### FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Agents</th>
<th>Indication</th>
<th>Dosing and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicle Stimulating Hormone (FSH)</td>
<td>● Induction of ovulation in women who have previously received pituitary suppression</td>
<td><strong>Ovulation induction:</strong> Initial (first cycle of treatment) starting dose of 150 International Units per day for 5 days, administered subcutaneously or intramuscularly. Subsequent cycles of treatment dose should be individualized based on clinical monitoring (including serum estradiol levels and vaginal ultrasound results). Do not make adjustments in dose more frequently than once every 2 days and do not exceed more than 75 to 150 International Units per adjustment. The maximum, individualized daily dose is 450 International Units per day.</td>
</tr>
<tr>
<td>Bravelle® (urofollitropin) injection</td>
<td>● Development of multiple follicles as part of an assisted reproductive technology (ART) cycle in ovulatory women who have previously received pituitary suppression</td>
<td><strong>ART:</strong> Initial dose of 225 International Units subcutaneously daily until sufficient follicular development, as determined by ultrasound evaluation of follicular growth and serum estradiol levels. Individualize dosage to attain sufficient follicular development. Do not make additional dosage adjustments more</td>
</tr>
<tr>
<td>Follistim® AQ (follitropin beta) injection</td>
<td>Induction of ovulation: Starting dose of 50 International Units subcutaneously daily for at least 7 days. Subsequent dosage adjustments of 25 or 50 International Units can be made at weekly intervals based upon ovarian response. The maximum daily dose is 250 International Units.</td>
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<tr>
<td>------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>In women for:</td>
<td><strong>Induction of ovulation:</strong> Starting dose of 50 International Units subcutaneously daily for at least 7 days. Subsequent dosage adjustments of 25 or 50 International Units can be made at weekly intervals based upon ovarian response. The maximum daily dose is 250 International Units.</td>
<td></td>
</tr>
<tr>
<td>• Induction of Ovulation and Pregnancy in anovulatory infertile women whom the cause of infertility in functional and not due to primary ovarian failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In men for:</td>
<td><strong>Induction of spermatogenesis:</strong> Serum testosterone levels must be normalized with human chorionic gonadotropin (hCG) treatment before starting Follistim AQ and hCG must be continued while on Follistim AQ. Dose is 450 International Units per week, subcutaneously, as</td>
<td></td>
</tr>
<tr>
<td>• 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</td>
<td></td>
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</tr>
</tbody>
</table>

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### Gonal-F® (follitropin alfa) injection

- **Induction of ovulation and pregnancy in oligo-ovulatory women in 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)**

### Ovulation induction:

**Starting (initial cycle) daily dose of 75 International Units subcutaneously 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 International Units. Thereafter if indicated by ovarian response increase dose by up to 37.5 International Units every 7 days. The maximum individualized dose is 300 International Units. In general treatment should not exceed 35 days unless an E2 rise indicates imminent follicular development.

### ART:

For women whose endogenous gonadotropin levels are normal or for women under 35 years of age whose endogenous gonadotropin levels are suppressed: starting dose of 150 International Units subcutaneously per day until sufficient follicular development, as determined.
- Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure by ultrasound in combination with measurement of serum estradiol levels.

In women 35 years of age and older whose endogenous gonadotropin levels are suppressed: starting dose of 225 International Units subcutaneously per day until sufficient follicular development, as determined by ultrasound in combination with measurement of serum estradiol levels.

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 International Units at each adjustment. Doses greater than 450 International Units per day are not recommended. In most cases, therapy should not exceed 10 days per cycle.

**Induction of spermatogenesis:** Serum testosterone levels must be normalized with human chorionic gonadotropin (hCG) treatment before starting Gonal-F and hCG must be continued while on Gonal-F. Dose of 150 International Units subcutaneously three times a week. If azoospermia persists, the
dose of Gonal-F may be increased to a maximum of 300 units three times per week. Gonal-F may need to be administered for up to 18 months to achieve adequate spermatogenesis.

