Gonadotropin Hormones Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

FDA APPROVED INDICATIONS AND DOSAGE[1-8]

Agent(s)	Indication(s)	Dosage
Follicle Stimulating Hormone (FSH)		
Follistim® AQ (follitropin beta) Injection	• Induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not due to primary ovarian failure	**Induction of ovulation:** Starting dose of 50 International Units (IU) subcutaneously (SC) daily for at least 7 days. Subsequent dosage adjustments of 25 or 50 IU can be made at weekly intervals based upon ovarian response. The maximum daily dose is 250 IU
	• Pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycle	**IVF or ICSI:** Starting dose of 200 IU SC daily for at least 7 days. Subsequent dosage adjustments down or up based upon the woman's ovarian response as determined by ultrasound evaluation of follicular growth and serum estradiol levels. Dosage reduction in high responders can be considered from the 6th day of treatment onward according to individual response. The maximum individualized daily dose is 500 IU
	• 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	**Induction of spermatogenesis:** Pretreatment with human chorionic gonadotropin (hCG) treatment is required prior to concomitant therapy

		with Follistim AQ and hCG , to normalized serum testosterone levels. After normal serum testosterone levels have been reached, dose is 450 IU per week, SC, as either 225 IU twice weekly or 150 IU three times weekly, on combination with the same hCG dose used to normalize testosterone levels. Therapy should be continued for at least 3 to 4 months before any improvement in spermatogenesis can be expected. If a man has not responded after this period, therapy may continue. Treatment response has been noted at up to 12 months
Gonal-F® (follitropin alfa) Injection	• Induction of ovulation and pregnancy in oligo-anovulatory infertile women for whom the cause of infertility is functional and not due to primary ovarian failure	**Ovulation induction:** Starting (initial cycle) daily dose of 75 IU SC for 14 days In subsequent cycles of treatment, the starting dose and dosage adjustments should be determined based on the history of the ovarian response to Gonal-F. If indicated by ovarian response after the initial 14 days, increase dose by up to 37.5 IU. Thereafter if indicated by ovarian response, increase dose by up to 37.5 IU every 7 days. The maximum individualized dose is 300 IU per day. In general treatment should not exceed 35 days unless an estradiol rise indicates imminent follicular development **ART:** beginning on cycle day 2 or 3, a starting dose of 150 IU SC per day until sufficient follicular development, as

	• Development of multiple follicles in ovulatory infertile women as part of an assisted reproductive technology (ART) cycle	determined by ultrasound in combination with measurement of serum estradiol levels. In women whose endogenous gonadotropin levels are suppressed, starting dose is 225 IU SC per day Adjust the dose after 5 days based on the woman's ovarian response, as determined by ultrasound evaluation of follicular growth and serum estradiol levels. Do not make additional dosage adjustments more frequently than every 3-5 days or by more than 75-150 IU at each adjustment. Do not use doses greater than 450 IU per. Continue treatment until adequate follicular development is evident. In most cases, therapy should not exceed 10 days **Induction of spermatogenesis:** Prior to concomitant therapy with Gonal-F, pretreatment with hCG alone is required to normalize serum testosterone levels. Gonal-F must be given in conjunction with hCG. Starting dose of Gonal- F is 150 IU SC three times a week. If azoospermia persists, the dose of Gonal-F may be increased to a maximum of 300 IU three times per week. Gonal-F may need to be administered for up to 18 months to achieve adequate spermatogenesis

	● Induction of spermatogenesis in infertile men with primary and secondary hypogonadotropic hypogonadism for whom the cause of infertility is not due to primary testicular failure	

Human Chorionic Gonadotropin (hCG)		
Novarel® (chorionic gonadotropin) Injection	● Prepubertal cryptorchidism not due to anatomic obstruction	**Prepubertal cryptorchidism:** o 4,000 USP Units intramuscularly (IM) three times weekly for three weeks OR o 5,000 USP Units IM every second day for four injections OR o 15 injections of 500 to 1,000 USP Units IM over a period of 6 weeks OR o 500 USP Units IM three times weekly for four to six weeks. If this course of treatment is not successful, another is begun one month later, giving 1,000 USP Units per injection
	● Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males	**Hypogonadotropic hypogonadism:** o 500 to 1,000 USP Units IM three times a week for three weeks, followed by the same dose twice a week for three weeks OR o 4,000 USP Units IM three times weekly for six to nine months, following which the dosage may be reduced to 2,000 USP Units three times weekly for an additional three months
	● Induction of ovulation and pregnancy in the	**Induction of ovulation:**

	anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menotropins	5,000 to 10,000 USP Units IM one day following the last dose of menotropins
Ovidrel® (choriogonadotropin alfa) Injection	• Induction of final follicular maturation and early luteinization in infertile women who have undergone pituitary desensitization and who have been appropriately pretreated with follicle simulating hormones as part of an assisted reproductive technology (ART) program • Induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure	**ART:** 250 µg SC one day following the last dose of the follicle stimulating agent **Ovulation induction:** 250 µg SC one day following the last dose of the follicle stimulating agent
Pregnyl® (chorionic gonadotropin) Injection	• Prepubertal cryptorchidism not due to anatomical obstruction • Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary	**Prepubertal cryptorchidism:** ○ 4,000 USP Units IM three times weekly for three weeks OR ○ 5,000 USP Units IM every second day for four injections OR ○ 15 injections of 500 to 1,000 USP Units IM over a period of 6 weeks OR ○ 500 USP Units IM three times weekly for four to six weeks. If this course of treatment is not successful, another is begun one month later, giving 1,000 USP Units per injection **Hypogonadotropic hypogonadism:** ○ 500 to 1,000 USP Units IM three times a week for three weeks, followed

	to a pituitary deficiency) in males ● Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who have been appropriately pretreated with human menotropins	by the same dose twice a week for three weeks OR ○ 4,000 USP Units IM three times weekly IM for six to nine months, following which the dosage may be reduced to 2,000 USP Units three times weekly for an additional three months **Induction of ovulation:** 5,000 to 10,000 USP Units IM one day following the last dose of menotropins
Gonadotropin Releasing Hormone (GnRH) analogs		
Cetrotide® (cetrorelix acetate) Injection	● Inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian stimulation	0.25 mg SC on either stimulation day 5 (morning or evening) or day 6 (morning) and continued daily until day of hCG administration
Ganirelix acetate Injection	● Inhibition of premature LH surges in women undergoing controlled ovarian hyperstimulation	250 mcg SC once daily during the mid to late portion of the follicular phase. Continue treatment daily until the day of hCG administration
Menotropins		
Menopur® (menotropins) Injection	● Development of multiple follicles and pregnancy in ovulatory women as part of an ART cycle	Starting dose (first cycle) of 225 IU SC daily, beginning on cycle day 2 or 3. Adjust the dose after 5 days based on the ovarian response, as determined by ultrasound evaluation of follicular growth and serum estradiol levels. Do not make additional dosage adjustments more frequently than every 2 days or by more than 150 IU at each adjustment. Daily dose should not exceed 450 IU.

		Continue treatment until adequate follicular development is evident. Therapy should not exceed 20 days

CLINICAL RATIONALE

Infertility[15]

Infertility is defined as the inability of a couple to conceive after 12 months of regular intercourse without use of contraception in women less than 35 years of age and after 6 months of regular intercourse without use of contraception in women 35 years and older. The incidence of infertility estimated from prospective studies in the United States ranges from 12 to 18%.

Infertility is a multifactorial condition and may be due to either the male or female partner or a combination of both. Some causes of infertility are easily identifiable; however, the situation is less clear in most couples. The most common causes of infertility are male factor (hypogonadism, post-testicular defects, seminiferous tubule dysfunction), ovulatory dysfunction, tubal damage, endometriosis, coital problems, and cervical factor. Up to 28% of infertility is unexplained.

Because infertility could be due to one partner or both it is recommended that an evaluation of both partners is performed concurrently. In addition to a complete initial diagnostic evaluation including a complete history and physical exam the following tests are useful in most couples with infertility:

- Semen analysis to assess male factors
- Menstrual history, assessment of luteinizing hormone surge in urine prior to ovulation, and/or luteal phase progesterone level to assess ovulatory function
- Hysterosalpingogram or sonohysterogram with a test of tubal patency such as hysterosalpingo-contrast-sonography to assess tubal patency and the uterine cavity
- Assessment of ovarian reserve with day 3 serum follicle-stimulating hormone and estradiol levels, anti-Müllerian hormone, and/or antral follicle count
- Thyroid-stimulating hormone

In select couples, the following additional tests may be warranted:

- Pelvic ultrasound to assess for uterine myomas and ovarian cysts
- Laparoscopy to identify endometriosis or other pelvic pathology

Once the cause of infertility is identified, therapy aimed at correcting reversible etiologies and overcoming irreversible factors can be implemented. Therapeutic interventions for treatment of male and female infertility may involve drug therapy, surgery, and/or procedures such as intrauterine insemination or invitro fertilization.

