HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

04 NOVEMBER 2020

The legally binding text is the original French opinion version

etravirine

INTELENCE 25, 100 and 200 mg tablets

Indication extension

Key points

Favourable opinion for reimbursement in the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-experienced children 2 to 6 years of age.

What therapeutic improvement?

Therapeutic improvement in management.

Role in the care pathway?

In the event of virologic failure, treatment should preferably combine a ritonavir-boosted protease inhibitor (active P/r, primarily darunavir/r; in exceptional cases tipranavir/r), combination of two PIs is not recommended, combined with another two active antiretrovirals from among:

- etravirine (which frequently remains active, even in the event of resistance to efavirenz and/or nevirapine, whereas there is cross-resistance with rilpivirine);
- raltegravir (particularly in combination with darunavir/r and etravirine);
- dolutegravir, which generally remains active, at a dosage of 50 mg x2/d, in the event of resistance mutations to raltegravir or elvitegravir. The dolutegravir plus etravirine combination should not be

used, except in combination with a PI/r to compensate for the enzyme inducing effect of etravirine on the metabolism of dolutegravir;
- maraviroc, if absence of virus using the CXCR4 coreceptor;
- enfuvirtide (but for which long-term use is limited by its injection form);
- one or more NRTIs. In the event of multiresistance to NRTIs (≥ 3 TAM + M184V), a residual activity of abacavir and tenofovir may persist. However, maintenance of NRTIs in the event of multiresistance to this class of antiretrovirals is not justified when fewer than three fully active antiretrovirals are available.

Role of the medicinal product in the care pathway

INTELENCE (etravirine) is an NNRTI that is frequently active on viruses resistant to the first NNRTIs (efavirenz and/or nevirapine). In accordance with its MA, INTELENCE (etravirine) is not recommended in antiretroviral treatment-naive patients.

In combination with a boosted protease inhibitor and other antiretrovirals, it is a therapeutic option for the treatment of HIV-1 infection in children of 2 to 6 years of age, as it is in previously treated adults, adolescents and children of 6 to < 18 years of age. These patients must have a detectable viral load under current antiretroviral therapy and have viral strains with resistance mutations to non-nucleoside reverse transcriptase inhibitors and protease inhibitors. Since cross-resistance with other NNRTIs is possible, genotype analysis of the reverse transcriptase should be performed prior to its prescription to verify the absence of 3 or more mutations reducing viral sensitivity to this drug.

Very rare cases of severe skin eruption, including toxic epidermal necrolysis and DRESS or severe hypersensitivity (rash, eosinophilia, which may be combined with, to varying degrees, adenopathy, hepatitis, interstitial nephritis, interstitial lung disease) have been reported within a period of 3 to 6 weeks following the start of etravirine therapy, reinforcing the need for monitoring precautions at treatment initiation. Prescribers should be informed that the incidence of skin rash was higher in female subjects (see SPC).

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ The condition concerned by these proprietary medicinal products leads to a marked deterioration in quality of life and is life-threatening.

◗ These medicinal products aim to prevent and/or correct the immune deficiency induced by HIV infection.

◗ In combination with a boosted protease inhibitor and other antiretrovirals, the efficacy/adverse effects ratio is high in the treatment of human immunodeficiency virus type 1 (HIV-1) infection.

◗ It is a first or second-line treatment in patients previously treated with antiretrovirals.

◗ There are few medicinal alternatives to these medicinal products in children and adolescents previously treated with other antiretroviral classes.

◗ Public health impact:

Considering:

- the seriousness and frequency of HIV-1 infection, and its transmissible nature,
- the frequency of resistance,
- the medical need to have access to new antiretrovirals, particularly in the event of failure of or resistance to first-line treatments,
- available data that demonstrate a favourable efficacy, safety and resistance profile, and hence an expected impact on morbidity and mortality and/or the quality of life of treated patients due to its activity on viral strains resistant to the other most widely used therapeutic classes,
- an expected impact on the care and life pathway, and in terms of breaking the HIV transmission chain with multidrug-resistant virus strains due to the reduction in viral load,

INTELENCE (etravirine) is likely to have an impact on public health.

Consequently, the Committee considers that the clinical benefit of INTELENCE (etravirine) 25, 100 and 200 mg tablets, administered in combination with a boosted protease inhibitor and other antiretrovirals, is substantial in the MA indication extension to children of 2 to 6 years of age.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the paediatric indication extension (2 to 6 years of age) and at the MA dosages.

Recommended reimbursement rate: 100%

Clinical Added Value

Considering:

- **available data in adults and children from the age of 6 years demonstrating its immuno-virologic efficacy in the treatment of HIV-1 infection in previously treated patients,**
- **the data available (phase I/II study) in children from the age of 2 years, suggesting an efficacy and safety profile comparable to that described in adults, adolescents and children from the age of 6 years,**

the Committee considers that, as in adults and children from 6 years of age, the proprietary medicinal product INTELENCE (etravirine), in combination with a boosted protease inhibitor and optimised antiretroviral treatment:

- **provides a moderate clinical added value (CAV III) in the treatment of a population limited to previously treated children 2 to <6 years of age, with a detectable viral load under current antiretroviral therapy and with viral strains with resistance mutations to non-nucleoside reverse transcriptase inhibitors and protease inhibitors and in the absence of mutations reducing viral sensitivity to this drug;**
- **provides no clinical added value (CAV V, no clinical added value) in previously treated patients without resistance mutations to non-nucleoside reverse transcriptase inhibitors and protease inhibitors.**