HAUTE AUTORITÉ DE SANTÉ

VIROLOGY
Focus
June 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ATRIPLA (efavirenz+emtricitabine+tenofovir disoproxil fumarate), antiviral combination

Second-line treatment in the management of HIV

Main points

- ATRIPLA has Marketing Authorisation in the treatment of HIV-1 infection in adults with virologic suppression on their current combination antiretroviral therapy for more than three months. Patients must not have experienced virological failure on any prior antiretroviral therapy and must be known not to have harboured virus strains with mutations conferring significant resistance to any of the three components contained in ATRIPLA prior to initiation of their first antiretroviral treatment regimen.
- ATRIPLA must no longer be used as first-line treatment, in view of:
  - the neurological toxicity (due to efavirenz), renal toxicity and toxic effects on calcium and phosphorus metabolism (due to tenofovir disoproxil fumarate) of this fixed-dose combination;
  - the existence of better tolerated treatment alternatives that are at least as effective, such as combinations based on an integrase inhibitor (dolutegravir, elvitegravir, raltegravir).
- It is a second-line treatment option and must be used alongside monitoring of renal function and of calcium and phosphorus metabolism. Good compliance with treatment is, moreover, advisable, on account of the low genetic barrier of efavirenz.

Therapeutic use

- The currently recommended first-line treatment is a combination therapy involving at least three highly active agents: two nucleoside reverse transcriptase inhibitors (NRTIs) plus a third agent (a protease inhibitor, a non-nucleoside reverse transcriptase inhibitors or an integrase inhibitor).

Role of the medicinal product in the therapeutic strategy

In view of:
- the neurological toxicity (due to efavirenz), renal toxicity and toxic effects on calcium and phosphorus metabolism (due to tenofovir disoproxil fumarate) of this fixed-dose combination;
- the existence of better tolerated treatment alternatives that are at least as effective, such as combinations based on an INI (dolutegravir, elvitegravir, raltegravir);

the Committee considers that, in the indication of the Marketing Authorisation, the proprietary medicinal product ATRIPLA:
- must no longer be used as first-line treatment;
- is a second-line treatment option and must be used alongside monitoring of renal function and of calcium and phosphorus metabolism. Good compliance with treatment is, moreover, advisable, on account of the low genetic barrier of efavirenz.

Clinical data

- The new studies submitted do not permit reassessment of the efficacy of ATRIPLA in its current therapeutic indication.
- Two phase III non-inferiority studies with ATRIPLA as the comparator have been carried out in patients who had not previously been treated with antiretrovirals. These are studies of off-label use outside the indication of the Marketing Authorisation.

Prescribing conditions

- Medicine for initial hospital prescription

Benefit of the medicinal product

- The actual benefit* of ATRIPLA is substantial in the indication of the Marketing Authorisation.
- Recommends continuation of inclusion on the list of reimbursable products for supply by pharmacists.

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This document was created on the basis of the Transparency Committee Opinion of 17 June 2015 (CT-13468) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".