In women with ovulatory failure or those who have unexplained infertility with normal estradiol and gonadotropin levels, clomiphene is considered a reasonable first approach to ovulation induction. It may be combined with IUI to increase the likelihood of conception, particularly in couples with oligospermia. If 3 or 4 cycles of clomiphene fail to result in a pregnancy, or the woman is of advanced fertility age, injectable FSH/LH may be tried for ovulation induction. When this approach also fails, assisted reproductive technologies (ART) can be tried. ART is used from the beginning in women with tubal factor infertility.[16]

Assisted Reproductive Technology[9]
The CDC definition of assisted reproductive technology (ART) includes all fertility treatments in which both eggs and embryos are handled. In general, ART procedures involve surgically removing eggs from a woman's ovaries, combining them with sperm in the laboratory, and returning them to the woman's body or donating them to another woman. They do NOT include treatments in which only sperm are handled (i.e., intrauterine or artificial insemination) or procedures in which a woman takes medicine only to stimulate egg production without the intention of having eggs retrieved.

Hypogonadotropic Hypogonadism
Hypogonadism is defined as inadequate gonadal function, as manifested by deficiencies in gametogenesis and/or the secretion of gonadal hormones. Hypogonadotropic hypogonadism (HH) is also known as secondary or central hypogonadism. Secondary hypogonadism is associated with decreased secretion of the gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), resulting in reductions in testosterone secretion and sperm production. This disorder should, in theory, respond to the administration of LH and FSH. In practice, testosterone secretion virtually always increases to normal after replacement of LH, and sperm production more often than not increases after replacement of LH alone or LH plus FSH. Testosterone replacement will not restore spermatogenesis. Sperm production can usually be stimulated to a level sufficient to restore fertility in men who are infertile as a result of secondary hypogonadism through the use of gonadotropins or gonadotropin-releasing hormone.[10]

The Practice Committee of the American Society for Reproductive Medicine recommends that for the infertile male, the minimum initial hormonal evaluation should include measurement of serum FSH and total testosterone. If the total testosterone level is low, a more extensive evaluation should include a second testosterone level, measurements of free testosterone, LH, and prolactin. The relationships among serum testosterone, LH, FSH, and prolactin concentrations help to provide an understanding of the source of the abnormal testosterone levels.[14]

Cryptorchidism[11]
Terms such as undescended testis, retention testis, cryptorchidism, and maldescended testis describe a testis that is not normally located at the bottom of the scrotum. Cryptorchidism is the most common congenital abnormality of the male genitourinary tract. Most cryptorchid testes are undescended, but some are absent (due to agenesis or atrophy). True undescended testes have stopped short along their normal path of descent into the scrotum. They may remain in the abdominal cavity or they may be palpable in the inguinal canal, or just outside the external ring.

The goal of management is to place and fix viable undescended testes in a normal scrotal position or to remove nonviable testicular remnants. Scrotal positioning reduces the risk of torsion and blunt traumatic injury (for intracanalicular testes) and permits easier examination of the testis. If performed sufficiently early, surgical correction also may reduce the risk of infertility and testicular cancer. Finally, having the testis in a normal, dependent scrotal position may improve body satisfaction, although the psychological impact of abnormal testicular position has not been studied.

Treatment for undescended testes is almost always surgical. Testicular descent depends upon local concentrations of testosterone considerably greater than can be achieved through systemic administration. However, administration of gonadotropins [either urine-

derived human chorionic gonadotropin (hCG) or gonadotropin-releasing hormone (GnRH) analogs] can stimulate the testes to increase production of testosterone sufficiently to achieve the necessary local concentration. Hormonal treatment is controversial. The Nordic consensus on treatment of undescended testes and the 2014 American Urological Association guideline on the evaluation and treatment of cryptorchidism recommend against hormonal treatment, whereas 2016 European guidelines suggest that hormonal treatment before or after surgical treatment may have a beneficial effect on fertility. Although, in some cases, descent following HCG administration is permanent, in most cases, the response is temporary.

