UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 1038-13
Program	Prior Authorization/Notification
Medication	Follistim® AQ (follitropin beta), Gonal-f® (follitropin alfa), Gonal-f RFF® (follitropin alfa)*ǂ
P&T Approval Date	5/2013, 5/2014, 8/2014, 5/2015, 5/2016, 5/2017, 5/2018, 5/2019, 6/2020, 6/2021, 6/2022, 8/2022, 8/2023
Effective Date	11/1/2023

1. Background:

The body produces two types of gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), both of which play a role in fertility and human reproduction. After they are produced by the pituitary gland, gonadotropins trigger production of other sex hormones which then promote production of egg and sperm. Gonadotropins are used in the treatment of infertility, a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse or therapeutic donor insemination.[1,2,14]

Follistim AQ (follitropin beta) is indicated for induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not due to primary ovarian failure. It is also indicated for pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycle. In males, Follistim AQ is indicated for induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism (HH) in whom the cause of infertility is not due to primary testicular failure.[3]

Gonal-f and Gonal-f RFF (follitropin alfa) are indicated for the induction of ovulation and pregnancy in oligo-anovulatory infertile women in whom the cause of infertility is functional and not due to primary ovarian failure. Gonal-f and Gonal-f RFF are also indicated for the development of multiple follicles in ovulatory women participating in an Assisted Reproductive Technology (ART) program. Gonal-f is indicated for the induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism for whom the cause of infertility is not due to primary testicular failure.[4, 5]

The clinically appropriate dosing for FSH agents is 450 IU/day or less when used for an ART cycle, or 225 IU/day or less when used for ovulation induction or controlled ovarian stimulation, for not more than 14 days of treatment. Exceeding this daily dose and duration of treatment has not been proven to be efficacious in terms of pregnancy outcome.[9, 13]

UnitedHealthcare®

2. Coverage Criteria[a]:

A. <u>Ovulation Induction</u>

1. **Follistim AQ, Gonal-f,** or **Gonal-f RFF** will be approved based on **<u>all</u>** of the following criteria*ǂ **:**

   a. Diagnosis of ovulatory dysfunction

   -AND-

   b. **<u>One</u>** of the following exists:

      (1) Anovulation
      (2) Oligo-ovulation
      (3) Amenorrhea

   -AND-

   c. Other specific causative factors (e.g., thyroid disease, hyperprolactinemia) have been excluded or treated

   -AND-

   d. Infertility is not due to primary ovarian failure

   -AND-

   e. For induction of ovulation

Authorization will be issued for 2 months.§

B. <u>Controlled Ovarian Stimulation</u>

1. **Follistim AQ, Gonal-f,** or **Gonal-f RFF** will be approved based on **<u>all</u>** of the following criteria*ǂ **:**

   a. Diagnosis of infertility

   -AND-

   b. For the development of multiple follicles (controlled ovarian stimulation)

   -AND-

   c. **<u>One</u>** of the following:

      (1) **<u>Both</u>** of the following:

(a) **One** of the following exists:

i. Diminished ovarian reserve
ii. Endometriosis
iii. Male factor infertility
iv. Tubal factor infertility
v. Unexplained infertility
vi. Uterine factor infertility
vii. Ovulatory dysfunction
viii. Recurrent pregnancy loss
ix. Failure to achieve conception with other treatment modalities

-AND-

(b) Will be used in conjunction with assisted reproductive technology (ART)

-OR-

(2) **Both** of the following:

(a) **One** of the following exists:

i. Diminished ovarian reserve
ii. Mild to moderate male factor infertility
iii. Minimal to mild endometriosis
iv. Unilateral tubal factor infertility
v. Unexplained infertility

-AND-

(b) Will be used in conjunction with intrauterine insemination (IUI)

Authorization will be issued for 2 months.§

C. Male Hypogonadotropic Hypogonadism

1. **Follistim AQ** or **Gonal-f** will be approved based on **all** of the following criteria*† **:**

a. **One** of the following:

(1) Diagnosis of male primary hypogonadotropic hypogonadism

-OR-

(2) Diagnosis of male secondary hypogonadotropic hypogonadism

-AND-

b. For induction of spermatogenesis

-AND-

c. Infertility is not due to primary testicular failure

Authorization will be issued for 2 months.§

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Programs:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.

