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.

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
04-01-2024

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Cetrotide® (cetrorelix acetate) Injection	Inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian stimulation	Gonadotropin Releasing Hormone (GnRH) analogs Available as generic	1
Follistim® AQ (follitropin beta) Injection	Induction of ovulation and pregnancy in anovulatory infertile women whom the cause of infertility is functional and not due to primary ovarian failure Pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycle 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	Follicle Stimulating Hormone (FSH)	2
Ganirelix acetate Injection	Inhibition of premature LH surges in women undergoing controlled ovarian hyperstimulation	Gonadotropin Releasing Hormone (GnRH) analogs Available as generic	3
Gonal-F® (follitropin alpha) Injection	Induction of ovulation and pregnancy in oligo-anovulatory women for whom the cause of infertility is functional and not due to primary ovarian failure Development of multiple follicles in ovulatory women as part of an assisted reproductive technology (ART) cycles Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism for whom the cause of infertility is not due to primary testicular failure	Follicle Stimulating Hormone (FSH)	4
Menopur® (menotropins)	Development of multiple follicles and pregnancy in ovulatory women as part of an assisted reproductive technology (ART) cycle	Menotropins	5

Agent(s)	FDA Indication(s)	Notes	Ref#
Injection			
Novarel® (chorionic gonadotropin) Injection	Prepubertal cryptorchidism not due to anatomic obstruction Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary 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 has been appropriately pretreated with human menotropins	Human Chorionic Gonadotropin (hCG)	6
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 (OI) and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure	Human Chorionic Gonadotropin (hCG)	7
Pregnyl®, Chorionic gonadotropin Injection	Prepubertal cryptorchidism not due to anatomical obstruction Selected cases of hypogonadotropic hypogonadism (hypogonadism secondary 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	Human Chorionic Gonadotropin (hCG)	8

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

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 of age 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 (LH) 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 (FSH) 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 (IUI) or invitro fertilization (IVF). 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 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 American Urological Association/American Society for Reproductive Medicine (AUA/ASRM) guideline recommends that clinicians should obtain hormonal evaluation, including FSH and testosterone, for infertile men with impaired libido, erectile dysfunction, oligozoospermia, atrophic testes, or evidence of hormonal abnormality on physical examination. Testosterone levels should be defined based on a blood sample drawn in the morning, since levels drop during the day. If the morning total testosterone level is low (less than 300 ng/dL), a more extensive evaluation should include a second testosterone level, measurements of free testosterone, LH, estradiol, and prolactin. The relationships among serum testosterone, LH, FSH, and prolactin concentrations helps to identify the clinical condition. The infertile male presenting with HH be treated with aromatase inhibitors, hCG, selective estrogen receptor

	modulators, or a combination thereof, after the etiology of the disorder has been evaluated.(18,19)
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)
Efficacy - 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 LH and 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 (less than 35 years old) • Lower body mass index (BMI) • Diagnosis of an ovulation disorder or polycystic ovary syndrome (PCOS) • Serum antimüllerian hormone (AMH) levels greater than 10 ng/mL • Antral follicle count (AFC) greater than or equal to 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 including dry natural rubber/latex • Known hypersensitivity to GnRH or any other GnRH analog • Known or suspected pregnancy Gonal-F has the following contraindications:(4) • Hypersensitivity to recombinant FSH products or one of their excipients • High levels of FSH indicating primary gonadal failure • Uncontrolled non-gonadal endocrinopathies (for example, thyroid, adrenal, or pituitary disorders)

	• 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 • Combined hCG and pregnant mare's serum therapy has been noted to induce high incidences of external congenital anomalies in the offspring of mice, in a dose-dependent manner. The potential extrapolation to humans has not been determined Ovidrel has the following contraindications:(7) • Prior hypersensitivity to hCG preparations or one of their excipients • Primary ovarian failure • Uncontrolled thyroid or adrenal dysfunction • 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) • Prior hypersensitivity reactions to human gonadotropins, including hCG, or any of the excipients • High serum FSH, indicating primary gonadal failure in women • Presence of uncontrolled non-gonadal endocrinopathies (e.g., thyroid, adrenal, or pituitary disorders) • Tumors of the hypothalamus or pituitary gland and ovary, breast, or uterus in females and breast or prostate in males • Malformations of the reproductive organs incompatible with pregnancy • Fibroid tumors of the uterus incompatible with pregnancy