Efficacy
Gonadotropins
Follicle-stimulating hormone (FSH) is synthesized and secreted by the gonadotropic cells of the anterior pituitary gland, and regulates the development, growth, pubertal maturation, and reproductive processes of the body. FSH stimulates the maturation of primordial germ cells in both males and females. In males, FSH induces Sertoli cells to secrete androgen-binding proteins and sustains spermatogenesis and stimulates inhibin B secretion. In females, FSH initiates follicular growth and recruitment of immature ovarian follicles on the ovary.[10]

Menopur is a preparation of gonadotropins FSH and luteinizing hormone (LH) activity. During the normal menstrual cycle, LH participates with FSH in the development and maturation of the normal ovarian follicle, and the mid-cycle LH surge triggers ovulation.[7]

Human Chorionic Gonadotropin[6]
Human chorionic gonadotropin (hCG) is structurally similar to luteinizing hormone (LH), although hCG appears to have a small degree of follicle-stimulating hormone (FSH) activity as well. HCG stimulates production of gonadal steroid hormones by stimulating the interstitial cells (Leydig cells) of the testis to produce androgens and the corpus luteum of the ovary to produce progesterone. Androgen stimulation in the male leads to the development of secondary sex characteristics and may stimulate testicular descent when no anatomical impediment to descent is present. This descent is usually reversible when HCG is discontinued.

During the normal menstrual cycle, LH participates with FSH in the development and maturation of the normal ovarian follicle, and the mid-cycle LH surge triggers ovulation. HCG can substitute for LH in this function.

Gonadotropin Releasing Hormone Analogs[1]
Gonadotropin Releasing Hormone (GnRH) analogs compete with natural GnRH for binding to membrane receptors on pituitary cells and thus control the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH). GnRH induces the production and release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the gonadotrophic cells of the anterior pituitary. Due to a positive estradiol (E2) feedback at midcycle, GnRH liberation is enhanced resulting in an LH-surge. This LH-surge induces the ovulation of the dominant follicle, resumption of oocyte meiosis and subsequently luteinization as indicated by rising progesterone levels.

Clomiphene citrate[13]
The majority of patients who are going to ovulate will do so after the first course of therapy with clomiphene citrate. If ovulation does not occur after three courses of therapy, further treatment with clomiphene citrate is not recommended and the patient should be reevaluated.

Safety[12]
Ovarian hyperstimulation syndrome (OHSS) is an uncommon but serious complication associated with controlled ovarian stimulation during assisted reproductive technology (ART). Moderate to severe OHSS occurs in approximately 1-5% of cycles. However, the true incidence is difficult to delineate as a strict, consensus definition is lacking. Symptoms of OHSS are often qualified by their severity (mild, moderate, or severe) and by the timing of onset (early or late). Severe OHSS can lead to serious complications, including pleural effusion, acute renal insufficiency, and venous thromboembolism.

OHSS could theoretically occur in any woman undergoing controlled ovarian stimulation with gonadotropins. However, evidence indicates there are some women who are at much higher risk. These risk factors may include:

- Younger age (< 35 years old)
- Lower BMI
- Diagnosis of an ovulation disorder or polycystic ovary syndrome (PCOS)
- Serum antimüllerian hormone (AMH) levels > 10 ng/mL
- Antral follicle count (AFC) ≥ 24
- Serum estradiol concentrations

Cetrotide has the following contraindications:[1]

- Hypersensitivity to cetrorelix acetate, extrinsic peptide hormones or mannitol
- Known hypersensitivity to GnRH or any other GnRH analogs
- Known or suspected pregnancy, and lactation
- Severe renal impairment

Follistim AQ has the following contraindications:[2]

- Prior hypersensitivity to recombinant hFSH products
- High levels of FSH indicating primary gonadal failure
- Presence of uncontrolled non-gonadal endocrinopathies
- Hypersensitivity reactions related to streptomycin or neomycin
- Tumors of the ovary, breast, uterus, testis, hypothalamus or pituitary gland
- Pregnancy
- Heavy or irregular vaginal bleeding of undetermined origin
- Ovarian cysts or enlargement not due to polycystic ovary syndrome

Ganirelix acetate has the following contraindications:[3]

- Known hypersensitivity to Ganirelix Acetate or to any of its components
- Known hypersensitivity to GnRH or any other GnRH analog
- Known or suspected pregnancy