<table>
<thead>
<tr>
<th>Human Chorionic Gonadotropin (hCG)</th>
<th>Prepubertal cryptorchidism:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Novarell® (chorionic gonadotropin) injection</strong></td>
<td>○ 4,000 USP Units intramuscularly (IM) three times weekly for three weeks OR</td>
</tr>
<tr>
<td></td>
<td>○ 5,000 USP Units IM every second day for four injections OR</td>
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<tr>
<td></td>
<td>○ 15 injections of 500 to 1,000 USP Units IM over a period of 6 weeks OR</td>
</tr>
<tr>
<td></td>
<td>○ 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</td>
</tr>
<tr>
<td></td>
<td>Prepubertal cryptorchidism:</td>
</tr>
</tbody>
</table>

- 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

<table>
<thead>
<tr>
<th>Hypogonadotropic hypogonadism:</th>
</tr>
</thead>
<tbody>
<tr>
<td>○ 500 to 1,000 USP Units intramuscularly (IM) three times a week for three weeks, followed by the same dose twice a week for three weeks OR</td>
</tr>
<tr>
<td>○ 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</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Induction of ovulation:</th>
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</thead>
<tbody>
<tr>
<td>5,000 to 10,000 USP Units intramuscularly (IM) one</td>
</tr>
<tr>
<td><strong>Ovidrel® (choriogonadotropin alfa) injection</strong></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>• 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</td>
</tr>
<tr>
<td>• Induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to primary ovarian failure</td>
</tr>
<tr>
<td><strong>ART:</strong> 250 µg subcutaneously one day following the last dose of the follicle stimulating agent</td>
</tr>
</tbody>
</table>
| **Ovulation induction:** 250 µg subcutaneously one day following the last dose of the follicle stimulating agent | 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 |
<p>| <strong>Hypogonadotropic hypogonadism:</strong>  |
| o 500 to 1,000 USP Units intramuscularly (IM) three times a week for three weeks, followed by |</p>
<table>
<thead>
<tr>
<th><strong>Gonadotropin Releasing Hormone (GnRH) analogs</strong></th>
<th><strong>Induction of ovulation: 5,000 to 10,000 USP Units intramuscularly (IM) one day following the last dose of menotropins</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cetrotide® (cetrorelix acetate) injection</strong></td>
<td>● 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</td>
</tr>
<tr>
<td></td>
<td>0.25 mg subcutaneously on either stimulation day 5 (morning or evening) or day 6 (morning) and continued daily until day of hCG administration</td>
</tr>
<tr>
<td><strong>Ganirelix acetate injection</strong></td>
<td>● Inhibition of premature LH surges in women undergoing controlled ovarian hyperstimulation</td>
</tr>
<tr>
<td></td>
<td>250 mcg subcutaneously one daily during the mid to late portion of the follicular phase. Continue treatment daily until the day of hCG administration</td>
</tr>
<tr>
<td><strong>Menotropins</strong></td>
<td>● Development of multiple follicles and pregnancy in ovulatory women as part of an assisted reproductive technology (ART) cycle</td>
</tr>
<tr>
<td><strong>Menopur® (menotropins) injection</strong></td>
<td>Starting dose (first cycle) of 225 International Units subcutaneously daily. 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 International Units at each adjustment. Menopur may be used with Bravelle and the total daily dose of the the same dose twice a week for three weeks OR</td>
</tr>
<tr>
<td></td>
<td>● 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</td>
</tr>
</tbody>
</table>
combination should not exceed 450 International Units. Continue treatment until adequate follicular development is evident. Therapy should not exceed 20 days.

**CLINICAL RATIONALE**

**Infertility**

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 oligosperma. 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.

**Assisted Reproductive Technology**

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**

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.

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.

**Cryptorchidism**

Cryptorchidism is the most common congenital abnormality of the 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 cell 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.12,14

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

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

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.