	• Abnormal vaginal bleeding of undetermined origin

REFERENCES

Number	Reference
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2	Follistim AQ prescribing information. Merck Sharp & Dohme LLC. June 2022.
3	Ganirelix acetate prescribing information. Organon USA Inc. June 2021.
4	Gonal-F prescribing information. EMD Serono Inc. December 2020.
5	Menopur prescribing information. Ferring Pharmaceuticals. May 2018.
6	Novarel prescribing information. Ferring Pharmaceuticals. November 2020.
7	Ovidrel prescribing information. EMD Serono Inc. February 2022.
8	Pregnyl prescribing information. Merck Sharp & Dohme LLC. March 2023.
9	Centers for Disease Control and Prevention. Assisted Reproductive Technology (ART). What is Assisted Reproductive Technology? Available at https://www.cdc.gov/art/whatis.html.
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12	Practice Committee of the American Society for Reproductive Medicine. American Society for Reproductive Medicine, Birmingham, Alabama. Prevention and treatment of moderate and severe ovarian hyperstimulation syndrome: a guideline. Fertility and Sterility® Vol. 106, No 7, December 2016.
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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.
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18	Schlegel PN, Sigman M, Collura B, et al. Diagnosis and Treatment of Infertility in Men: AUA/ASRM Guideline Part I. *J Urol*. 2021;205(1):36-43. doi:10.1097/JU.0000000000001521.
19	Schlegel PN, Sigman M, Collura B, et al. Diagnosis and Treatment of Infertility in Men: AUA/ASRM Guideline Part II. J Urol. 2021;205(1):44-51. doi:10.1097/JU.0000000000001521

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Cetrotide	cetrorelix acetate for inj kit	0.25 MG	M ; N ; O ; Y	O ; Y		

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Ovidrel	choriogonadotropin alfa inj	250 MCG/0.5ML	M ; N ; O ; Y	N		
Novarel ; Pregnyl ; Pregnyl w/diluent benzyl	chorionic gonadotropin for im inj	10000 UNIT ; 5000 UNIT	M ; N ; O ; Y	N		
Gonal-f ; Gonal-f rff	follitropin alfa for inj ; follitropin alfa for subcutaneous inj	1050 UNIT ; 450 UNIT ; 75 UNIT	M ; N ; O ; Y	N		
Gonal-f rff rediject	follitropin alfa subcutaneous soln pen-inj	300 UNIT/0.5ML ; 450 UNT/0.75ML ; 900 UNIT/1.5ML	M ; N ; O ; Y	N		
Follistim aq	follitropin beta inj	300 UNT/0.36ML ; 600 UNT/0.72ML ; 900 UNT/1.08ML	M ; N ; O ; Y	N		
Fyremadel	ganirelix acetate soln prefilled syringe	250 MCG/0.5ML	M ; N ; O ; Y	O ; Y		
Menopur	menotropins for subcutaneous inj	75 UNIT	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Cetrotide	Cetrorelix Acetate For Inj Kit 0.25 MG	0.25 MG	5	Kits	30	DAYS			
Follistim aq	Follitropin Beta Inj 300 Unit/0.36ML	300 UNT/0.36ML	15	Cartridges	30	DAYS	Each cartridge is billed as 0.420 mL		
Follistim aq	Follitropin Beta Inj 600 Unit/0.72ML	600 UNT/0.72ML	8	Cartridges	30	DAYS	Each cartridge is billed as 0.780 mL		
Follistim aq	Follitropin Beta Inj 900 Unit/1.08ML	900 UNT/1.08ML	5	Cartridges	30	DAYS	Each cartridge is billed as 1.170 mL		
Fyremadel	Ganirelix Acetate Soln Prefilled Syringe 250 MCG/0.5ML	250 MCG/0.5ML	5	Syringes	30	DAYS			
Gonal-f	Follitropin Alfa For Inj 1050 Unit	1050 UNIT	4	Syringes	30	DAYS			
Gonal-f	Follitropin Alfa For Inj 450 Unit	450 UNIT	10	Syringes	30	DAYS			
Gonal-f rff	Follitropin Alfa For Subcutaneous Inj 75 Unit	75 UNIT	20	Syringes	30	DAYS			
Gonal-f rff	Follitropin Alfa For Subcutaneous Inj 75 Unit	75 UNIT	20	Syringes	30	DAYS			
Gonal-f rff rediject	Follitropin Alfa Subcutaneous Soln Pen-inj	300 UNIT/0.5ML	15	Pens	30	DAYS			
Gonal-f rff rediject	Follitropin Alfa Subcutaneous Soln Pen-inj	450 UNT/0.75ML	10	Pens	30	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Gonal-f rff rediject	Follitropin Alfa Subcutaneous Soln Pen-inj	900 UNIT/1.5ML	5	Pens	30	DAYS			
Menopur	Menotropins For Subcutaneous Inj 75 Unit	75 UNIT	60	Vials	30	DAYS			
Novarel	Chorionic Gonadotropin For IM Inj 5000 Unit	5000 UNIT	4	Vials	30	DAYS			
Novarel ; Pregnyl ; Pregnyl w/diluent benzyl	Chorionic Gonadotropin For IM Inj 10000 Unit	10000 UNIT	2	Vials	30	DAYS			
Ovidrel	Choriogonadotropin Alfa Inj 250 MCG/0.5ML	250 MCG/0.5ML	2	Syringes	30	DAYS			

