HAUTE AUTORITÉ DE SANTÉ

GYNAECOLOGY AND OBSTETRICS
New medicinal product
December 2014

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

BEMFOLA (recombinant follitropin alfa), gonadotropin

As a biosimilar medicine, BEMFOLA provides no demonstrated clinical benefit when compared with GONAL-F, the standard biological product.

Main points

- BEMFOLA is a biosimilar of GONAL-F. It has Marketing Authorisation in the stimulation of follicle growth and spermatogenesis (see the indications below)
- The clinical equivalence of BEMFOLA and GONAL-F has been demonstrated in a study relating to the stimulation of multifollicular development in women undergoing superovulation for assisted reproductive technologies.

Indications

"In adult women

- Anovulation (including polycystic ovarian disease (PCOD)) in women who have been unresponsive to treatment with clomiphene citrate.
- Stimulation of multifollicular development in patients undergoing superovulation for assisted reproductive technologies (ART) such as in vitro fertilisation (IVF), gamete intra-fallopian transfer (GIFT) and zygote intra-fallopian transfer (ZIFT).
- Follitropin alfa in association with a luteinising hormone (LH) preparation is recommended for the stimulation of follicular development in women with severe LH and FSH deficiency. In clinical trials these patients were defined by an endogenous serum LH level < 1.2 IU/l.

In adult men

- Follitropin alfa is indicated for the stimulation of spermatogenesis in men who have congenital or acquired hypogonadotrophic hypogonadism with concomitant human Chorionic Gonadotrophin (hCG) therapy."

Therapeutic use

Products containing human FSH are part of the strategies for medical management of human infertility. The fact that around half of couples who do not conceive after 1 year will do so the next year must be considered before resorting to these treatments.
After a first administration of a biologic medicine derived from biotechnology, it is recommended not to change the product administered to the patient (whether the biosimilar or the standard product) and to ensure the traceability of the pharmacovigilance monitoring in order to monitor and limit the risks of immunisation.

Role of the medicinal product in the therapeutic strategy

As a biosimilar of GONAL-F, BEMFOLA plays the same role as the latter in the therapeutic strategy in each of its indications: it is a first-line treatment in all the indications except in patients with anovulation (including PCOD) where it is a second-line treatment after failure of or intolerance to clomiphene citrate.

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Clinical data

- A multicentre randomised open-label study (with blinded evaluators) performed in 372 women undergoing superovulation as an ART technique determined the clinical equivalence of BEMFOLA and GONAL-F based on the result of the number of oocytes siphoned at 12 weeks (primary endpoint) 10.8 versus 10.6 (rounded) or 0.27 [CI = -1.34 to 1.32], which was in line with the equivalence point predefined in the protocol.
- The safety profiles of BEMFOLA and GONAL-F were similar overall but with a higher incidence of ovarian hyperstimulation syndrome in patients who received BEMFOLA. Nevertheless, this difference appears to be linked more with different monitoring between the two groups than with true differences between the safety profiles of the two proprietary medicinal products. Monitoring this syndrome is a routine pharmacovigilance measure provided for in the Risk Management Plan for BEMFOLA and GONAL-F.

Special prescribing conditions

Prescription restricted to doctors specialising in gynaecology, gynaecology-obstetrics, endocrinology and metabolism or urology. Medicine requiring special monitoring during treatment

Benefit of the medicinal product

- The actual benefit* of BEMFOLA is substantial in all the indications of the Marketing Authorisation.
- As a biosimilar medicine, BEMFOLA does not provide any clinical added value relative to the standard biotherapy, GONAL-F (CAV** V, non-existent).
- 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 03 December 2014 (CT-13788) and is available at **www.has-sante.fr**

[i] * 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".

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