HAUTE AUTORITÉ DE SANTÉ

VIROLOGY
Focus
October 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

EVIPLERA (rilpivirine, emtricitabine, tenofovir disoproxil fumarate), antiviral combination

Second-line treatment in the management of HIV

Main points

- EVIPLERA has Marketing Authorisation in the treatment of adult patients infected with the human immunodeficiency virus type 1 (HIV-1) without any known mutations associated with resistance to the non-nucleoside class of reverse transcriptase inhibitors (NNRTI) or to tenofovir or emtricitabine, and who present a viral load ≤ 100 000 copies/ml of HIV-1 RNA.
- EVIPLERA is a second-line treatment option because of:
  - its renal toxicity and toxic effects on calcium and phosphorus metabolism (due to tenofovir disoproxil fumarate), and its neurological toxicity (due to rilpivirine),
  - the low genetic barrier to resistance of rilpivirine and the absence of demonstrated superiority in terms of efficacy by comparison with the efavirenz/emtricitabine/tenofovir DF combination,
  - the existence of treatment alternatives with a better efficacy and/or safety profile, and with a higher genetic barrier to resistance, such as the combinations based on integrase inhibitors (INI) or protease inhibitors/ritonavir (PI/r),
- 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 rilpivirine.

Therapeutic use

- The preferred first-line treatments currently recommended are combination therapies involving at least three highly active agents, two nucleoside reverse transcriptase inhibitors (NRTI) plus a third agent (a protease inhibitor, a non-nucleoside reverse transcriptase inhibitor [NNRTI] or an integrase inhibitor).
- **Role of the medicinal product in the therapeutic strategy**
  EVIPLERA is a second-line treatment option.

Clinical data

- The efficacy and safety data are based on:
  - two controlled phase III studies versus a triple therapy based on an NNRTI + 2 NRTIs (the emtricitabine/tenofovir DF + efavirenz combination), performed in previously untreated patients
  - two studies performed in patients pretreated with virological success and without any mutations associated with resistance to the agents in EVIPLERA.
- In the various studies, EVIPLERA was non-inferior to the comparators in terms of immunological and virological efficacy. However, a higher percentage of virological failures among previously untreated patients, particularly among the subpopulation of patients with a viral load > 100,000 copies/ml, explains why this subgroup has been excluded from the Marketing Authorisation for EVIPLERA.
- The resistance data reflect the relatively low genetic barrier of resistance to rilpivirine (one component of EVIPLERA) with a higher risk of the selection of resistant variants in the event of virological failure and a risk of this occurring more rapidly than with a treatment including a protease inhibitor. In addition, the resistance is cross-resistance with other NNRTIs (efavirenz, nevirapine, etravirine).

Overall, the safety profile of rilpivirine was better than that of efavirenz in the two studies carried out in previously untreated patients. In the course of the studies carried out in patients displaying virological control, the known safety profile of EVIPLERA was confirmed and no new safety signals were identified. On the other hand, in the study carried out in patients displaying virological control under triple therapy based on PI/r, adverse effects were more frequent among the patients who switched to treatment with EVIPLERA (24.9%) compared with those who remained on their initial treatment based on PI/r (2.5%), with more frequent premature discontinuations of treatment due to the occurrence of adverse effects (2.8% versus 0%). An improvement in the lipid parameters was, however, noted after switching to EVIPLERA, compared with patients who continued the initial antiretroviral treatment based on PI/r, and in particular patients whose prior treatment based on PI/r was lopinavir/ritonavir (KALETRA).

Prescribing conditions

- Medicine requiring initial annual hospital prescription. Unrestricted renewal.

Benefit of the medicinal product

- The actual benefit* of EVIPLERA is substantial.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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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.