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VIROLOGY
NEW MEDICINAL PRODUCT
June 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

DESCOVY (emtricitabine, tenofovir alafenamide), antiretroviral combination

No clinical benefit demonstrated for this second-line treatment in the treatment of HIV infection.

Main points

- DESCOVY, in combination with other antiretrovirals, has the Marketing Authorisation in the treatment of adults and adolescents (aged 12 years and older, weighing at least 35 kg) infected with type 1 human immunodeficiency virus (HIV-1).
- In adults, it is an alternative to TRUVADA (emtricitabine, tenofovir disoproxil fumarate).
- In adolescents and patients with moderate renal failure (estimated creatinine clearance ≥ 30 mL/min), it is a therapeutic option only in cases in which it is not possible to prescribe first-line medicinal products that are not associated with a risk of kidney and bone damage.
- It must be used alongside monitoring of renal function, calcium and phosphorus metabolism, and lipid parameters.

Therapeutic use

- The currently recommended first-line treatments are combination therapies including at least 3 highly active agents: 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 proprietary medicinal product in the therapeutic strategy**
- DESCOVY has a composition of active ingredients similar to TRUVADA (emtricitabine, tenofovir disoproxil fumarate [TDF]), which is currently available. TDF was replaced by tenofovir alafenamide (TAF), which was developed to reduce the renal and bone toxicity observed with TDF, through a mechanism of action that allows a more significant intracellular concentration of tenofovir to be obtained, while reducing systemic exposure by 90%.
- In naïve patients, when tritherapy including 2 NRTIs (emtricitabine/tenofovir or abacavir/lamivudine) + a third agent (1 PI, 1 NNRTI or 1 INI) is envisaged, considering:
  - the important potential risk of renal toxicity and on calcium and phosphorus metabolism (linked to tenofovir alafenamide),
  - the absence of comparative data in naïve patients versus the available therapeutic alternatives,

  DESCOVY is a second-line treatment option and an alternative to TRUVADA, keeping in mind, however, that the efficacy of DESCOVY has not been demonstrated in these patients.
- In patients treated with TRUVADA and virologically controlled, DESCOVY can replace TRUVADA. The modest change in renal function, lack of evidence of decreased fracture risk and disruption of lipid parameters that may require the introduction of lipid-lowering therapy observed with DESCOVY do not justify systematic replacement of TRUVADA by DESCOVY. This replacement could be useful in patients with adverse effects related to tenofovir disoproxil, but there are no clinical data to support this hypothesis.
- In adolescents and patients with moderate renal failure (estimated creatinine clearance ≥ 30 mL/min), due to the significant potential risk of nephrotoxicity and of impact on bone mineralization, or even on growth in children, DESCOVY is a therapeutic option only in cases in which it is not possible to prescribe first-line medicinal products that are not associated with a risk of kidney and bone damage.
- DESCOVY must be used alongside monitoring of renal function, calcium and phosphorus metabolism, and lipid parameters.

Clinical data

- No studies have assessed the efficacy and safety of DESCOVY in treatment-naïve patients (adults and adolescents).
- In adults treated with TRUVADA and virologically controlled, one study demonstrated the non-inferiority, in terms of efficacy, of replacing TRUVADA with DESCOVY versus maintenance of this treatment at week 48. Virologic control was maintained in 94.3% of patients who changed to DESCOVY versus 93.0% of patients who continued their original treatment with TRUVADA, regardless of the third agent. The data at 96 weeks support the non-inferiority demonstrated at week 48; virologic control was maintained in 88.6% of patients who changed to DESCOVY versus 89.1% of patients who continued their original treatment with TRUVADA.
- Overall, the safety profile was comparable between the two medicines. A modest improvement on parameters measuring renal and bone function was observed in patients who changed to DESCOVY relative to those who maintained their original treatment with TRUVADA. The long-term persistence and the impact on the reduction in the risk of fractures and nephrotoxicity (renal failure and proximal tubulopathy, including Fanconi syndrome) remains to be demonstrated:
  - modest change in blood creatinine (-0.08 mg/dL versus -0.04 mg/dL) and glomerular filtration rate (eGFR CKD-EPI: +5.2% versus +3.1%) at 48 and 96 weeks,
  - increase of 2% in terms of hip bone and spine mineral density, which is not a good replacement efficacy endpoint for estimating fracture risk and identical fracture risk at 48 and 96 weeks.

  However, the increase in lipid parameters (hypercholesterolaemia, LDL-C, triglycerides) was greater with DESCOVY than with TRUVADA.
- The available data do not permit DESCOVY to be situated relative to another regimen with no tenofovir, particularly in patients with renal failure or having renal failure or renal risk factors and bone fragility or fracture.

Special prescribing conditions

- Medicinal product for initial hospital prescription

Benefit of the medicinal product

- The actual benefit* of DESCOVY is substantial
- DESCOVY does not provide clinical added value** (CAV V) in the management of patients infected with HIV-1.
- 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 07 June 2017 (CT-16046) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a 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 ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product 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 (equivalent to “no CAV”) means “no clinical added value”.