Contributor Disclosures

For additional information see "Follitropin alfa (recombinant human follicle stimulating hormone): Patient drug information"

For abbreviations, symbols, and age group definitions show table

Brand Names: US

Gonal-f; Gonal-f RFF Rediject; Gonal-f RFF [DSC]

Brand Names: Canada

Gonal-f; Gonal-f Pen

Pharmacologic Category

Gonadotropin; Ovulation Stimulator

Dosing: Adult

Note: Dose should be individualized. Use the lowest dose consistent with the expectation of good results. Over the course of treatment, doses may vary depending on individual patient response.

Ovulation induction

Ovulation induction: SubQ: Initial: 75 units daily for 14 days in the first cycle; incremental dose adjustments of up to 37.5 units may be considered after 14 days based on ovarian response; further dose increases of the same magnitude can be made, if necessary, every 7 days (maximum dose: 300 units daily). Treatment should be continued until follicular growth and/or serum estradiol levels indicate an adequate ovarian response. If response to follitropin is appropriate, human chorionic gonadotropin (hCG) is given 1 day following the last dose to

induce final oocyte maturation and ovulation. Follow current clinical practice to reduce the risk of ovarian hyperstimulation syndrome. In general, therapy should not exceed 35 days.

Multifollicular development during assisted reproductive technology

Multifollicular development during assisted reproductive technology: SubQ: Initiate therapy with follitropin alfa in the early follicular phase (cycle day 2 or day 3) at a dose of 150 units daily, until sufficient follicular development is attained. In most cases, therapy should not exceed 10 days. In patients whose endogenous gonadotropin levels are suppressed, initiate follitropin alfa at a dose of 225 units daily. Continue treatment until adequate follicular development is indicated as determined by ultrasound in combination with measurement of serum estradiol levels. Consider adjustments to dose after 5 days based on the patient's response; adjust subsequent dosage every 3 to 5 days by ≤75 to 150 units additionally at each adjustment. Doses >450 units daily are not recommended. Once adequate follicular development is evident, administer hCG to induce final follicular maturation in preparation for oocyte retrieval. Withhold hCG if the ovaries are abnormally enlarged.

Spermatogenesis induction

Spermatogenesis induction: *Gonal-f:* **SubQ:** Therapy should begin with hCG pretreatment until serum testosterone is in normal range, then initiate follitropin alfa at 150 units 3 times weekly with hCG 3 times weekly; continue with lowest dose needed to induce spermatogenesis (maximum dose: 300 units 3 times weekly); may be given for up to 18 months.

Dosing: Kidney Impairment: Adult

There are no dosage adjustments provided in the manufacturer's labeling. Limited information is available regarding the use of follitropin alfa in this population (Ref).

Dosing: Liver Impairment: Adult

There are no dosage adjustment provided in the manufacturer's labeling (has not been studied).

Dosing: Older Adult

Refer to adult dosing. Clinical studies did not include patients >65 years.

Adverse Reactions

The following adverse drug reactions and incidences are derived from product labeling unless otherwise specified. Percentage may vary by indication, product formulation. As reported with females, unless otherwise noted.

>10%:

Dermatologic: Acne vulgaris (males: 27%)

Endocrine & metabolic: Ovarian cyst (4% to 15%)

Gastrointestinal: Abdominal pain (5% to 23%), enlargement of abdomen (14%)

Local: Pain at injection site (males: 11%; females: 5% to 6%)

Nervous system: Headache (10% to 27%)

1% to 10%:

Dermatologic: Seborrhea (males: 5%)

Endocrine & metabolic: Decreased libido (males: 3%), gynecomastia (males: 6%), intermenstrual bleeding (5%), ovarian hyperstimulation syndrome (5% to 7%)

Gastrointestinal: Diarrhea (4%), flatulence (4% to 6%), nausea (4% to 8%)

Genitourinary: Pelvic pain (7%)

Local: Bruising at injection site (10%), inflammation at injection site (2% to 4%), injection site reaction (4%), swelling at injection site (3%)

Nervous system: Fatigue (males: 10%), pain (5%)

Postmarketing:

Cardiovascular: Thromboembolism

Endocrine & metabolic: Ovary enlargement

Hematologic & oncologic: Ovarian neoplasm

Hypersensitivity: Anaphylaxis, hypersensitivity reaction (including severe hypersensitivity reaction), nonimmune anaphylaxis

Respiratory: Asthma, pulmonary complications (including atelectasis, acute respiratory distress syndrome, exacerbation of asthma)

Miscellaneous: Ovarian torsion

Contraindications

Hypersensitivity to recombinant human follicle-stimulating hormone (FSH) products or any component of the formulation; high levels of FSH indicating primary gonadal failure; sex hormone dependent tumors of the reproductive tract and accessory organs; pituitary or hypothalamus tumors; uncontrolled thyroid, pituitary, or adrenal dysfunction; abnormal uterine bleeding of undetermined origin; ovarian cysts or enlargement of undetermined origin.

