HAUTE AUTORITÉ DE SANTÉ

VIROLOGY
New form
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**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

# **ISENTRESS** 100 mg (raltegravir), granules for oral suspension, antiretroviral

**Next-line treatment in infants aged 4 weeks to 2 years and weighing between 3 and 20 kg who are infected with HIV**

## Main points

- ISENTRESS 100 mg, granules for oral suspension, has Marketing Authorisation, in combination with other antiretroviral medicinal products, in the treatment of infection with the human immunodeficiency virus (HIV-1) in adults, adolescents, children, young children and infants over 4 weeks old and weighing between 3 and < 20 kg.
- It is a treatment option, only for children at a therapeutic impasse and in the absence of viral mutations reducing the sensitivity to this substance and to the at least two other ARVs that will be used in combination.
- On account of the high risk of resistant mutations emerging in cases of virological failure, it is essential to use raltegravir with at least 2 active antiretroviral agents.

## Therapeutic use

- In children, combinations including two nucleoside reverse transcriptase inhibitors (NRTIs) and 1 protease inhibitor (PI)/ritonavir are favoured. The choice of PI/r is preferably lopinavir/ritonavir (KALETRA). A combination including 2 NRTIs and 1 NNRTI must be reserved for the very rare situations where there is certainty about the compliance of the child and his/her family to the therapeutic project.
- **Role of the medicinal product in the therapeutic strategy**

  The data concerning the use of ISENTRESS in the form of granules for oral suspension in children from 4 weeks to 2 years old are currently very limited. For this group of children, this new formulation of raltegravir may be considered as a therapeutic option in special circumstances as a combination product for multiresistant patients in whom the sensitivity of the HIV virus to raltegravir has been tested in advance.

  In children over 2 years old and weighing less than 20 kg, this presentation is an addition to the range of other presentations of ISENTRESS available in the form of chewable tablets (of 25 and 100 mg) intended for children who are 2 to 11 years old.

## Clinical data

- In infants and young children aged from 4 weeks to 2 years, the efficacy and safety profile of raltegravir is based on the results of a non-comparative phase I/II study that included 26 patients aged from 4 weeks to 2 years (18 of them included in South Africa). All the patients had previously been treated with a retroviral as prophylaxis for mother-to-child transmission of the virus and/or during perinatal treatment for HIV infection. The majority of the patients had previously been treated with NNRTIs (73%) and INIs (46%), and only 19% had been treated with PI/r.

  At inclusion, 69% of the patient had a high plasma viral load (HIV-1 RNA > 100 000 copies/ml). The median number of CD4+ cells was 1400 and the median percentage of CD4+ was 18.6%.

  Raltegravir was administered in the form of granules for oral suspension, taken independently of the consumption of food, together with optimised maintenance therapy including at least 2 active medicinal products in the majority of cases (about 50%, combined with ≥ 3 active medicinal products), including lopinavir/ritonavir in two-thirds of the patients.

  After 48 weeks of treatment, a reduction of at least 1 log10 in the HIV-1 RNA viral load was obtained in 85% of the patients and a RNA < 50 copies/ml was obtained in 52.6% of the patients. The mean change in the number of CD4+/mm3 was +492 CD4+ cells/mm3, or an increase of +7.8% compared with inclusion.

- Overall, the immunological and virological response observed in week 48 in the infants and young children aged from 4 weeks to less than 2 years thus appears to be of the same order as that described in the other cohorts of older patients (2 to 18 years old) in the study, with a similar safety profile. However, these data are currently very limited and do not allow definite conclusions about the efficacy and safety of this medicinal product in this age group to be drawn.

## Prescribing conditions

- Medicine for initial hospital prescription

## Benefit of the medicinal product

- The actual benefit* ISENTRESS 100 mg, granules for oral suspension, is substantial.
- ISENTRESS 100 mg, granules for oral suspension, provides clinical added value** (CAV IV, minor) in children aged from 4 weeks to 2 years in therapeutic impasse and in the absence of viral mutations reducing the sensitivity to this substance and to the at least two other ARVs that will be used in combination.
- In children above 2 years old and weighing less than 20 kg, it is an addition to the range of other presentations of ISENTRESS.
- 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 18 November 2015 (CT-14458) 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.

** 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 means "no clinical added value".