Safety

Ovarian hyperstimulation syndrome (OHSS) occurs when the ovaries are hyper-stimulated and enlarged due to fertility treatments (or rarely, mutations in the follicle-stimulating hormone [FSH] receptor), resulting in the shift of serum from the intravascular space to the third space, mainly to the abdominal cavity. In its severe form, OHSS is a life-threatening condition because it can cause venous or arterial thromboembolic events, including stroke and loss of perfusion of an extremity.
**Clomiphene citrate**

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.

**References**

Gonadotropin Hormones Prior Authorization with Quantity Limit Criteria

OBJECTIVE
The intent of Gonadotropin Hormones Prior Authorization with quantity limit (PAQL) program is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines.

TARGET AGENT(S)
Preferred Agents
Follistim AQ® (follitropin beta)
Ganirelix Acetate (ganirelix) a
Menopur® (menotropin)
Novarel® (chorionic gonadotropin) a
Pregnyl® (chorionic gonadotropin) a

Nonpreferred Agents
Bravelle® (urofollitropin)
Cetrotide® (cetrorelix acetate)
Gonal-F® Kit (follitropin alfa)
Gonal-F® RFF (follitropin alfa)
Gonal-F® RFF Pen (follitropin alfa)
Ovidrel® (chioriogonadotropin alfa)

a Generic available and included in this program

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bravelle (urofollitropin) injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75 unit vials</td>
<td>30062090102112</td>
<td>M, N, O, or Y</td>
<td>60 vials per 30 days</td>
</tr>
<tr>
<td>Cetrotide (cetrorelix acetate) injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25 mg kit</td>
<td>30090025106420</td>
<td>M, N, O, or Y</td>
<td>5 kits per 30 days</td>
</tr>
<tr>
<td>Follistim AQ (follitropin beta) injection</td>
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<td></td>
</tr>
<tr>
<td>75 unit/0.5 mL cartridge</td>
<td>30062030102003</td>
<td>M, N, O, or Y</td>
<td>10 mL (20 cartridges) per 30 days</td>
</tr>
<tr>
<td>300 unit/0.36 mL cartridge</td>
<td>30062030102020</td>
<td>M, N, O, or Y</td>
<td>5.4 mL (15 cartridges) per 30 days</td>
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<tr>
<td>600 unit/0.72 mL cartridge</td>
<td>30062030102030</td>
<td>M, N, O, or Y</td>
<td>5.76 mL (8 cartridges) per 30 days</td>
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<tr>
<td>900 unit/1.08 mL cartridge</td>
<td>30062030102040</td>
<td>M, N, O, or Y</td>
<td>5.4 mL (5 cartridges) per 30 days</td>
</tr>
</tbody>
</table>

Ganirelix Acetate injection

| 250 mcg/0.5 mL prefilled syringe a       | 30090040102020         | M, N, O, or Y    | 2.5 mL (5 syringes) per 30 days |

Gonal-F (follitropin alfa) injection
CRITERIA FOR APPROVAL
PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Follicle Stimulating Hormone Evaluation
Bravelle, 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. The patient has a diagnosis of infertility (either current or anticipated) AND ONE of the following:
   A. The requested agent will be used for ovulation induction AND ONE of the following:
      i. There is documentation that the patient is currently being treated with the requested agent
         OR
      ii. The prescriber states the patient is currently being treated with the requested agent AND is at risk if therapy is changed

