HAUTE AUTORITÉ DE SANTÉ

INFECTIOUS DISEASE
New indication
April 2018

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

HARVONI (sofosbuvir/ledipasvir), direct-acting antiviral

High clinical benefit and moderate clinical added value for the treatment of chronic hepatitis C in adolescents aged from 12 to < 18 years.

Main points

- HARVONI has now been granted a marketing authorisation for the treatment of chronic hepatitis C in adolescents aged from 12 to < 18 years.
- The efficacy and safety in adolescents were assessed for the treatment of chronic hepatitis C virus (HCV) genotype 1-related infection with a similar profile to that described in adults. For genotypes 3, 4, 5 and 6, the marketing authorisation is extrapolated from the clinical data obtained on HCV genotype 1 and clinical feedback in adults.
- It is a first-line option for the treatment of chronic hepatitis C infection associated with HCV genotypes 1, 3 (pretreated), 4, 5 and 6.

Pre-existing indication*

HARVONI has been granted a marketing authorisation for the treatment of chronic hepatitis C in adults.

Therapeutic strategy

In children, the natural course of hepatitis C is poorly elucidated since this infection is rare and generally asymptomatic. The risk of adulthood complications would be relatively low and of late onset in the absence of other liver disease or alcohol absorption which are known factors in the acceleration of fibrosis.
Treatment, the indication of which is based on clinical factors, the existence or not of risk factors and histology, is exceptionally urgent. It should be discussed on a case-by-case basis from 12 years of age within the framework of a consultation between the adult and paediatric hepatologist or infectious disease specialist.
Direct-acting antivirals (SOVALDI and HARVONI) are recommended as conventional treatments for adolescents. Interferon is no longer recommended for this population.

- **Role of the medicinal product in the therapeutic strategy**
  HARVONI is a first-line option for the treatment of chronic hepatitis C infection associated with HCV genotype 1, 3 (pretreated), 4, 5 and 6.

Clinical data

- The extension of the indication of the fixed sofosbuvir/ledipasvir combination for the treatment of HCV-infected adolescents is based on the intermediate analysis of the findings of a non-comparative phase II trial in which the population included 100 patients infected with HCV genotype 1 aged from 12 years to < 18 years, who were treated with HARVONI for 12 weeks (80 naive patients and 20 pretreated patients).
- The median patient age was 15 years (12 to 17 years). The mean body mass index was 23 kg/m2; 55% has HCV RNA counts at inclusion ≥ 800,000 IU/mL in 55% of patients. The mode of HCV transmission was vertical in the majority of cases (84%).

* This summary does not concern this indication.

- The sustained virological response percentage (SVR at 12 weeks of treatment) was 97% (95 CI: [91.5%; 99.4%]): 77/80 for the naive patients and 20/20 for the pretreated patients. The only treatment-naive patient having cirrhosis obtained an SVR12. No virological failure or relapse under treatment was observed. Three patients were lost to follow-up.

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 HARVONI is high for the treatment of chronic hepatitis C in adolescents aged from 12 to under 18 years.
- HARVONI provides a moderate clinical added value** (CAV III) for the treatment of chronic hepatitis C in adolescents aged over 12 years.
- Approval for non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 18 April 2018 (CT-16717) 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".