has not been conclusively demonstrated and therefore concerns about the risk of cardiovascular disease should not lead to the withholding of CART when indicated for these patients.
- The ongoing studies of long-term cardiovascular complications (the DAD and the VA studies) should be continued for an extended follow-up time, at least until January 2005. The CPMP regards this extension and any additional follow-up that may be necessary to provide conclusive results as part of the ongoing commitment from MAHs.

[1] A large multi-cohort prospective study to evaluate cardiovascular risk know as The Data Collection on Adverse Events of Anti-HIV Drugs.

[2] A study entitled "A Retrospective Cohort Study of the Risk of Cardiovascular Events in HIV Patients on HAART" utilizing the Veterans Administration Database.

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