HAUTE AUTORITÉ DE SANTÉ

INFECTIOUS DISEASE
New indication
June 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

PEGASYS (peginterferon alfa-2a), interferon

High clinical benefit in chronic hepatitis B in children over the age of 3 and minor clinical added value like VIREAD and BARACLUDE

Main points

- PEGASYS has now a marketing authorization (MA) in the treatment of HBe antigen (HBeAg)-positive chronic hepatitis B in non-cirrhotic children and adolescents aged 3 years and over, with viral replication and confirmed persistently elevated serum ALAT levels.
- Its superiority has been demonstrated compared to no treatment in terms of HBe seroconversion at 24 weeks after 48 weeks of treatment.
- Despite its safety, it can lead to a sustained virological response (HBs seroconversion) and does not induce resistance.
- It should be started on a case by case basis, taking predictive factors of response to interferon into account along with the risk of adverse effects.

Pre-existing indications*

PEGASYS also has MA in the treatment of hepatitis B in adults and hepatitis C (see MA for further details).

Therapeutic strategy

- In children and adolescents, treatments for chronic hepatitis B must be prescribed as part of specific protocols and include specialised monitoring.
- When antiviral treatment is indicated, two first-line strategies can be discussed:
  - Peginterferon alfa-2a (PEGASYS) for a limited 48-week period,
  - A nucleoside or nucleotide analogue for an extended period: tenofovir disoproxil fumarate (VIREAD) or entecavir (BARACLUDE), the only ones to have MA in this indication.
- **Role of the medicinal product in the therapeutic strategy**
  PEGASYS is a first-line therapeutic option in the treatment of chronic hepatitis B in children and adolescents aged 3 years and over, in the same way as tenofovir disoproxil fumarate (VIREAD) or entecavir (BARACLUDE).

Clinical data

- A study compared a 48-week peginterferon alfa-2a treatment versus an untreated control group, in anti-HBV treatment-naive children and adolescents, aged 3 to 18 years, with chronic hepatitis B, HBeAg and HBsAg-positive, and compensated liver disease.
- The proportion of patients without severe fibrosis achieving HBe seroconversion (HBeAg undetectable and anti-HBe antibody detectable) 24 weeks after the end of the treatment/observation period (primary endpoint) was higher in the peginterferon alfa-2a group compared to the control group (25.7% versus 6.0%, $CI_{95\%}$ [1.54; 19.20]; p=0.0043). Eight patients (7.9%) from the peginterferon alfa-2a group achieved HBs seroconversion (secondary endpoint), synonymous with cure, compared to none in the control group.

* This summary does not concern these indications.

- Use of peginterferon alfa-2a in children and adolescents with or with a previous history of severe psychiatric disorders is contraindicated.
- The safety profile observed in children was similar to that observed in adults, although there is a paediatric-specific concern in relation to delayed height and weight growth.

Special prescription requirements

- Initial half-yearly prescription by gastroenterology, hepatology, internal medicine or infectious disease specialists and/or specialised services.

Benefit of the medicinal product

- The actual clinical benefit* of PEGASYS is high in the treatment of chronic hepatitis B in children.
- PEGASYS provides clinical added value** (CAV IV, minor) in the same way as VIREAD and BARACLUDE in this indication.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was drafted on the basis of the Transparency Committee opinion dated 13 June 2018 (CT-16805) available at **www.has-sante.fr**

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