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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ZEPATIER (elbasvir grazoprevir), fixed combination of direct-acting antivirals

Minor clinical added value, like other direct-acting antivirals (HARVONI, DAKLINZA, OLYSIO, VIEKIRAX, EXVIERA), in the treatment of genotype 1 and 4 chronic hepatitis C.

Main points

- ZEPATIER has Marketing Authorisation in the treatment of chronic hepatitis C in adults infected with genotype 1 and 4 hepatitis C virus (HCV).
- It represents minor clinical added value in treatment, given:

- its substantial virological efficacy in patients infected with genotype 1 and 4 HCV with a treatment duration of 12 to 16 weeks (± ribavirin) for patients with or without compensated cirrhosis (Child-Pugh A only),
- the demonstration of efficacy superior to sofosbuvir + peg-interferon/ribavirin triple therapy (comparator that is no longer optimal), with an extent of effect comparable to the alternatives currently recommended,
- the demonstration of significant efficacy in specific populations, such as renal failure or dialysis patients, for whom the alternatives are limited and insufficiently evaluated,
- its satisfactory safety profile,
- its significant risk of developing resistance in the case of treatment failure,
- the absence of comparison with the other direct-acting antiviral combinations available, such as sofosbuvir + NS5A inhibitor combinations which most often allow a shorter treatment duration (8-12 weeks) without addition of ribavirin.

Therapeutic use

- Currently the therapeutic strategy for chronic hepatitis C relies on direct-acting antiviral combinations, with or without ribavirin, enabling substantial efficacy (>90%) to be obtained.
- The quality of therapeutic results and good tolerance currently observed with direct-acting antivirals, the fact that the majority of severe patients were treated in the past 3 years and the expected benefit on quality of life, treatment can now be offered to all patients infected with HCV, including asymptomatic carriers with F0 or F1-stage fibrosis who are not at risk of transmission of HCV, not included in previous recommendations. In this group of patients, detailed information on the treatment, its necessary compliance, its constraints, advantages and disadvantages must be provided; the therapeutic decision must be made in agreement with the patient, taking into account the slowly progressive nature of the disease, the benefits and risks expected from treatment and the possibilities for further treatment with shorter regimens.
- **Role of the medicinal product in the therapeutic strategy**

  ZEPATIER is one of the therapeutic options for treatment of patients with chronic genotype 1 and 4 hepatitis C with or without compensated cirrhosis (Child-Pugh A only).

Clinical data

- Studies have shown a significant (> 90%) efficacy of ZEPATIER in terms of sustained virological response in HCV-infected patients of genotype 1 and 4, after 12 to 16 weeks of treatment. The addition of ribavirin and a treatment duration of 16 weeks was required in patients with genotype 1a with an HCV RNA count > 800,000

IU/mL and/or pre-existing NS5A variants as well as in patients of genotype 4 with an HCV RNA count > 800,000 IU/mL. The quantity of effects observed are of the same level as those reported with the therapeutic options currently recommended for patients of genotype 1 and 4.

- The safety profile was satisfactory and comparable to that of other currently available protease-based combinations (ombitasvir/paritaprevir/ritonavir + dasabuvir, or sofosbuvir + simeprevir). These combinations are not recommended in patients with moderate hepatic impairment (Child-Pugh B) and are contraindicated in patients with hepatic impairment (Child-Pugh C) due to a risk of liver decompensation and liver failure during treatment. On the other hand, they represent preferential options in patients with severe renal failure (GFR < 30 mL/min) or on dialysis.

Special prescribing conditions

- Medicine for hospital prescription restricted to specialists in gastroenterology and hepatology, internal medicine, and infectious diseases.

Benefit of the medicinal product

- The actual benefit* of ZEPATIER is substantial
- ZEPATIER provides minor clinical added value** (CAV IV) in the same way as the other direct-acting antivirals available (HARVONI, DAKLINZA, OLYSIO, VIEKIRAX, EXVIERA), in treating adult patients infected by genotype 1 and 4 HCV.
- 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 19 October 2016 (CT-15357) 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”.