ADDITIONAL QUANTITY LIMIT INFORMATION

Wildcard	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Additional QL Information	Targeted NDCs When Exclusions Exist	Effective Date	Term Date
30062030102020	Follistim aq	Follitropin Beta Inj 300 Unit/0.36ML	300 UNT/0.36ML	Each cartridge is billed as 0.420 mL			
30062030102030	Follistim aq	Follitropin Beta Inj 600 Unit/0.72ML	600 UNT/0.72ML	Each cartridge is billed as 0.780 mL			
30062030102040	Follistim aq	Follitropin Beta Inj 900 Unit/1.08ML	900 UNT/1.08ML	Each cartridge is billed as 1.170 mL			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Cetrotide	cetrorelix acetate for inj kit	0.25 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Follistim aq	follitropin beta inj	300 UNT/0.36ML ; 600 UNT/0.72ML ; 900 UNT/1.08ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Fyremadel	ganirelix acetate soln prefilled syringe	250 MCG/0.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f ; Gonal-f rff	follitropin alfa for inj ; follitropin alfa for subcutaneous inj	1050 UNIT ; 450 UNIT ; 75 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f rff rediject	follitropin alfa subcutaneous soln pen-inj	300 UNIT/0.5ML ; 450 UNT/0.75ML ; 900 UNIT/1.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ;

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Health Insurance Marketplace/BasicRx ; KeyRx
Menopur	menotropins for subcutaneous inj	75 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Novarel ; Pregnyl ; Pregnyl w/diluent benzyl	chorionic gonadotropin for im inj	10000 UNIT ; 5000 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Ovidrel	choriogonadotropin alfa inj	250 MCG/0.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Cetrotide	Cetrorelix Acetate For Inj Kit 0.25 MG	0.25 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Follistim aq	Follitropin Beta Inj 300 Unit/0.36ML	300 UNT/0.36ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Follistim aq	Follitropin Beta Inj 600 Unit/0.72ML	600 UNT/0.72ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Follistim aq	Follitropin Beta Inj 900 Unit/1.08ML	900 UNT/1.08ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Fyremadel	Ganirelix Acetate Soln Prefilled Syringe 250 MCG/0.5ML	250 MCG/0.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f	Follitropin Alfa For Inj 1050 Unit	1050 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f	Follitropin Alfa For Inj 450 Unit	450 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f rff	Follitropin Alfa For Subcutaneous Inj 75 Unit	75 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Gonal-f rff	Follitropin Alfa For Subcutaneous Inj 75 Unit	75 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f rff rediject	Follitropin Alfa Subcutaneous Soln Pen-inj	900 UNIT/1.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f rff rediject	Follitropin Alfa Subcutaneous Soln Pen-inj	450 UNT/0.75ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Gonal-f rff rediject	Follitropin Alfa Subcutaneous Soln Pen-inj	300 UNIT/0.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Menopur	Menotropins For Subcutaneous Inj 75 Unit	75 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Novarel	Chorionic Gonadotropin For IM Inj 5000 Unit	5000 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Novarel ; Pregnyl ; Pregnyl w/diluent benzyl	Chorionic Gonadotropin For IM Inj 10000 Unit	10000 UNIT	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Ovidrel	Choriogonadotropin Alfa Inj 250 MCG/0.5ML	250 MCG/0.5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Follicle Stimulating Hormone	**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: 1. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy

