VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

# BRAVELLE™; FOLLISTIM® AQ; GONAL-F®; GONAL-F™ RFF (Follitropins)

Effective Date: 7/28/5

Date Developed: 07.14.05 by C. Wilhelmy MD

Last Approval Date: 1/26/16, 1/24/17

(Archived 1/1/18), 1/22/19, 2/18/20

**Unarchived Date: 1/22/19 (Formulary Exclusion – For Exception Review Use Only)**

Follitropins are Gonadotropin Ovulation Stimulators. Urofollitropin is a preparation of highly purified follicle-stimulating hormone (FSH) extracted from the urine of postmenopausal women. Follitropin alfa and follitropin beta are human FSH preparations of recombinant DNA origin. Follitropins stimulate ovarian follicular growth in women who do not have primary ovarian failure, and stimulate spermatogenesis in men with hypogonadotrophic hypogonadism. FSH is required for normal follicular growth, maturation, gonadal steroid production, and spermatogenesis.

**Pre-Authorization Criteria:**

**Urofollitropin (Bravelle™):**

Development of multiple follicles with assisted reproductive technologies (ART) in women who have previously received pituitary suppression.

**Follitropin alfa (Gonal-f®, Gonal-f RFF):** ®

**Females:** Induction of ovulation in oligo-anovulatory infertile women in whom the cause of infertility is functional and not caused by primary ovarian failure; development of multiple follicles with assisted reproductive technologies (ART, e.g. in vitro fertilization, IVF )

**Males:** Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure (Gonal-f only)

**Follitropin beta (Follistim® AQ):**

**Females:** Induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not caused by primary ovarian failure; induction of pregnancy in normal ovulatory women undergoing Assisted Reproductive Technology (ART, e.g. in vitro fertilization, IVF )
**Males:** Induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.

VCHCP requires that these medications be prescribed by an infertility specialist.
Indications and Usage Guidelines:

- For the induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not caused by primary ovarian failure.

  OR

- To stimulate the development of multiple follicles in ovulatory patients undergoing Assisted Reproductive Therapy (ART), e.g., in vitro fertilization.

  OR

- Inhibition of premature luteinizing hormone in women undergoing controlled ovarian hyperstimulation.

  OR

- Induction of ovulation in women with primary hypothalamic amenorrhea.

  OR

- Fertility coverage with the following restrictions per state:
  - CT: $\leq$ 40 years of age
  - NJ: $\leq$ 45 years of age
  - NY: Between 21-44 years of age

  AND

- Failure or clinically significant adverse effects to Gonal-F and Bravelle.

Coverage is Not Authorized For Non-FDA approved indications

MONITORING PARAMETERS — Monitor sufficient follicular maturation. This may be directly estimated by sonographic visualization of the ovaries and endometrial lining or measuring serum estradiol levels. The combination of both ultrasonography and measurement of estradiol levels is useful for monitoring for the growth and development of follicles and timing hCG administration.

The clinical evaluation of estrogenic activity (changes in vaginal cytology and changes in appearance and volume of cervical mucus) provides an indirect estimate of the estrogenic effect upon the target organs and, therefore, it should only be used adjunctively with more direct estimates of follicular development (ultrasonography and serum estradiol determinations).

The clinical confirmation of ovulation is obtained by direct and indirect indices of progesterone production. The indices most generally used are: rise in basal body temperature, increase in serum progesterone, and menstruation following the shift in basal body temperature.

Spermatogenesis: Monitor serum testosterone levels, sperm coun
DOSING: ADULTS – See Lexi-Comp Online™ and Epocrates.com for details.

DOSING: ELDERLY — Refer to adult dosing. Clinical studies did not include patients >65 years of age.

Recommended Dosing Regimen and Authorization Limit:

| Drug | Dosing Regimen | Authorization Limit |
|---|---|---|
| All listed above Various, see package inserts | | CT:<br>4 cycles per lifetime<br>NJ/NY:<br>Unlimited cycles |

ADMINISTRATION — See packet insert.

