HAUTE AUTORITÉ DE SANTÉ

IMMUNOLOGY
New medicinal product
September 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

HYQVIA, (Human normal immunoglobulin)

No clinical benefit demonstrated relative to other immunoglobulins in replacement therapy for adults with primary or secondary immunodeficiency

Main points

- HYQVIA has Marketing Authorisation in replacement therapy for adults with primary or secondary immunodeficiency in myeloma or chronic lymphocytic leukaemia (CLL) with severe secondary hypogammaglobulinaemia and recurrent infections
- The combination of human normal immunoglobulin G with recombinant human hyaluronidase permits HYQVIA to be administered in a single subcutaneous injection every 3 or 4 weeks.
- It makes it possible to obtain an annual rate of acute serious bacterial infections of 0.025, below the limit of 1 predefined by health agencies.
- The advantage of HYQVIA, which permits monthly SC administration at a single site is not reflected by an improvement in quality of life relative to IGIV administered monthly at a single site or IGSC administered weekly at several sites.
- Given the lack of direct comparative data versus other immunoglobulins and the lack of data in secondary immunodeficiencies and Ig treatment initiation in primary immunodeficiencies, the choice of one Ig over another cannot be determined.

Therapeutic use

- In primary immunodeficiency (PID), the benefit of replacement therapy for humoral deficiency is established and the medicinal product is recommended.
- In secondary immunodeficiency, immunoglobulins are recommended in the management of infectious complications related to hypogammaglobulinaemia (<5 to 6 g/l) associated with repetitive infectious episodes in patients with CLL or myeloma.

Role of the medicinal product in the therapeutic strategy

The role of HYQVIA is the same as for other proprietary medicinal products based on human normal immunoglobulins with the same indications and used IV or SC.

Clinical data

- The efficacy of HYQVIA was evaluated in a multi-centre, non-comparative phase III study in 83 PID patients (including 14 aged 2 to 12 years), and pretreated with human normal immunoglobulin intravenously (at regular intervals of 3 or 4 weeks, n = 56) or with human normal immunoglobulin subcutaneously (at weekly intervals, n = 31) during period 1 of the study. During period 2, patients received HYQVIA at intervals of 3 or 4 weeks for a median of 12 months (after a titration period of approximately 6 weeks).
  The annual acute serious bacterial infection rate (primary endpoint) was 0.025 during HYQVIA treatment. This rate is below the predefined threshold of 1 (upper limit of the one-sided 99% confidence interval: 0.046, p<0.001).
  The median quality of life scores were comparable in the IGSC, IGIV and IGHy treatment arms.
  During the 3 years of follow-up, the all-cause infection rate was stable (3.25, 3.36 and 2.33).
- The main adverse events observed were systemic with: headache (rate per injection = 0.031), fatigue (0.012), nausea (0.010), fever (0.009), vomiting (0.008) and chills (0.003). Longer-term follow-up data are necessary to assess the immunogenicity profile of subcutaneous administration of recombinant human hyaluronidase.

Special prescribing conditions

- Blood-derived medicine
- Medicine for hospital prescription

Benefit of the medicinal product

- The actual benefit* of HYQVIA is substantial.
- HYQVIA does not provide clinical added value** (CAV V) relative to other immunoglobulins in replacement therapy in adult patients with primary and secondary immunodeficiencies in view of the available data and the lack of comparative data versus immunoglobulins administered intravenously or subcutaneously.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 16 September 2015 (CT-14312) 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".