- Supply limits and/or Step Therapy may be in place.

*Infertility is typically excluded from coverage for UnitedHealthcare. Please refer to member's specific benefits for coverage determination.

ǂ OptumHealth review only: Please refer to the Clinical Policy on Follicle Stimulating Hormones (FSH) Used in the Treatment of Infertility for state-specific requirements that may apply.

§ OptumHealth review only: Subsequent authorizations will be reviewed according to the Infertility Clinical Performance Guideline.

4. References:

1. World Health Organization web site. https://www.who.int/health-topics/infertility#tab=tab_Accessed July 16, 2023.
2. American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril 2013;Jan;99(1):63
3. Follistim AQ [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2023.
4. Gonal-f [package insert]. Rockland, MA: EMD Serono, Inc.; December 2020.
5. Gonal-f RFF [package insert]. Rockland, MA: EMD Serono, Inc.; December 2020.
6. Muasher SJ. Use of gonadotrophin-releasing hormone agonists in controlled ovarian hyperstimulation for in vitro fertilization. Clin Ther 1992;14(Suppl A):74-86.
7. Ferraretti A, Marca A, Fauser B, et al. ESHRE consensus on the definition of 'poor response' to ovarian stimulation for in vitro fertilization: the Bologna criteria. Human Reprod 2011; 26: 1616-24.
8. Andoh K, Mizunuma H, Liu X, et al. A comparative study of fixed-dose, stepdown, and low-dose step-up regimens of human menopausal gonadotropin for patients with polycystic ovary syndrome. Fertil Steril m1998: 70; 840-846.
9. Pal L, Jindal S, Witt B, Santoro N. Less is more: increased gonadotropin use for ovarian stimulation adversely influences clinical pregnancy and live birth after in vitro fertilization. Fertil Steril 2008;89:1694-701.
10. Fauser B, Nargund G, Anderson A, et al. Mild ovarian stimulation for IVF: 10 years later. Human Reprod 2010; 25: 2678-84.
11. Baart E, Martini E, Eijkemans M, et al. Milder ovarian stimulation for in-vitro fertilization reduces aneuploidy in the human preimplantation embryo: a randomized controlled trial. Human Reprod 2007; 22: 980-8.

12. Sunkara S, Rittenberg V, Raine-Fenning N, et al. Association between the number of eggs and live birth in IVF treatment: an analysis of 400,135 treatment cycles. Human Reprod 2011; 26: 1768-74.
13. The Practice Committee of the American Society for Reproductive Medicine. Use of exogenous gonadotropins in anovulatory women: a technical bulletin. Fertil Steril 2008;90:S7–12.
14. Practice Committee of the American Society for Reproductive Medicine. Electronic address: asrm@asrm.org. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril. 2020;113(3):533-535. doi:10.1016/j.fertnstert.2019.11.025

Program	Prior Authorization/Notification – Follistim AQ (follitropin beta), Gonal-f (follitropin alfa), Gonal-f RFF (follitropin alfa)
Change Control	
5/2014	Annual review. No change to the criteria. Updated references.
8/2014	Separated Gonadotropin Notification into individual documents. Revised criteria for controlled ovarian stimulation and ovulation induction. Updated background and references.
5/2015	Updated background and references.
5/2016	Annual review. Updated criteria for controlled ovarian stimulation. Updated background and references.
5/2017	Annual review. No changes to criteria. Updated references.
5/2018	Annual review. No changes to criteria. Updated references.
5/2019	Annual review. No changes to coverage criteria. Updated references.
6/2020	Annual review. Removed Bravelle (off market). Updated references.
6/2021	Annual review. No changes to criteria. Updated references.
6/2022	Annual review. Updated references.
8/2022	Removed coverage for Gonal-f RFF for hypogonadotropic hypogonadism as this brand formulation is not approved by the FDA for this indication.
8/2023	Annual review. Clarified that criteria for induction of spermatogenesis are specific to male hypogonadotropic hypogonadism. Removed broken hyperlink to Infertility Clinical Performance Guideline. Updated background, added state mandate, and updated references.