HAUTE AUTORITÉ DE SANTÉ

GYNAECOLOGY
New medicinal product
April 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

REKOVELLE (follitropin delta), ovulation stimulant

No clinical benefit demonstrated in comparison to GONAL-f to induce controlled ovarian stimulation for the development of multiple follicles in women undergoing an assisted reproductive technology program.

Main points

- REKOVELLE has Marketing Authorisation to induce controlled ovarian stimulation for the development of multiple follicles in women undergoing an assisted reproductive technology program, such as in-vitro fertilisation (IVF) or IVF with intracytoplasmic sperm injection (ICSI).
- The non-inferiority of REKOVELLE in comparison to GONAL-F was demonstrated in the ongoing pregnancy rate and the ongoing implantation rate 10-11 weeks after transfer.

Therapeutic use

- For induction of ovulation in the context of IVF, the protocol generally combines a gonadotropin with a GnRH analogue, agonist or antagonist. No benefit has been demonstrated in exceeding 450 IU/day of gonadotropin, even in poor responders. Long protocols using GnRH agonists have historically been the most widely used in France. GnRH antagonists allow a reduction in the duration of treatment, the number of injections and (according to some studies) in the risk of ovarian hyperstimulation.
- The transfer and freezing strategy must be discussed with the couple. The number of embryos transferred must consider the patient's age and medical history, previous attempts, fertilisation rate and embryos quality.
- Eight medicinal products are indicated in controlled ovarian stimulation to obtain the development of multiple follicles in women undergoing an assisted reproductive technology program, including five with FSH activity alone.
- **Role of the proprietary medicinal product in the therapeutic strategy**
  REKOVELLE is a first-line treatment in ovulation stimulation used in IVF with or without ICSI.

Clinical data

- A single-blind, non-inferiority study compared the efficacy of REKOVELLE with that of GONAL-F in patients undergoing a first cycle of controlled ovarian stimulation for IVF/ICSI with a GnRH antagonist. The co-primary endpoints were the ongoing pregnancy rate and the ongoing implantation rate 10-11 weeks after transfer. For these co-endpoints, the margin of non-inferiority was – 8%, corresponding to a loss of efficacy of 20%, clinically significant. The ongoing pregnancy rate was 31.8% in the REKOVELLE group and 32.6% in the GONAL-F group, and the ongoing implantation rate was 36.2% and 36.9%, respectively. The non-inferiority of REKOVELLE in comparison to GONAL-F was demonstrated for these two co-primary endpoints.
- The most common adverse events were headaches, pain related to the procedures (primarily oocyte retrieval) and pelvic pain.
- Ovarian hyperstimulation was reported in 3.5% of patients treated with REKOVELLE and 4.8% of patients treated with GONAL-F. The most common serious events were ovarian hyperstimulation: 3 in the REKOVELLE group and 6 in the GONAL-F group, with a longer duration of hospitalisation in the GONAL-F group, as well as bleeding during pregnancy: 5 in the REKOVELLE group and 1 in the GONAL-F group.

Special prescribing conditions

- Prescription restricted to doctors specialising in medical gynaecology, gynaecology-obstetrics or endocrinology, diabetology and nutrition.
- Medicinal product requiring special monitoring during treatment.

Benefit of the medicinal product

- The actual benefit* of REKOVELLE is substantial.
- REKOVELLE does not provide clinical added value** (CAV V) by comparison with GONAL-F.
- 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 05 April 2017 (CT-15912) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a 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”.