PREFERRED SPECIALTY MANAGEMENT POLICY

POLICY: Infertility – Follitropins, Clomiphene Preferred Specialty Management Policy

- Clomid® (clomiphene tablets – Cosette)
- Clomiphene Citrate tablets (generic – multiple manufacturers)
- Gonal-f®, Gonal-f® RFF, Gonal-f® RFF Redi-ject (follitropin alfa injection – EMD Serono)
- Follistim® AQ (follitropin beta injection – Merck)

REVIEW DATE: 02/21/2024

OVERVIEW

The Gonal-f products and Follistim AQ are gonadotropins (follicle stimulating hormones [FSH]).[1-5] The Gonal-f products and Follistim AQ are indicated for the induction of **ovulation and pregnancy in the anovulatory infertile patient**, in whom the cause of infertility is functional and not due to primary ovarian failure. The Gonal-f products are also indicated for the development of multiple follicles in ovulatory patients participating in an assisted reproductive technology (ART) program.[1-3] Follistim AQ is also indicated in normal ovulatory women undergoing controlled ovarian stimulation as part of an *in vitro* fertilization or intracytoplasmic sperm injection cycle.[4] Gonal-f (but not Gonal-f RFF) and Follistim AQ are also indicated for the induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.[1-4]

Clomiphene citrate tablets are indicated for the treatment of **ovulatory dysfunction in women who desire pregnancy**.[5] Patients most likely to achieve success with clomiphene therapy include patients with polycystic ovarian syndrome (PCOS), amenorrhea-galactorrhea syndrome, psychogenic amenorrhea, post-oral contraceptive amenorrhea, and certain cases of secondary amenorrhea of undetermined etiology.

Guidelines

American Society for Reproductive Medicine (ASRM) committee opinion (2020) on the use of exogenous gonadotropins for ovulation induction in anovulatory women note that gonadotropin therapy has more risks than oral ovulation induction.[7] The publication states that gonadotropin therapy should only be used by clinicians who have the training and experience to use these products. Most women will respond to ovulation induction with oral medications, but exogenous gonadotropin treatment may be an option in women who fail to respond to lifestyle modifications and oral agents. The ASRM opinion states that there is no significant advantage to using any specific gonadotropin preparation.

An international evidence-based guideline for the management of PCOS was released in 2018.[6] The guideline was a collaborative effort from the Centre for Research Excellence in PCOS research, the European Society of Human Reproduction and Embryology, the ASRM, and professional societies and consumer advocacy groups. The guidelines note letrozole as the first-line pharmacological treatment in women with PCOS and anovulatory infertility without other infertility factors. Letrozole is used to improve ovulation, pregnancy, and live birth rates. Both metformin and clomiphene can be used alone in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation and pregnancy rates. Clomiphene may be preferred over metformin for this use in women who are obese (body mass index ≥ 30 kg/m^2). Gonadotropins (e.g., FSH) can be used as second-line therapy for women with PCOS who have failed first-line oral ovulation induction therapy and are anovulatory and infertile with no other infertility factors. Gonadotropins may be preferred over the combination therapy of clomiphene and metformin in patients who are clomiphene-resistant.

POLICY STATEMENT

This Preferred Specialty Management program has been developed to encourage the use of the Preferred Products. Utilization of the follitropin products and clomiphene is not managed by *Prior Authorization* criteria, but is based on whether the patient's benefit includes infertility coverage. The program directs the patient to try the Preferred Products prior to the approval of a Non-Preferred Product. Requests for Non-Preferred Products (Step 3) will also be reviewed using the exception criteria (below). All approvals are provided for the duration noted below.

Automation: A patient with a of either clomiphene citrate tablets or the Gonal-f injectable products (including Gonal-f RFF and Gonal-f RFF Redi-ject pens) within the 130-day look-back period is excluded from this Preferred Specialty Management program.

Preferred Products

Step 1: Clomid, Clomiphene citrate
Step 2: Gonal-f, Gonal-f RFF, Gonal-f RFF Redi-ject

Non-Preferred Products

Step 3: Follistim AQ

RECOMMENDED EXCEPTION CRITERIA

REFERENCES

1. Gonal-f multi-dose vials [prescribing information]. Rockland, MA: EMD Serono; November 2023.
2. Gonal-f RFF vial [prescribing information]. Rockland, MA: EMD Serono; November 2023.
3. Gonal-f RFF Redi-ject pens [prescribing information]. Rockland, MA: EMD Serono; February 2020.
4. Follistim AQ Cartridge [prescribing information]. Whitehouse Station, NJ: Merck; March 2023.
5. Clomid tablets [prescribing information]. South Plainfield, NJ: Cosette; May 2022.
6. Teede HJ, Misso ML, Costello MF, et al. International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018. Available at: https://www.monash.edu/__data/assets/pdf_file/0004/1412644/PCOS_Evidence-Based-Guidelines_20181009.pdf. Accessed on February 19, 2024.
7. Use of exogenous gonadotropins for ovulation induction in anovulatory women: a committee opinion. American Society for Reproductive Medicine. *Fertil Steril*. 2020;113(1):66-70.