HAUTE AUTORITÉ DE SANTÉ

INFECTIOUS DISEASES
New medicinal product
July 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

JULUCA (dolutegravir/rilpivirine), combination of anti-viral agents

High clinical benefit in the treatment of HIV infection in adults who are virologically-suppressed**, but no demonstrated clinical benefit over conventional tritherapies or over the free-dose combination of its two components.**

Main points

- JULUCA has been granted marketing authorisation for the treatment of virus type 1 (HIV-1) infection in adults who are virologically-suppressed (HIV-1 RNA <50 copies/mL), receiving stable anti-retroviral treatment for at least the past 6 months, with no history of virological treatment failure and with no known or suspected resistance to non-nucleoside reverse transcriptase inhibitors or to integrase inhibitors.
- This dual therapy should preferably be reserved for patients whose viral load has been undetectable for at least one year and with no history of virological failure or resistance, with a CD4 count greater than 400 cells/mm^3 and whose CD4 count has never dropped below 200 cells/mm^3.
- Considering the potential risk of congenital malformation with dolutegravir, JULUCA is not recommended in women of child-bearing 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).
- Once virological success is achieved (VL <50 copies/ml), whether after first-line treatment or following relay treatment, a change in anti-retroviral treatment may be useful or necessary, under variable circumstances and for variable purposes. Treatment should be tailored to enhance safety and/or administration simplicity, while maintaining immuno-virological efficacy.

Role of the medicinal product in the therapeutic strategy

- Dolutegravir/rilpivirine dual therapy fits into the various recommended therapeutic optimisation strategies in virologically- suppressed patients, following first or second line of conventional tritherapy and with no history of failure, under specific circumstances and with variable objectives (to maximise efficacy, to minimise toxicity, to minimise drug interactions or to minimise the emergence of resistance in the event of failure, etc.). Replacement of tritherapy with the dolutegravir + rilpivirine combination may be considered in patients with no prior virological failure and to whom treatment without NRTI or PI/ritonavir is to be offered.
- JULUCA can be used to simplify treatment compared to the separate administration of the two components (1 tablet per day instead of 2), when prescription of this dual therapy is considered in virologically-suppressed patients with no history of virological failure or resistance.
- Good treatment observance is recommended due to the low rilpivirine genetic barrier.

Clinical data

- Two studies demonstrated the efficacy of dolutegravir (TIVICAY) + rilpivirine (EDURANT) free dose dual therapy in the context of a change strategy (de-escalation strategy) in patients pretreated and virologically suppressed by conventional tritherapy (comprising 2 NRTIs + 1 NNRTI, or 1 INI or 1 boosted or non-boosted PI) for at least the past 6 months and with no history of failure or resistance, in terms of maintenance of virological suppression after 48 weeks of treatment.

- The selected population, however, limited the scope of the results. Indeed, multiple non-inclusion criteria were applied, including in particular: pregnant or breast-feed women or women planning to become pregnant during the trial, liver failure, co-infection with HBV during selection, or need for anti-HCV treatment during the trial and high risk of suicide.
- There is a high risk of adverse events occurrence, particularly neuropsychiatric, due to the cumulative toxicity of each of the products.

Special prescription requirements

- Medicinal product subject to initial annual hospital prescription
- Prescription reserved for certain specialists

Benefit of the medicinal product

- The actual clinical benefit* of JULUCA is high.
- JULUCA does not provide any clinical added value** (CAV V)) over conventional tritherapies or the free-dose combination of its two components.
- Approved for non-hospital pharmacy reimbursement or for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 25 July 2018 (CT-16942) available at **www.has-sante.fr**

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