Gonal-F has the following contraindications:[4]

- Hypersensitivity to recombinant FSH preparations or one of their excipients
- High levels of FSH indicating primary gonadal failure
- Pregnancy
- Uncontrolled non-gonadal endocrinopathies
- Sex hormone dependent tumors of the reproductive tract and accessory organ
- Tumors of pituitary gland or hypothalamus
- Abnormal uterine bleeding of undetermined origin
- Ovarian cyst or enlargement of undetermined origin, not due to poly cystic ovary syndrome

Menopur has the following contraindications:[5]

- Prior hypersensitivity to Menopur or menotropins products or one of their excipients
- High levels of FSH indicating primary ovarian failure
- Pregnancy
- Presence of uncontrolled non-gonadal endocrinopathies (e.g., thyroid, adrenal, or pituitary disorders)
- Sex hormone dependent tumors of the reproductive tract and accessory organs
- Tumors of the pituitary gland or hypothalamus
- Abnormal uterine bleeding of undetermined origin
- Ovarian cyst or enlargement of undetermined origin, not due to polycystic ovary syndrome

Novarel has the following contraindications:[6]

- Precocious puberty
- Prostatic carcinoma or other androgen-dependent neoplasm
- Prior allergic reaction to hCG
- HCG may cause fetal harm when administered to a pregnant woman

Ovidrel has the following contraindications:[7]

- Prior hypersensitivity to hCG preparations or one of their excipients
- Primary ovarian failure
- An uncontrolled organic intracranial lesion such as a pituitary tumor
- Abnormal uterine bleeding of undetermined origin
- Ovarian cyst or enlargement of undetermined origin
- Sex hormone dependent tumors of the reproductive tract and accessory organs Pregnancy

Pregnyl has the following contraindications:[8]

- Precocious puberty
- Prostatic carcinoma or other androgen-dependent neoplasm
- Prior allergic reaction to hCG

References

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of moderate and severe ovarian hyperstimulation syndrome: a guideline. Fertility and Sterility® Vol. 106, No 7, December 2016.
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15. Lindsay TJ, Vitrikas KR. Evaluation and Treatment of Infertility. Am Fam Physician. 2015 Mar 1;91(5):308-314.
16. Practice Committee of the American Society for Reproductive Medicine. American Society for Reproductive Medicine, Birmingham, Alabama. Evidence-based treatments for couples with unexplained infertility: a guideline. Fertility and Sterility® Vol. 113, No2, February 2020.

Gonadotropin Hormones Prior Authorization with Quantity Limit Criteria

TARGET AGENT(S)

Preferred Agents	Non-Preferred Agents
Follistim AQ® (follitropin beta)	Gonal-F® Kit (follitropin alfa) Gonal-F® RFF (follitropin alfa) Gonal-F® RFF Pen (follitropin alfa)
Novarel® (chorionic gonadotropin) Pregnyl® (chorionic gonadotropin)[a]	Ovidrel® (choriogonadotropin alfa)
Ganirelix Acetate[a] (ganirelix)	Cetrotide® (cetrorelix acetate)
Menopur® (menotropin)	NA

[a] Generic available and included as preferred in this program

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)
Cetrotide (cetrorelix acetate) injection			
0.25 mg kit	30090025106420	M, N, O, or Y	5 kits per 30 days
Follistim AQ (follitropin beta) injection			
300 unit/0.36 mL cartridge	30062030102020	M, N, O, or Y	6.3 mL (15 cartridges) per 30 days
600 unit/0.72 mL cartridge	30062030102030	M, N, O, or Y	6.24 mL (8 cartridges) per 30 days
900 unit/1.08 mL cartridge	30062030102040	M, N, O, or Y	5.85 mL (5 cartridges) per 30 days
Ganirelix Acetate injection[a]			
250 mcg/0.5 mL prefilled syringe	3009004010E520	M, N, O, or Y	2.5 mL (5 syringes) per 30 days
Gonal-F (follitropin alfa) injection			
75 unit RFF pre-filled syringe	30062030052115	M, N, O, or Y	20 syringes per 30 days
300 unit/0.5 mL Rediject multi-dose delivery system	30062030052020	M, N, O, or Y	7.5 mL (15 pens) per 30 days
450 unit/0.75 mL Rediject multi-dose delivery system	30062030052025	M, N, O, or Y	7.5 mL (10 pens) per 30 days
450 unit multi-dose pre-filled	30062030052140	M, N, O. or Y	10 syringes per 30 days

