SUMMARY

cabotegravir

APRETUDE 30 mg and 600 mg

film-coated tablets and prolonged-release suspension for injection

First listing

Adopted by the Transparency Committee on 29 May 2024

Summary of opinion

Favourable opinion for reimbursement in the indication for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg.

Transparency Committee's conclusions

Clinical Benefit

- HIV infection is a serious, life-threatening disease.
- This proprietary medicinal product, in combination with safer sex practices, is a preventive treatment to reduce the risk of sexually acquired HIV-1 infection in high-risk adults.
- The efficacy/adverse effects ratio is high, subject to strict compliance with treatment and regular monitoring.
- There is only one therapeutic alternative with an MA in PrEP: the proprietary medicinal product TRUVADA (emtricitabine/tenofovir disoproxil). APRETUDE (cabotegravir) is administered as part of an overall HIV prevention strategy, as an additional tool along with other preventive measures, based, in particular, on compliance with basic HIV and STI prevention measures, such as condom use.
- This proprietary medicinal product is a first-line treatment in individuals at high risk of HIV-1 infection.

Public health benefit

Considering:

- the seriousness of HIV infection;
- the incidence of HIV infection, which has remained high and stable in France since 2010, particularly in high-risk populations, demonstrating that the epidemic is not under control;

- the medical need to have access to new approaches and effective prevention tools to combat the HIV epidemic;
- the theoretical response provided by APRETUDE (cabotegravir) to the identified medical need, but for which the real impact on both an individual and collective level is still to be demonstrated in practice: an impact that will depend on the adherence of the populations concerned to this practice, compliance with the treatment, which is essential to its efficacy, and the risks associated with this practice that cannot be totally excluded currently (increase in other STIs in the event of a decrease in condom use, long-term metabolic and cardiovascular toxicity);
- the expected impact on the health system in terms of management of this practice: the required training for healthcare players and professionals, increase in healthcare use associated with the initiation of treatment, and its regular monitoring, including laboratory tests;

APRETUDE (cabotegravir) as pre-exposure prophylaxis of HIV-1 is likely to have an impact on public health in subjects at high risk of HIV transmission, but this impact is still to be demonstrated in real world conditions.

Considering all these elements, the Committee deems that the clinical benefit of APRETUDE (cabotegravir), in combination with safer sex practices, is high in pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg.

The Committee issues a favourable opinion for inclusion of APRETUDE (cabotegravir), in combination with safer sex practices, in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg, and at the MA dosages.

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%**

Clinical Added Value

Considering:

- the partially met medical need in pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg;
- evidence of the superiority of cabotegravir (APRETUDE) in terms of reduction in the incidence of documented new HIV-1 infections compared to the emtricitabine / tenofovir disoproxil (TRUVADA) combination as continuous administration:
  - in the HPTN 083 study (HIV-uninfected cisgender men who have sex with men and HIV-uninfected transgender women who have sex with men) with a relative risk reduction of 66%,
  - in the HPTN 084 study (HIV-uninfected cisgender women who have sex with men) with a relative risk reduction of 89%;
- pharmacokinetic data (“Pop PK-adults” model and HPTN 083-01 and HPTN 084-01 study extensions) demonstrating similar exposure to cabotegravir in the adolescent population (12 years and over and weighing at least 35 kg) and in adults, without demonstrating any clinically relevant difference between these two populations;

- a satisfactory safety profile, although marked by injection site reactions, and the fact that no new safety signals have been identified. The important identified risks (risk management plan) include hepatotoxicity, HIV-1 seroconversion and development of resistance;

but:

- a limited transposability of the available data (HPTN 083 and HPTN 084 studies) to the population liable to receive PrEP with APRETUDE (cabotegravir) in France, i.e.:
  - risky behaviours or practices of the subjects included in the studies not very or not transposable to those in the French population liable to receive HIV PrEP,
  - non-inclusion of pregnant or breastfeeding women and IV drug users in the clinical studies,
  - uncertainties with respect to long-term compliance for a long acting treatment, particularly since adherence was already lower in both groups in the HPTN-083 study after the first year,
  - the absence of data on cabotegravir enabling its role to be assessed compared to the other method of administration of the emtricitabine / tenofovir disoproxil combination (TRUVADA), a regimen that is off-label but validated by the WHO and national recommendations;
- a risk of selection of INI-resistant virus strains in individuals not complying with the injection schedule and of transmission of these viruses, whereas INIs are the pillars of first-line antiretroviral (ARV) therapy;

the Committee deems that APRETUDE (cabotegravir) provides a minor clinical added value (CAV IV) compared to the emtricitabine / tenofovir disoproxil (TRUVADA) fixed-dose combination as a continuous administration regimen, when APRETUDE (cabotegravir) is combined with safer sex practices, in pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in high-risk adults and adolescents, weighing at least 35 kg.