CONTRAINDICATIONS — Hypersensitivity to follitropins or any component of the formulation; high levels of FSH indicating primary gonadal failure (ovarian or testicular); uncontrolled thyroid or adrenal dysfunction; the presence of any cause of infertility other than anovulation; tumor of the ovary, breast, uterus, hypothalamus, testis, or pituitary gland; abnormal vaginal bleeding of undetermined origin; ovarian cysts or enlargement not due to polycystic ovary syndrome; pregnancy

WARNINGS / PRECAUTIONS — These medications should only be used by physicians who are thoroughly familiar with infertility problems and their management. To minimize risks, use only at the lowest effective dose. Monitor ovarian response with serum estradiol and vaginal ultrasound on a regular basis.

Ovarian enlargement which may be accompanied by abdominal distention or abdominal pain, occurs in ~20% of those treated with urofollitropin and hCG, and generally regresses without treatment within 2-3 weeks. Ovarian hyperstimulation syndrome, characterized by severe ovarian enlargement, abdominal pain/distention, nausea, vomiting, diarrhea, dyspnea, and oliguria, and may be accompanied by ascites, pleural effusion, hypovolemia, electrolyte imbalance, hemoperitoneum, and thromboembolic events is reported in about 6% of patients. If hyperstimulation occurs, stop treatment and hospitalize patient. This syndrome develops rapidly within 24 hours to several days and generally occurs during the 7-10 days immediately following treatment. Hemoconcentration associated with fluid loss into the abdominal cavity has occurred and should be assessed by fluid intake & output, weight, hematocrit, serum & urinary electrolytes, urine specific gravity, BUN and creatinine, and abdominal girth. Determinations should be performed daily or more often if the need arises. Treatment is primarily symptomatic and consists of bed rest, fluid and electrolyte replacement and analgesics. The ascitic, pleural and pericardial fluids should never be removed because of the potential danger of injury.

Serious pulmonary conditions (atelectasis, acute respiratory distress syndrome and exacerbation of asthma) have been reported. Thromboembolic events, both in association with and separate from ovarian hyperstimulation syndrome, have been reported.

Multiple pregnancies have been associated with these medications, including triplet and quintuplet gestations. Advise patient of the potential risk of multiple births before starting the treatment.

Follistim® AQ: Contains trace amounts of neomycin and streptomycin. Must be administered using the Follistim Pen™; dose adjustment required when switching from powder for injection to solution for injection due to accuracy of pen device.

PREGNANCY RISK FACTOR — X

PREGNANCY IMPLICATIONS — Ectopic pregnancy, congenital abnormalities, and multiple births have been reported. The incidence of congenital abnormality is similar during natural conception.

LACTATION — Excretion in breast milk unknown/not recommended

PATIENT EDUCATION — Discontinue immediately if possibility of pregnancy. Prior to therapy, inform patients of the following: Duration of treatment and monitoring required; possible adverse reactions; risk of multiple births.

References:



**Revision History:**
Date Revised: 10/4/11 by A. Reeves MD
Date Reviewed: 4/2/12; 1/16/13 by A. Reeves MD
Date Approved by P&T Committee: 7/28/05; 10/25/11; 4/24/12; 1/29/13 Date Reviewed/No Updates: 1/28/14 by C. Sanders MD
Date Approved by P&T Committee: 1/28/14
Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD
Date Approved by P&T Committee: 1/27/15
Date Reviewed/Updated: 1/13/15 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/26/16
Date Reviewed/No Updates: 1/24/17 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/24/17
Date Reviewed/Archived: 1/1/18 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/23/18
Date Reviewed/No Updates/Unarchived: 1/22/19 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/22/19
Date Reviewed/No Updates/Unarchived: 2/18/20 by H. Taekman, MD; R. Sterling, MD
Date Approved by P&T Committee: 2/18/20

| Revision Date | Content Revised (Yes/No) | Contributors | Review/Revision Notes |
|---|---|---|---|
| 1/24/17 | No | Catherine Sanders, MD; Robert Sterling, MD | Annual review |

| | | | |
|---|---|---|---|
| 1/1/18 | No | Catherine Sanders, MD;<br>Robert Sterling, MD | Archived – excluded from the Formulary effective 1/1/18 |
| 1/22/19 | Yes | Catherine Sanders, MD;<br>Robert Sterling, MD | Unarchived – Formulary Exclusion – For Exception Review Use Only<br>Annual Review |
| 2/18/20 | No | Howard Taekman, MD; Robert Sterling, MD | Annual Review |