HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

2 DECEMBER 2020

The legally binding text is the original French opinion version

ledipasvir/sofosbuvir

HARVONI 90 mg/400 mg film-coated tablets

HARVONI 45 mg/200 mg film-coated tablets

HARVONI 45 mg/200 mg coated granules in sachet

HARVONI 33.75 mg/150 mg coated granules in sachet

New indication

and

Availability of new forms

Key points

Favourable opinion for reimbursement in the treatment of chronic hepatitis C (CHC) in paediatric patients aged 3 to < 12 years.

Favourable opinion for reimbursement of the new HARVONI (ledipasvir/sofosbuvir) 45 mg/200 mg film-coated tablets, 45 mg/200 mg coated granules in sachet and 33.75 mg/150 mg coated granules in sachet forms.

What therapeutic improvement?

No clinical added value in the therapeutic strategy in children aged 3 to < 12 years.

Role in the care pathway?

The reference treatment for chronic hepatitis C in adults and adolescents (from 12 years of age) is now based on direct-acting antiviral combinations. These combinations usually enable a sustained virological response (> 90%) to be obtained, including in cirrhosis patients. The majority of patients can now benefit for 8 to 12 weeks of treatment with ribavirin-free pangenotypic direct-acting antiviral combinations. These pangenotypic regimens are recommended preferentially since they reduce the needs for genotyping or resistance tests to guide treatment decisions.

In children aged under 12 years, due to the slow-progressing nature of the infection in paediatric patients, the guidelines recommend delaying the initiation of treatment pending the availability of pangenotypic combinations: EPCLUSA (sofosbuvir/velpatasvir) and MAVIRET (pibrentasvir/glecaprevir), which are reference options.

Role of the medicinal product in the care pathway

In children who meet the treatment criteria, HARVONI (ledipasvir/sofosbuvir), is a first-line option for the treatment of chronic hepatitis C related to genotype 1, 3, 4, 5 and 6 HCV. However, its role becomes very limited (or even non-existent) following the availability of ribavirin-free pangenotypic direct-acting antiviral combinations, which simplify treatment and shorten the treatment duration (8 to 12 weeks for the majority of patients).

COMMITTEE'S CONCLUSIONS

Clinical benefit

- Hepatitis C is a viral disease in which the seriousness is related to the potential long-term complications of its chronicisation: cirrhosis, hepatocellular carcinoma. HCV infection is rare in children and generally asymptomatic. The outcome of the disease is not identical to that in adults, as time to progression is longer. Hepatitis C in children is therefore a non-serious disease in most cases.

- HARVONI (ledipasvir/sofosbuvir), used with or without ribavirin, is a curative treatment.

- The efficacy/adverse effects ratio of this medicinal product is high in this indication.

- This proprietary medicinal product is a first-line treatment. However, it only has a very restricted, or even non-existent, role following the availability of pangenotypic combinations.

- There are therapeutic alternatives in the treatment of hepatitis C in children aged 3 to < 12 years, particularly pangenotypic combinations, which have become the reference options.

Public health impact

Considering:

- the seriousness of the disease and its prevalence,
- the medical need that is currently met by pangenotypic antiviral combinations, which have become the reference options, opening up new treatment opportunities, particularly in terms of reducing the treatment duration or simplifying treatment (reduced need for genotyping or resistance tests),
- the absence of an additional impact of HARVONI (ledipasvir/sofosbuvir) in terms of morbidity and mortality, on the care and life pathway, in particular due to a longer treatment duration (8 to 24 weeks) and the need to sometimes combine it with ribavirin,

HARVONI (ledipasvir/sofosbuvir) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of HARVONI (ledipasvir/sofosbuvir) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of HARVONI (ledipasvir/sofosbuvir) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the new indication and at the MA dosages.

- **Recommended reimbursement rate: 100%**

Clinical Added Value

Considering:

- **the data available in adults, demonstrating significant virological efficacy,**
- **the data available (phase 2 study) in children aged from 3 years, suggesting an efficacy and safety profile comparable to that described in adults,**
- **the rapidly evolving care pathway, following the availability of pangenotypic antiviral combinations, which have become the reference options,**

the Committee considers that HARVONI (ledipasvir/sofosbuvir) provides no clinical added value (CAV V) in the treatment of chronic hepatitis C in children aged 3 to < 12 years.