HAUTE AUTORITÉ DE SANTÉ

INFECTIOUS DISEASES
New medicinal product
April 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

PIFELTRO (doravirine), antiretroviral

High clinical benefit in the treatment of HIV-1 in patients with a low viral load ≤ 100,000 copies/mL, when a non-nucleoside reverse transcriptase inhibitor (NNRTI) is indicated and the use of rilpivirine is not appropriate, but no demonstrated clinical added value in the management of these patients.

Main points

- Doravirine is an NNRTI available in free form (PIFELTRO) or as a fixed-dose combination (DELSTRIGO).
- PIFELTRO has an MA for the treatment of adults infected with HIV-1 without past or present evidence of resistance to the NNRTI class.
- It is a therapeutic option in patients whose viral load is ≤ 100,000 copies /mL, when an NNRTI is indicated and the prescription of rilpivirine is not appropriate, particularly for reasons related to interactions with other medicinal products.
- PIFELTRO has no role in the current therapeutic strategy for patients with virologic failure or in whom the virus is resistant to other non-nucleoside reverse transcriptase inhibitors.

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], NNRTI, or integrase inhibitor [INI]).
- **Role of the medicinal product in the therapeutic strategy**
- When a treatment strategy with an NNRTI is envisaged, PIFELTRO is a second-line treatment option, in adults infected with HIV-1, whose viral load is ≤ 100,000 copies /mL, without past or present evidence of resistance to the NNRTI class.
- In the absence of an MA and data, PIFELTRO has no role in the therapeutic strategy for patients with virologic failure or in whom the virus is resistant to other non-nucleoside reverse transcriptase inhibitors.

Clinical data

- Two studies have demonstrated the non-inferiority of doravirine (in free form [PIFELTRO] or as a fixed-dose combination [DELSTRIGO]) versus active comparators (darunavir/ritonavir [PIs] or efavirenz [ATRIPLA]), in terms of immuno-virologic efficacy after 96 weeks of treatment, in antiretroviral treatment-naive adult patients with no history of resistance mutation to doravirine and related medicinal products.
- Uncertainties remain with respect to the efficacy of doravirine in patients with a high viral load (> 100,000 copies/ml), a subpopulation in which a low level of virologic success has been observed (approximately 70% at 96 weeks).
- The efficacy of the doravirine/lamivudine/tenofovir disoproxil combination (DELSTRIGO) has also been demonstrated in pre-treated patients with virologic control for at least 6 months, with no history of virologic failure and resistance to the NNRTI class, emtricitabine, tenofovir or lamivudine, but the absence of a per protocol population analysis means that it is not possible to reach a conclusion concerning its non-inferiority versus maintenance of initial therapy (PI/ritonavir or elvitegravir/cobicistat mainly).

- The safety profile was comparable to that of darunavir/ritonavir, and more favourable than that of efavirenz (ATRIPLA), particularly for dizziness and headaches, but with no significant difference for the most severe neuropsychiatric adverse reactions (depression, suicide and bipolar disorders).
- The available data suggested a relatively low genetic barrier to doravirine resistance due to the high frequency of resistance to doravirine and related NRTIs in the event of virologic failure, particularly in the context of its use in combination with tenofovir disoproxil fumarate/lamivudine (DELSTRIGO).
- No study has assessed doravirine (PIFELTRO or DELSTRIGO) in pre-treated patients with virologic failure of NNRTIs.

Special prescription requirements

- Medicinal product subject to initial hospital prescription

Benefit of the medicinal product

- The actual clinical benefit* of PIFELTRO is high in HIV-1 patients with a low viral load ≤ 100,000 copies/mL, when an NNRTI is indicated and the use of rilpivirine is not appropriate.
- PIFELTRO does not provide any clinical added value** (CAV V) in the management of patients infected with HIV-1.
- Approved for non-hospital pharmacy reimbursement and for hospital treatment.

HAUTE AUTORITÉ DE SANTÉ
This document was drafted on the basis of the Transparency Committee opinion dated 03 April 2019 (CT-17495) 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 may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) corresponds to the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV level from I, major, to IV, minor. A level V CAV (equivalent to "no clinical added value") denotes a "lack of clinical improvement".