<table>
<thead>
<tr>
<th>Product Description</th>
<th>Code</th>
<th>Code Description</th>
<th>30 syringes per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 unit RFF pre-filled syringe</td>
<td>30062030052115</td>
<td>M, N, O, or Y</td>
<td>20 syringes per 30 days</td>
</tr>
<tr>
<td>300 unit/0.5 mL Rediject multi-dose delivery system</td>
<td>30062030052020</td>
<td>M, N, O, or Y</td>
<td>7.5 mL (15 pens) per 30 days</td>
</tr>
<tr>
<td>450 unit/0.75 mL Rediject multi-dose delivery system</td>
<td>30062030052025</td>
<td>M, N, O, or Y</td>
<td>7.5 mL (10 pens) per 30 days</td>
</tr>
<tr>
<td>450 unit multi-dose pre-filled syringe multi-dose delivery system</td>
<td>30062030052140</td>
<td>M, N, O, or Y</td>
<td>10 syringes per 30 days</td>
</tr>
<tr>
<td>900 unit/1.5 mL Rediject multi-dose delivery system</td>
<td>30062030052040</td>
<td>M, N, O, or Y</td>
<td>7.5 mL (5 pens) per 30 days</td>
</tr>
<tr>
<td>1050 unit multi-dose pre-filled syringe</td>
<td>30062030052150</td>
<td>M, N, O, or Y</td>
<td>4 syringes per 30 days</td>
</tr>
</tbody>
</table>

**Menopur (menotropins) injection**

<table>
<thead>
<tr>
<th>Product Description</th>
<th>Code</th>
<th>Code Description</th>
<th>30 syringes per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 unit vial</td>
<td>30062050002175</td>
<td>M, N, O, or Y</td>
<td>60 vials per 30 days</td>
</tr>
</tbody>
</table>

**Novarel (chorionic gonadotropin) injection**

<table>
<thead>
<tr>
<th>Product Description</th>
<th>Code</th>
<th>Code Description</th>
<th>30 syringes per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>5,000 unit vial&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30062020002130</td>
<td>M, N, O, or Y</td>
<td>4 vials per 30 days</td>
</tr>
<tr>
<td>10,000 unit vial&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30062020002140</td>
<td>M, N, O, or Y</td>
<td>2 vials per 30 days</td>
</tr>
</tbody>
</table>

**Ovidrel (choriogonadotropin alfa) injection**

<table>
<thead>
<tr>
<th>Product Description</th>
<th>Code</th>
<th>Code Description</th>
<th>30 syringes per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mcg/0.5 mL pre-filled syringe</td>
<td>30062022052220</td>
<td>M, N, O, or Y</td>
<td>1 mL (2 syringes) per 30 days</td>
</tr>
</tbody>
</table>

**Pregnyl (chorionic gonadotropin) injection**

<table>
<thead>
<tr>
<th>Product Description</th>
<th>Code</th>
<th>Code Description</th>
<th>30 syringes per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>10,000 unit multi-dose vial&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30062020002140</td>
<td>M, N, O, or Y</td>
<td>2 vials per 30 days</td>
</tr>
</tbody>
</table>

<sup>a</sup> generic available
iii. ALL of the following:
   1. ONE of the following:
      a. The patient has tried and had an inadequate response to an adequate trial of clomiphene citrate (i.e., 3 courses of at least 50 mg daily for 5 days) OR
      b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to clomiphene citrate 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. ONE of the following:
      a. The requested agent is the preferred agent Follistim AQ OR
      b. The patient has tried and had an inadequate response to Follistim AQ OR
      c. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Follistim AQ that is NOT expected to occur with the requested agent OR

B. The requested agent will be used for the development of multiple follicles as part of an assisted reproductive technology (ART) [e.g., in vitro 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. There is documentation that the patient is currently being treated with the requested agent OR
   ii. The prescriber states the patient is currently being treated with the requested agent AND is at risk if therapy is changed OR
   iii. 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 human chorionic gonadotropin (hCG) following completion of the requested agent unless there are risks present for ovarian hyperstimulation syndrome (OHSS) AND
      4. ONE of the following:
         a. The requested agent is the preferred agent Follistim AQ
b. The patient has tried and had an inadequate response to Follistim AQ

OR

c. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Follistim AQ that is NOT expected to occur with the requested agent