syringe multi-dose delivery system			
900 unit/1.5 mL Rediject multi-dose delivery system	30062030052040	M, N, O, or Y	7.5 mL (5 pens) per 30 days
1050 unit multi-dose pre-filled syringe	30062030052150	M, N, O, or Y	4 syringes per 30 days
Menopur (menotropins) injection			
75 unit vial	30062050002175	M, N, O, or Y	60 vials per 30 days
Novarel (chorionic gonadotropin) injection			
5,000 unit vial	30062020002130	M, N, O, or Y	4 vials per 30 days
10,000 unit vial	30062020002140	M, N, O, or Y	2 vials per 30 days
Ovidrel (choriogonadotropin alfa) injection			
250 mcg/0.5 mL pre-filled syringe	30062022052220	M, N, O, or Y	1 mL (2 syringes) per 30 days
Pregnyl (chorionic gonadotropin) injection			
10,000 unit multi-dose vial[a]	30062020002140	M, N, O, or Y	2 vials per 30 days

[a] generic available

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Follicle Stimulating Hormone Evaluation
Follistim AQ and Gonal-F will be approved when ALL of the following are met:

1. The patient's benefit plan covers agents for infertility
   AND
2. ONE of the following:
   A. The requested agent will be used for ovulation induction AND ONE of the following:
      i. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days
      OR
      ii. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed
      OR
      iii. ALL of the following:
         a. ONE of the following:
            1. The patient has tried and had an inadequate response to clomiphene citrate
            OR
            2. The patient has an intolerance or hypersensitivity to clomiphene citrate
            OR
            3. The patient has an FDA labeled contraindication to clomiphene citrate
            OR
            4. The patient is currently being treated with the requested agent as indicated by ALL of the following:

A. A statement by the prescriber that the patient is currently taking the requested agent
AND
B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
AND
C. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

5. The prescriber has provided documentation that clomiphene citrate cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

AND

b. The patient is NOT pregnant
AND
c. The patient does NOT have primary ovarian failure
AND
d. The patient will receive human chorionic gonadotropin (hCG) following completion of the requested agent unless there are risks present for ovarian hyperstimulation syndrome (OHSS)
AND
e. ONE of the following:
    1. The requested agent is a preferred agent
    OR
    2. The patient has tried and had an inadequate response to ONE of the preferred agent(s)
    OR
    3. The patient has an intolerance or hypersensitivity to ONE of the preferred agent(s) that is NOT expected to occur with the requested agent
    OR
    4. The patient has an FDA labeled contraindication to ALL of the preferred agent(s) that is NOT expected to occur with the requested agent
    OR
    5. The patient is currently being treated with the requested agent as indicated by ALL of the following:
        A. A statement by the prescriber that the patient is currently taking the requested agent
        AND
        B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
        AND
        C. The prescriber states that a change in therapy is expected to be ineffective or cause harm

    OR

6. The prescriber has provided documentation ALL of the preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

OR

B. The requested agent will be used for the development of multiple follicles as part of an assisted reproductive technology (ART) [e.g., invitro fertilization (IVF), gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), tubal embryo transfer (TET), cryopreservation, intracytoplasmic sperm injection (ICSI)] AND ONE of the following:
   i. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days
   OR
   ii. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed
   OR
   iii. ALL of the following:
      a. The patient is NOT pregnant
      AND
      b. The patient does NOT have primary ovarian failure
      AND
      c. The patient will receive human chorionic gonadotropin (hCG) following completion of the requested agent unless there are risks present for ovarian hyperstimulation syndrome (OHSS)
      AND
      d. ONE of the following:
         1. The requested agent is a preferred agent
         OR
         2. The patient has tried and had an inadequate response to ONE of the preferred agent(s)
         OR
         3. The patient has an intolerance or hypersensitivity to ONE of the preferred agent(s) that is NOT expected to occur with the requested agent
         OR
         4. The patient has an FDA labeled contraindication to ALL of the preferred agent(s) that is NOT expected to occur with the requested agent
         OR
         5. The patient is currently being treated with the requested agent as indicated by ALL of the following:
            A. A statement by the prescriber that the patient is currently taking the requested agent
            AND
            B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
            AND

C. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

6. The prescriber has provided documentation that ALL of the preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

OR

C. The requested agent will be used for hypogonadotropic hypogonadism AND ALL of the following:
   i. The requested agent is Follistim AQ or Gonal-F
   AND
   ii. The patient does not have primary testicular failure
   AND
   iii. The requested agent will be used in combination with human chorionic gonadotropin (hCG)
   AND
   iv. The requested agent will not be started until the patient's serum testosterone level is at normal levels
   AND
   v. ONE of the following:
      a. The requested agent is a preferred agent
      OR
      b. The patient has tried and had an inadequate response to ONE of the preferred agent(s)
      OR
      c. The patient has an intolerance or hypersensitivity to ONE of the preferred agent(s) that is NOT expected to occur with the requested agent
      OR
      d. The patient has an FDA labeled contraindication to ALL of the preferred agent(s) that is NOT expected to occur with the requested agent
      OR
      e. The patient is currently being treated with the requested agent as indicated by ALL of the following:
         1. A statement by the prescriber that the patient is currently taking the requested agent
         AND
         2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
         AND
         3. The prescriber states that a change in therapy is expected to be ineffective or cause harm

      OR

      f. The prescriber has provided documentation that ALL of the preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause

an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

AND

3. The patient has undergone a complete medical and endocrinologic evaluation
AND
4. The fertility status of the patient's partner has also been evaluated (if applicable)
AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
6. ONE of the following:
    A. The requested quantity (dose) does NOT exceed the program quantity limit
    OR
    B. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
        AND
        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
    OR
    C. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
        AND
        iii. The prescriber has provided information in support of therapy with a higher dose for the requested indication

Length of Approval: 3 months for ART or ovulation induction
6 months for hypogonadotropic hypogonadism

Human Chorionic Gonadotropin Evaluation
Novarel, Ovidrel, Pregnyl, or **hCG** will be approved when ALL of the following are met:

1. ONE of the following:
    A. The requested agent will be used for a diagnosis of cryptorchidism AND ALL of the following:
        i. The requested agent is Novarel, Pregnyl, or hCG
        AND
        ii. The diagnosis is not due to an anatomical obstruction
        AND
        iii. The patient is prepubertal
        AND
        iv. ONE of the following:

a. The patient has had surgery to correct the cryptorchidism
OR
b. The patient will have surgery to correct the cryptorchidism after using the requested agent
OR
c. The patient is unable to have surgery to correct the cryptorchidism

OR

B. The requested agent will be used for a diagnosis of hypogonadotropic hypogonadism AND BOTH of the following:
   i. The requested agent is Novarel, Pregnyl, or hCG
   AND
   ii. ONE of the following:
      a. The patient is not currently receiving treatment for the diagnosis AND has ONE of the following pretreatment levels:
         1. Total serum testosterone level that is below the testing laboratory's normal range or is less than 300 ng/dL
         OR
         2. Free serum testosterone level that is below the testing laboratory's normal range

      OR

      b. The patient is currently receiving treatment for the diagnosis AND has ONE of the following current levels:
         1. Total serum testosterone level that is within OR below the testing laboratory's normal range OR is less than 300 ng/dL
         OR
         2. Free serum testosterone level is within OR below the testing laboratory's normal range

OR

C. The requested agent will be used for the development of multiple follicles as part of an assisted reproductive technology (ART) [e.g., invitro fertilization (IVF), gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), tubal embryo transfer (TET), cryopreservation, intracytoplasmic sperm injection (ICSI)] OR for ovulation induction AND BOTH of the following:
   i. The patient's benefit plan covers agents for infertility
   AND
   ii. ONE of the following:
      a. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days
      OR
      b. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed
      OR
      c. ALL of the following:
         1. The patient is NOT pregnant
         AND
         2. The patient does NOT have primary ovarian failure
         AND
         3. The patient will receive follicle stimulating hormone (FSH) OR clomiphene before the requested agent unless

there are risks present for ovarian hyperstimulation syndrome (OHSS)

AND

4. The patient has undergone a complete medical and endocrinologic evaluation

AND

5. The fertility status of the partner also been evaluated (if applicable)

AND

6. ONE of the following:
    A. The requested agent is a preferred agent

    OR

    B. The patient has tried and had an inadequate response to ONE of the preferred agents

    OR

    C. The patient has an intolerance or hypersensitivity to ONE preferred agent that is NOT expected to occur with the requested agent

