HAUTE AUTORITÉ DE SANTÉ

INFECTIOUS DISEASE
New medicinal product
September 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

BIKTARVY (bictegravir, emtricitabine, tenofovir alafenamide), antiretroviral combination

High clinical benefit in HIV-1 infection, but no demonstrated clinical improvement compared to TRIUMEQ.

Main points

- BIKTARVY has MA for the treatment of HIV-1 infection in treatment-naive or virologically controlled pre-treated patients, in the absence of integrase inhibitor, emtricitabine or tenofovir resistance.
- Where a treatment strategy including an integrase inhibitor (INI) is envisaged, BIKTARVY is a first-line therapeutic option for treatment-naive or virologically controlled pre-treated patients.
- BIKTARVY has no role in the therapeutic strategy of patients in virological failure or in whom the virus is resistant to other integrase inhibitors.
- In view of the recent data on the potential risk of congenital malformation after a treatment with dolutegravir at the time of conception and during the first trimester of pregnancy, and pending supplementary data on a potential class effect, women exposed to INIs (including bictegravir) should be reminded of the precautions (information and prescription of effective contraception) for women of reproductive age.

Therapeutic strategy

- Combination therapies combining at least 3 highly active agents are recommended for first-line treatment; these should include 2 nucleoside reverse transcriptase inhibitors NRTIs + a third agent (protease inhibitor [PI], non-nucleoside reverse transcriptase inhibitor [NNRTI], or integrase inhibitor [INI]).
- **Role of the medicinal product in the therapeutic strategy**
- BIKTARVY is a new first-line option, only for treatment-naive or virologically controlled pre-treated patients, in whom the virus contains no integrase inhibitor, emtricitabine or tenofovir resistance mutation.
- In this population, it is an alternative to dolutegravir-based tritherapies (TRIUMEQ or TIVICAY + 2 NRTIs), due to comparable efficacy and safety profiles and a higher genetic barrier to resistance to that of first-generation INIs (raltegravir and elvitegravir). Nevertheless, uncertainties remain in relation to its efficacy in patients with negative prognostic factors (viral load > 100,000 copies/mL, CD4 count < 200 cells/mm^3) and in patients with HIV-HBV coinfection.

Clinical data

- Two studies have demonstrated the non-inferiority of BIKTARVY versus active comparators (TRIUMEQ or TIVICAY + DESCOVY) in antiretroviral treatment-naive adults having an estimated glomerular filtration rate ≥ 50 ml/min and ≥ 30 ml/min.
- Three switch studies have demonstrated the non-inferiority of BIKTARVY compared to retaining the initial tritherapy, in virologically controlled adults having an estimated glomerular filtration rate ≥ 50 ml/min, including one study conducted solely on women.
- The efficacy, safety (particularly renal and bone safety), and resistance profiles were favourable and comparable to those of TRIUMEQ. The data are limited for patients with negative prognostic factors (viral load > 100,000 copies/mL, CD4 count < 200 cells/mm3) and for patients with HIV-HBV coinfection, limiting the transposability of the findings to all of these populations.

- No study has assessed BIKTARVY in pre-treated patients in virological failure.

Special prescription requirements

- Medicinal product subject to initial hospital prescription

Benefit of the medicinal product

- The actual clinical benefit* of BIKTARVY is high.
- BIKTARVY does not provide an improvement in actual clinical benefit** compared to TRIUMEQ in the treatment of treatment-naive or virologically pre-treated HIV-1 adults.
- Reimbursement approved for non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 5 September 2018 (CT-1704) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The improvement in actual clinical benefit (IACB) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the IACB rating from I, major, to IV, minor. An IACB rating of V (equivalent to "no IACB") denotes a "lack of clinical improvement"