UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2026 P 2149-11
Program	Prior Authorization/Medical Necessity Supported By Fertility Solutions
Medication	Follistim® AQ (follitropin beta), Gonal-f™ (follitropin alfa), Gonal-f™ RFF (follitropin alfa) *, Menopur® (menotropins)*ǂ
P&T Approval Date	7/2018, 11/2018, 5/2019, 8/2019, 8/2020, 9/2021, 10/2022, 10/2023, 5/2024, 6/2025, 6/2026
Effective Date	9/1/2026

1. Background:

Gonadotropins are used in the treatment of infertility, a disease of the reproductive system defined as one of the following:

- inability to achieve a successful pregnancy due to an individual's medical, sexual, or reproductive history;
- failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse when the female partner is less than 35 years;
- failure to achieve a pregnancy after 6 months or more of regular unprotected sexual intercourse when the female partner is 35 years or older

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.

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 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.

Menopur (menotropins) is indicated for the development of multiple follicles and pregnancy in women participating in an assisted reproductive technology (ART) program. Human menopausal gonadotropins (hMG) is used for the treatment of ovulation induction in women with ovulatory dysfunction including polycystic ovary syndrome (PCOS) who failed on clomiphene as well for ovulation induction in the setting of hypogonadotropic hypogonadism.
hMG is also used for induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.

The clinically appropriate dosing for hMG agents when used in an ART cycle without an FSH product is 450 IU/day or less for not more than 14 days of treatment. When used as part of a mixed

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stimulation protocol (hMG + FSH) or when used alone for ovulation induction or ovarian stimulation, the clinically appropriate maximum dosing for hMG agents is 225 IU/day and 150 IU/day, respectively. Exceeding this daily dose and duration of treatment has not been proven to be efficacious in terms of pregnancy outcome. The clinically appropriate dosing for gonadotropin (FSH or hMG alone or in combination) agents is 450 IU/day or less when used for an ART cycle, or 225 IU/day and 150 IU/day or less when used for ovulation induction or ovarian stimulation, respectively, 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.

This is an optional program that is put in place for clients or businesses that have elected to provide coverage for gonadotropins, managed through the Optum Fertility Solutions program.

2. Coverage Criteria[a]:

A. Coverage Criteria for Ovarian Stimulation, Ovulation Induction, and Assisted Reproductive Technology

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

   a. Prognosis for conception must be ≥ 5%

   -AND-

   b. Adequate ovarian reserve as indicated, but not limited to, at least **two** of the following markers within the previous 6 months:

      (1) FSH level < 15 mIU/ml;
      (2) AMH level > 0.2 ng/ml;
      (3) Antral follicle count > 3;
      (4) The risk for aneuploidy for all embryos is ≤ 85%

   -AND-

   c. Evidence of adequate ovarian response to stimulation if there has been previously monitored, medicated-stimulated infertility treatment within the previous 6 months. Examples of adequate ovarian response are:

      (1) One follicle ≥ 15 mm diameter for IUI
      (2) Minimum of 1 follicle ≥ 15 mm diameter for ART

   -AND-

   d. If the request is for Gonal-f/Gonal-f RFF, the following criterion:

      (1) History of failure, contraindication, or intolerance to Follistim AQ

   -AND-

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e. **Follistim AQ, Gonal-f, Gonal-f RFF,** or **Menopur** will be utilized for one of the following indications (See additional coverage criteria for each indication):

(1) Ovulation Induction (see Section B)
(2) Ovarian Stimulation (see Section C)
(3) Assisted Reproductive Technology (see Section D)

B. Ovulation Induction

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

a. Patient meets the coverage criteria in section A

-AND-

b. **One** of the following:

(1) Failure to ovulate with either Clomid (clomiphene citrate) or Femara (letrozole)
(2) Patient diagnosed with hypothalamic amenorrhea

-AND-

c. **One** of the following exists:

(1) Anovulation
(2) Oligo-ovulation
(3) **Both** of the following:

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

-AND-

d. **Both** of the following:

(1) Dose does not exceed 225 IU/day
(2) **One** of the following:

i. Duration of therapy does not exceed 14 days per cycle
ii. Patient diagnosed with hypothalamic amenorrhea

-AND-

e. The use of **Follistim AQ, Gonal-f, Gonal-f RFF,** or **Menopur** applies to **NONE** of the following situations:

(1) Use of gonadotropins beyond the 6th gonadotropin induced ovulatory cycle.
(2) When there are ≥ 4 follicles which are ≥15 mm in diameter from a previously

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gonadotropin-induced ovulation, despite a dosage adjustment (e.g., doses of gonadotropin down to 37.5 IU per day).
(3) When used alone for individuals with unexplained infertility.
(4) When there is a failure to respond to ovulation induction (e.g., doses of gonadotropins up to 225 IU per day and no follicles ≥ 15 mm in diameter).
(5) In lieu of clomiphene or letrozole to correct a thin endometrial lining.
(6) An estradiol level <100 pg/ml/follicle ≥15 mm in diameter.
(7) Doses that exceed 225 IU/day for ovulation induction.
(8) Duration of therapy that exceeds 14 days per cycle. Note that a longer than 14 day stimulation may be considered in the setting of hypothalamic amenorrhea.

Authorization will be issued for 3 months.§

C. Ovarian Stimulation

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

   a. Patient meets the coverage criteria in section A.

   -AND-

   b. **One** of the following:

      (1) **All** of the following:

         (a) Used alone or in conjunction with intrauterine insemination (IUI)

         -AND-

         (b) **One** of the following:

            i. Treatment in individuals with diminished ovarian reserve that have not responded to clomiphene or letrozole
            ii. In the setting of unilateral tubal disease in conjunction with IUI when there is no evidence of tubal compromise on the patent side when at least 2 cycles of oral agents (clomiphene or letrozole) have failed to yield a dominant follicle on the side with a patent fallopian tube

         -AND-

         (c) Dose does not exceed 150 IU/day, for no more than 14 days per cycle.