    OR

    D. The patient has an FDA labeled contraindication to ALL of the preferred agent(s) that is NOT expected to occur with the requested agent

    OR

    E. The patient is currently being treated with the requested agent as indicated by ALL of the following:
        i. A statement by the prescriber that the patient is currently taking the requested agent

        AND

        ii. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent

        AND

        iii. The prescriber states that a change in therapy is expected to be ineffective or cause harm

    OR

    F. The prescriber has provided documentation that ALL of the preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

AND

2. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

3. ONE of the following:
    A. The requested quantity (dose) does NOT exceed the program quantity limit

    OR

B. ALL of the following:
   i. The requested quantity (dose) is greater than the program quantity limit
   AND
   ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
   AND
   iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

OR

C. ALL of the following:
   i. The requested quantity (dose) is greater than the program quantity limit
   AND
   ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
   AND
   iii. The prescriber has provided information in support of therapy with a higher dose for the requested indication

Length of Approval: 3 months for ovulation induction or ART
6 months for hypogonadotropic hypogonadism
3 months for cryptorchidism

Gonadotropin Releasing Hormone (GnRH) Analogs Evaluation

Cetrotide or **ganirelix** acetate will be approved when ALL of the following are met:

1. The patient's benefit plan covers agents for infertility
   AND
2. ONE of the following:
   A. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days
   OR
   B. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed
   OR
   C. ALL of the following:
      i. The patient is undergoing ovarian stimulation
      AND
      ii. The patient is NOT pregnant
      AND
      iii. The patient has undergone a complete medical and endocrinologic evaluation
      AND
      iv. The fertility status of the patient's partner has also been evaluated (if applicable)
      AND

v. The patient will receive human chorionic gonadotropin (hCG) following completion of the requested agent unless there are risks present for ovarian hyper-stimulation syndrome (OHSS)
AND

vi. ONE of the following:
a. The requested agent is a preferred agent
OR
b. The patient has tried and had an inadequate response to ONE of the preferred agent(s)
OR
c. The patient has an intolerance or hypersensitivity to ONE of the preferred agent(s) that is NOT expected to occur with the requested agent
OR
d. The patient has an FDA labeled contraindication to ALL of the preferred agent(s) that is NOT expected to occur with the requested agent
OR
e. The patient is currently being treated with the requested agent as indicated by ALL of the following:
1. A statement by the prescriber that the patient is currently taking the requested agent
AND
2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
AND
3. The prescriber states that a change in therapy is expected to be ineffective or cause harm
OR
f. The prescriber has provided documentation that ALL of the preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

AND

3. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
4. ONE of the following:
A. The requested quantity (dose) does NOT exceed the program quantity limit
OR
B. ALL of the following:
i. The requested quantity (dose) is greater than the program limit
AND
ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
AND
iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
OR

C. ALL of the following:
   i. The requested quantity (dose) is greater than the program quantity limit
   AND
   ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
   AND
   iii. The prescriber has provided information in support of therapy with a higher dose for the requested indication

Length of Approval: 3 months

Menotropins
Menopur will be approved when ALL of the following are met:
1. The patient's benefit plan covers agents for infertility
   AND
2. ONE of the following:
   A. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days
   OR
   B. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed
   OR
   C. ALL of the following:
      i. The requested agent will be used for the development of multiple follicles as part of an assisted reproductive technology (ART) [e.g., invitro fertilization (IVF), gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), tubal embryo transfer (TET), cryopreservation, intracytoplasmic sperm injection (ICSI)
      AND
      ii. The patient is NOT pregnant
      AND
      iii. The patient does NOT have primary ovarian failure
      AND
      iv. The patient will receive human chorionic gonadotropin (hCG) following completion of the requested agent unless there are risks present for ovarian hyperstimulation syndrome (OHSS)
      AND
      v. The patient has undergone a complete medical and endocrinologic evaluation
      AND
      vi. The fertility status of the patient's partner has also been evaluated (if applicable)

   AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND

4. ONE of the following:
    A. The requested quantity (dose) does NOT exceed the program quantity limit
    OR
    B. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
        AND
        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
    OR
    C. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
        AND
        iii. The prescriber has provided information in support of therapy with a higher dose for the requested indication

Length of Approval: 3 months