Module	Clinical Criteria for Approval

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**

2. 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:

Preferred Target Agents	Non-Preferred Target Agents
Follistim AQ (follitropin beta)	Gonal F Kit (follitropin alfa) Gonal F RFF (follitropin alfa) Gonal F RFF Pen (follitropin alfa)

      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**

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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:

1. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
All target agents are eligible for continuation of therapy

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**

2. 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:

Preferred Target Agents	Non-Preferred Target Agents
Follistim AQ (follitropin beta)	Gonal F Kit (follitropin alfa) Gonal F RFF (follitropin alfa) Gonal F RFF Pen (follitropin alfa)

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

Module	Clinical Criteria for Approval
	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: 1. The requested agent is Follistim AQ or Gonal-F **AND** 2. The patient does not have primary testicular failure **AND** 3. The requested agent will be used in combination with human chorionic gonadotropin (hCG) **AND** 4. The requested agent will not be started until the patient's serum testosterone level is at normal levels **AND** 5. ONE of the following: **Preferred Target Agents** / **Non-Preferred Target Agents** Follistim AQ (follitropin beta) / Gonal F Kit (follitropin alfa), Gonal F RFF (follitropin alfa), Gonal F RFF Pen (follitropin alfa) 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 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 been evaluated (if applicable) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of approval:** 3 months for ART or ovulation induction 6 months for hypogonadotropic hypogonadism NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents
Gonadotropin Releasing Hormone (GnRH) Analogs	**Gonadotropin Releasing Hormone (GnRH) Analogs Evaluation** **Cetrotide and 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. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy**

Module	Clinical Criteria for Approval
	All target agents are eligible for continuation of therapy 1. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days **OR** 2. 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** B. ALL of the following: 1. The patient is undergoing ovarian stimulation **AND** 2. The patient is NOT pregnant **AND** 3. The patient has undergone a complete medical and endocrinologic evaluation **AND** 4. The fertility status of the patient's partner has been evaluated (if applicable) **AND** 5. 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** 6. ONE of the following: **Preferred Target Agents**: Ganirelix acetate* *generic available and included as preferred in this program **Non-Preferred Target Agents**: Cetrotide (cetrorelix acetate) 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 **Length of Approval:** 3 months NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents
Human Chorionic	**Human Chorionic Gonadotropin Evaluation**

Module	Clinical Criteria for Approval
Gonadotropin Evaluation	**Novarel, Ovidrel, Pregnyl, and Chorionic gonadotropin** will be approved when BOTH 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: 1. The requested agent is Novarel, Pregnyl, or hCG **AND** 2. The diagnosis is not due to an anatomical obstruction **AND** 3. The patient is prepubertal **AND** 4. 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: 1. The requested agent is Novarel, Pregnyl, or hCG **AND** 2. 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: 1. The patient's benefit plan covers agents for infertility **AND** 2. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** Ovidrel (chorionic gonadotropin) Pregnyl (chorionic gonadotropin) 1. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days **OR** 2. 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** B. ALL of the following: 1. The patient is NOT pregnant **AND** 2. The patient does NOT have primary ovarian failure **AND**

<table>
<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
<tr><td></td><td>
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 been evaluated (if applicable) AND
6. ONE of the following:

<table>
<tr><th>Preferred Target Agents</th><th>Non-Preferred Target Agents</th></tr>
<tr><td>Ovidrel (chorionic gonadotropin)

Pregnyl (chorionic gonadotropin) (50090-5923-**, 00052-0315-**)</td><td>Chorionic gonadotropin (63323-0030-**)

Novarel (chorionic gonadotropin) (55566-1501-**, 55566-1502-**)</td></tr>
</table>
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 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
2. The patient does NOT have any FDA labeled contraindications to the requested agent

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

NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents</td></tr>
<tr><td>Menotropins</td><td>Menotropins Evaluation</td></tr>
</table>

Module	Clinical Criteria for Approval
	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. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. Information has been provided that indicates the patient has been treated with the requested agent within the past 90 days **OR** 2. 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** B. ALL of the following: 1. 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** 2. The patient is NOT pregnant **AND** 3. The patient does NOT have primary ovarian failure **AND** 4. 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** 5. The patient has undergone a complete medical and endocrinologic evaluation **AND** 6. The fertility status of the patient's partner has been evaluated (if applicable) **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 3 months NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. 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