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 patient will receive human chorionic gonadotropin concomitantly with the requested agent
   AND
   iv. The requested agent will not be started until the patient’s serum testosterone level is at normal levels (documentation requirement to be determined by client)
   AND
   v. ONE of the following:
      1. The requested agent is the preferred agent Follistim AQ
         OR
      2. The patient has tried and had an inadequate response to Follistim AQ
         OR
      3. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to Follistim AQ that is NOT expected to occur with the requested agent

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 contraindication(s) 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 above 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 submitted documentation in support of therapy with a higher dose for the intended diagnosis

Length of approval: 3 months for ART or ovulation induction
   6 months for hypogonadotrophic 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:
         1. The patient has had surgery to correct the cryptorchidism
            OR
         2. The patient will have surgery to correct the cryptorchidism after using the requested agent
            OR
         3. The patient is unable to have surgery to correct the cryptorchidism
   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 (documentation requirement to be determined by client):
         1. The patient is not currently receiving treatment for the diagnosis AND has ONE of the following pretreatment levels
            a. Total serum testosterone level that is below the testing laboratory’s lower limit of the normal range or is less than 300 ng/dL
            OR
            b. Free serum testosterone level that is below the testing laboratory’s lower limit of the normal range
            OR
2. The patient is currently receiving treatment for the diagnosis AND has ONE of the following current levels:
   a. Total serum testosterone level that is within OR below the testing laboratory’s lower limit of the normal range OR is less than 300 ng/dL
   OR
   b. 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:
      1. There is documentation that the patient is currently being treated with the requested agent
      OR
      2. The prescriber states the patient is at risk if therapy is changed
      OR
      3. The patient has a diagnosis of infertility (either current or anticipated) AND 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 follicle stimulating hormone (FSH) OR clomiphene before the requested agent unless there are risks present for ovarian hyperstimulation syndrome (OHSS)
         AND
         d. The patient has undergone a complete medical and endocrinologic evaluation
         AND
         e. The fertility status of the partner also been evaluated (if applicable)
         AND
   f. ONE of the following:
      i. The requested agent is a preferred agent: generic hCG, Novarel, or Pregnyl
      OR
      ii. The patient has tried and had an inadequate response to ONE of the preferred agents: generic hCG, Novarel, or Pregnyl
      OR
iii. The patient has a documented intolerance, FDA labeled contraindication or hypersensitivity to ALL of the preferred agents: generic hCG, Novarel, or Pregnyl that is NOT expected to occur with the requested agent

**AND**

3. The patient does not have any FDA labeled contraindication(s) 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 for the requested indication
      **AND**
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis

**Approval length:** 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. The patient has a diagnosis of infertility (either current or anticipated) AND ONE of the following:
   A. There is documentation that the patient is currently being treated with the requested agent
   **OR**
   B. The prescriber states the patient is currently being treated with the requested agent 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:
       1. The requested agent is the preferred agent Ganirelix acetate
          OR
       2. The patient has tried and had an inadequate response to the preferred agent Ganirelix acetate
          OR
       3. The patient has a documented intolerance, FDA labeled indication, or hypersensitivity to the preferred agent Ganirelix acetate that is NOT expected to occur with the requested agent
          AND
   3. The patient does not have any FDA labeled contraindication(s) 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 dose 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 submitted documentation in support of therapy with a higher dose for the intended diagnosis
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. The patient has a diagnosis of infertility (either current or anticipated) AND ONE of the following:
   A. There is documentation that the patient is currently being treated with the requested agent
      OR
   B. The prescriber states the patient is currently being treated with the requested agent 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
2. The patient does not have any FDA labeled contraindication(s) 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 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 submitted documentation in support of therapy with a higher dose for the intended diagnosis

Length of Approval: 3 months
Step Therapy Supplement

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

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. 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

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

OR

3. The prescriber has provided documentation that the required prerequisite/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

Length of Approval: As per program specific criteria