HAUTE AUTORITÉ DE SANTÉ

INFECTIOLOGY
NEW MEDICINAL PRODUCT
April 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VIEKIRAX (ombitasvir/paritaprevir/ritonavir), fixed-dose direct-acting antiviral combination,
EXVIERA (dasabuvir), direct-acting antiviral

Minor improvement, as with DAKLINZA (daclatasvir) and OLYSIO (simeprevir), in the treatment of adults infected with hepatitis C virus (HCV) genotypes 1 and 4

Main points

- VIEKIRAX, like EXVIERA, has Marketing Authorisation in the treatment of chronic hepatitis C, in combination with other medicinal products, in adults infected with HCV genotype 1.
- VIEKIRAX also has Marketing Authorisation in adults infected with HCV genotype 4.
- VIEKIRAX and EXVIERA may provide a cure for the majority of patients with hepatitis C, with or without extrahepatic manifestations. Treatment should be offered as a priority in all patients whose hepatic disease is at fibrosis stage F3 or F4 and in certain special populations. A specific mention concerns patients infected with the genotype 3 virus, for whom early treatment is desirable. Patients at fibrosis stage F2 should also receive new treatments within a short time. For stages F0 or F1, treatment may be delayed depending on the progression of the disease and the context of the pathology.
- They provide a minor improvement, as do DAKLINZA and OLYSIO, in the treatment of chronic hepatitis C genotypes 1 and 4 given:
  - their significant virological efficacy similar to that observed with the available sofosbuvir-based combinations (sofosbuvir/daclatasvir, sofosbuvir/simeprevir and sofosbuvir/ledipasvir) with a good level of evidence,
  - their satisfactory safety profile,
  - the significant risk of developing cross-resistance in the event of treatment failure,
  - the potential for drug interactions,
  - the current therapeutic strategy which mainly includes a combination with sofosbuvir, without interferon.

Therapeutic use

Currently the therapeutic strategy for chronic hepatitis C is based on combinations of direct-acting antivirals, with or without ribavirin, providing substantial efficacy (> 90%), including in patients who previously were difficult to treat (including those with cirrhosis, co-infected with HIV or who have undergone liver transplantation). The role of interferon is becoming very limited even null in the majority of patients.

Role of the medicinal product in the therapeutic strategy

For genotype 1 patients: The ombitasvir/paritaprevir/ritonavir + dasabuvir (VIEKIRAX + EXVIERA) combination is a good therapeutic option due to a high level of evidence of efficacy and safety.
For genotype 4 patients: The ombitasvir/paritaprevir/ritonavir + dasabuvir (VIEKIRAX) combination is a therapeutic option but still has limited clinical data (phase II studies).

Clinical data

- Genotype 1 patients

The efficacy and safety of the VIEKIRAX + EXVIERA combination (ombitasvir/paritaprevir/ritonavir + dasabuvir), with or without ribavirin, for 12 or 24 weeks, was evaluated in six phase III studies, carried out in patients infected with HCV genotype 1 with compensated liver disease (three studies in treatment-naïve patients without cirrhosis, two studies in patients who have failed previous treatment, without cirrhosis, and one study in treatment-naïve or pretreated compensated cirrhotic patients).
The treatment duration evaluated in the studies was 12 weeks (with or without ribavirin) for non-cirrhotic patients and 12 or 24 weeks in cirrhotic patients.
The sustained virologic response rates, defined by a HCV RNA level < 25 IU/mL 12 weeks after the end of treatment (primary endpoint) were significant (> 90%) in all the studies in the various treatment groups according to the regimen adopted by the Marketing Authorisation.

- Other populations

The efficacy of VIEKIRAX and EXVIERA was also observed in HCV/HIV co-infected patients, liver transplant patients, genotype 4 patients (VIEKIRAX only), but these data are still very limited and additional studies are needed to validate these preliminary results.

- Resistance

Data from *in vitro* studies and clinical studies show that the genetic barriers of the three antivirals (ombitasvir/paritaprevir/dasabuvir) used in the association are low.

- Safety

The safety profile is satisfactory overall. The available data have not shown any major concerns.

Benefit of the medicinal product

- The actual benefit* of VIEKIRAX and EXVIERA is substantial.
- VIEKIRAX and EXVIERA clinical added value** (IAB IV, minor), as do DAKLINZA and OLYSIO, in the treatment of adults infected with HCV genotypes 1 and 4.
- 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 01 April 2015 (CT-14068) 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".