         -AND-

         (d) The use of **Follistim AQ, Gonal-f, Gonal-f RFF,** or **Menopur** applies to **NONE** of the following situations:

            i. Treatment in individuals with unexplained infertility, endometriosis, bilateral tubal factor infertility, unilateral isthmic, ampullary, fimbrial or

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peri tubal compromise (e.g., loculated spill, dilatation, phimosis, occlusion), recurrent pregnancy loss, isolated male factor infertility
ii. When there is a failure to respond to ovarian stimulation, (e.g., doses of gonadotropins up to 150 IU per day and no follicles ≥ 15 mm in diameter)
iii. An estradiol level <100 pg/ml/follicle ≥15 mm in diameter
iv. When there are ≥ 4 follicles which are ≥15 mm in diameter from a previously gonadotropin-induced ovulation, despite a dosage adjustment.
v. Following ART cycles that fail to result in conception due to poor ovarian response or poor-quality oocytes or embryos.
vi. Doses that exceed 150 IU/day for ovulation stimulation
vii. Duration of therapy that exceeds 14 days per cycle.
viii. Beyond 3 cycles

-OR-

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

(a) Used for fertility preservation

-AND-

(b) The individual will undergo gonadotoxic therapy (e.g., exposure to cytotoxic agents, invasive surgery, prolonged hormonal ovarian suppression, radiation therapy)

-AND-

(c) Will be used as part of an assisted reproductive technology (e.g., in vitro fertilization) procedure

Authorization will be issued for 3 months.§

D. Assisted Reproductive Technology

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

a. Patient meets the coverage criteria in section A.

-AND-

b. If used for the preparation of the endometrial lining, then there has been a failure to achieve a sufficient endometrial thickness (>6 mm) or trilaminar pattern with conventional preparation methods (e.g., estrogen and progesterone)**

** Gonadotropins are not indicated for use in the preparation of the endometrial lining unless there has been a failure to achieve a sufficient endometrial thickness (>6 mm) or trilaminar pattern with conventional preparation methods (e.g., estrogen and progesterone)

-AND-

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c. For assisted reproductive technologies (ART)[b], total gonadotropin dose does not exceed 450 IU/day, for no more than 14 days per cycle

-AND-

d. The use of **Follistim AQ, Gonal-f, Gonal-f RFF,** or **Menopur** applies to **NONE** of the following situations:

(1) Following ART cycles that fail to result in conception due to poor ovarian response or poor-quality oocytes or embryos.
(2) Doses that exceed 450 IU/day for ART
(3) Duration of therapy that exceeds 14 days per cycle.

Authorization will be issued for 3 months.[§]

E. <u>Male Hypogonadotropic Hypogonadism</u>

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

a. **<u>One</u>** 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

-AND-

d. If the request is for Gonal-f, the following criterion:

(1) History of failure, contraindication, or intolerance to Follistim AQ

Authorization will be issued for 3 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.

[b] ART includes all fertility treatments in which both eggs and embryos are handled, including in vitro fertilization.

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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 may be in place.

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

ǂ Optum Fertility Solutions review only: Please refer to the Clinical Policy on Human Menopausal Gonadotropin (hMG) Used in the Treatment of Infertility for state-specific requirements that may apply.

§ Optum Fertility Solutions review only: Authorizations will be reviewed according to the Fertility Solutions Medical Necessity Clinical Guideline - Infertility.

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Program	Prior Authorization/Medical Necessity (For Optum Fertility Solutions) - Follistim AQ (follitropin beta), Gonal-f (follitropin alfa), Gonal-f RFF (follitropin alfa)
Change Control	
7/2018	New program
11/2018	Corrected maximum dosing for ovulation induction to 225 IU/day and controlled ovarian stimulation to 150 IU/day. Added definition of ART. Moved Follistim AQ criteria in to general requirements sections.
5/2019	Annual review. Revised coverage rationale for ovulation induction and controlled ovarian stimulation. Updated references.
8/2019	Revised coverage rationale to change step therapy criteria. Require trial of Follistim AQ before Gonal F.

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8/2020	Annual review with no changes to coverage criteria.
9/2021	Annual review. Updated coverage rationale for ovulation induction and controlled ovarian stimulation.
10/2022	Annual review. Added Assisted Reproductive Technology section and clarified when gonadotropins are indicated for use in the preparation of the endometrial lining. Updated Coverage Criteria for Controlled Ovarian Stimulation, Ovulation Induction, and Assisted Reproductive Technology with revised FSH and AMH levels as well as antral follicle count and risk for aneuploidy to specify indicators for adequate ovarian reserve. Clarified situations to which the use of Follistim AQ, Gonal-f, Gonal-f RFF, or Menopur applies.
10/2023	Annual review with no changes to coverage criteria. Updated references.
5/2024	Added coverage criteria for fertility preservation for iatrogenic infertility. Updated term "controlled ovarian stimulation" to "ovarian stimulation".
6/2025	Revised definition of infertility in background to correlate with ASRM. Added criteria bypassing step requirement for patients diagnosed with hypothalamic amenorrhea. Clarified situations to which the use of gonadotropins applies. Removed criterion for initial treatment of diminished ovarian reserve. Updated coverage criteria for fertility preservation for iatrogenic infertility to include additional examples of gonadotoxic therapy such as prolonged hormonal ovarian suppression. Updated references.
6/2026	Annual review with no changes to coverage criteria. Updated background and references.

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