HAUTE AUTORITÉ DE SANTÉ

INFECTIOUS DISEASE
New medicinal product
December 2017

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VOSEVI (sofosbuvir / velpatasvir / voxilaprevir), fixed direct-acting antiviral combination

High clinical benefit for the treatment of chronic Hepatitis C genotypes 1 to 6 and minor clinical added value compared to the current therapeutic strategy for adults patients infected with HCV genotypes 1 to 6

Main points

- VOSEVI has been granted a marketing authorisation for the treatment of chronic hepatitis C in adults infected with hepatitis C virus (HCV) genotypes 1 to 6.
- Its pan-genotypic virological efficacy is high (>90%), with a treatment duration between 8 and 12 weeks based on the patients' liver disease with or without compensated cirrhosis (Child-Pugh A only).
- Its efficacy has been demonstrated in patients for whom treatment with previously available direct-acting antivirals has failed, in particular for whom NS5A inhibitor therapy has failed, for whom the therapeutic options available are very limited and insufficiently validated.
- Its safety and resistance profile is satisfactory but it has a high medicinal interaction potential.

Therapeutic strategy

- The therapeutic management of chronic hepatitis C relies on combinations based on direct-acting antivirals (DAAs), capable of obtaining a high level of efficacy (> 90%).
- Since 2017, most patients have been able to benefit from an 8- to 12-week ribavirin-free treatment. These ribavirin-free regimens should be preferred.

Role of the medicinal product in the therapeutic strategy

VOSEVI is among the therapeutic options for the treatment of patients with chronic hepatitis C genotypes 1 to 6, without or with compensated cirrhosis (Child-Pugh A only). As for other proprietary medicinal products containing an NS3A/4A protease inhibitor, its use is not recommended for patients with decompensated liver disease, unlike EPCLUSA which contains no NS3A/4A protease inhibitor.

Moreover, in view of:

- the fact that this is the first medicinal product to be granted a marketing authorisation for the treatment of cases of failure of the DAAs currently available,
- the lack of proven benefit of 8 weeks of VOSEVI treatment compared to 12 weeks of EPCLUSA treatment in naive patients,
- uncertainties in respect of retreatment possibilities (therapeutic options in the event of failure of VOSEVI),

its use should be preferentially reserved for patients presenting with factors predictive of poor response to the alternatives available; this particularly applies to:

- patients for whom treatment with previously available direct-acting antivirals has failed, in particular for whom NS5A inhibitor therapy has failed, for whom the therapeutic options available are very limited and insufficiently validated,
- genotype 3 patients, in particular those with compensated cirrhosis.

The risk of HBV reactivation common to all DAAs and the risk of severe bradycardia and conduction disorders associated with the use of proprietary medicinal products based on sofosbuvir in combination with amiodarone must be taken into account.

Clinical data

- The phase III studies conducted on patients with or without compensated cirrhosis show pan-genotypic virological recovery of > 90%, with 8 to 12 weeks of ribavirin-free treatment.
- The benefit of VOSEVI compared to EPCLUSA or to the other alternatives available is therefore based on:
  - the reduction in the treatment duration in particular for DAA treatment-naive genotype 3 patients (8 weeks), without cirrhosis or with compensated cirrhosis,
  - its efficacy in patients for whom currently available DAAs have failed, with a treatment duration of 12 weeks for all patients, regardless of viral genotype.
- The safety profile was satisfactory and similar to that of other sofosbuvir-based combinations currently available.

Special prescription requirements

- Hospital prescription reserved for specialists in gastroenterology and hepatology, in internal medicine and in infectious disease.

Benefit of the medicinal product

- The actual clinical benefit* of VOSEVI is high.
- VOSEVI provides a minor clinical added value (CAV IV) for the therapeutic strategy of adult patients infected with HCV genotypes 1 to 6.
- Approval for non-hospital pharmacy reimbursement and for hospital treatment.

HAUTE AUTORITÉ DE SANTÉ
This document was drafted on the basis of the Transparency Committee opinion dated 6 December 2017 (CT-16443)
available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) consists of 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".