Canadian labeling: Additional contraindications (not in US labeling): Presence of any cause for infertility other than anovulation (unless candidate for assisted reproductive technology); breastfeeding; pregnancy.

Warnings/Precautions

Concerns related to adverse effects:

• Hypersensitivity: Serious hypersensitivity reactions including anaphylaxis have been reported; discontinue use for serious reactions and treat appropriately.

• Ovarian enlargement: The lowest effective dose should be used to decrease the risk of abnormal ovarian enlargement. If ovaries are abnormally enlarged on the last day of follitropin alfa treatment, follow current clinical practice to reduce the risk of ovarian hyperstimulation syndrome (OHSS).

• Ovarian hyperstimulation syndrome: OHSS is a rare, exaggerated response to ovulation induction therapy (Corbett 2014; Fiedler 2012). This syndrome may begin within 24 hours of human chorionic gonadotropin treatment but may become most severe 7 to 10 days after therapy (Corbett 2014). Mild/moderate OHSS signs/symptoms may include abdominal distention/discomfort, diarrhea, nausea, vomiting, and mild/moderate enlargement of ovaries/ovarian cysts. Severe OHSS signs/symptoms may include severe abdominal pain, anuria/oliguria, ascites, severe dyspnea, hypotension, hydrothorax, nausea/vomiting (intractable), pleural effusion, rapid weight gain, venous thrombosis, and large ovarian cysts. Decreased CrCl, hemoconcentration, hypoproteinemia, elevated liver enzymes,

elevated WBC, and electrolyte imbalances may also be present (ASRM 2016; Corbett 2014; Fiedler 2012). Treatment is primarily symptomatic and includes fluid and electrolyte management, analgesics, and prevention of thromboembolic complications (ASRM 2016; Shmorgun 2017).

• Ovarian torsion: Has been reported following gonadotropin treatment; may be related to OHSS, prior ovarian torsion, prior or current ovarian cyst, polycystic ovaries, pregnancy, or prior abdominal surgery. Early diagnosis and prompt detorsion may limit the extent of ovarian damage.

• Pulmonary effects: Serious pulmonary conditions (atelectasis, acute respiratory distress syndrome, and exacerbation of asthma) have been reported.

• Thromboembolic events: In association with and separate from OHSS, thromboembolic events have been reported. Risk may be increased in patients with severe obesity, thrombophilia, or a personal or family history of risk factors for thrombosis.

Dosage form specific issues:

• Multiple-dose injection pens: According to the Centers for Disease Control and Prevention, pen-shaped injection devices should never be used for more than one person (even when the needle is changed) because of the risk of infection. The injection device should be clearly labeled with individual patient information to ensure that the correct pen is used (CDC 2012).

Other warnings/precautions:

• Appropriate use: To minimize risks, use only at the lowest effective dose. Monitor ovarian response with transvaginal ultrasound; concurrent measurement of estradiol levels may also be useful.

• Experienced physician: These medications should only be used by physicians who are thoroughly familiar with infertility problems and their management.

• Multiple births: May result from the use of these medications; advise patient of the potential risk of multiple births before starting the treatment.

Dosage Forms Considerations

Gonal-f 450 unit and 1050 unit multi-dose vials are packaged with a diluent (bacteriostatic water for injection in a prefilled syringe) that contains benzyl alcohol.

Dosage Forms: US

Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Solution Pen-injector, Subcutaneous:

Gonal-f RFF Rediject: 300 units/0.48 mL (0.48 mL); 450 units/0.72 mL (0.72 mL); 900 units/1.44 mL (1.44 mL) [contains metacresol]

Solution Reconstituted, Injection:

Gonal-f: 450 units (1 ea); 1050 units (1 ea [DSC]) [contains benzyl alcohol]

Solution Reconstituted, Subcutaneous:

Gonal-f RFF: 75 units (1 ea [DSC])

Generic Equivalent Available: US

No

Pricing: US

Solution (reconstituted) (Gonal-f Injection)

450 unit (per each): $1,738.87

Solution Pen-injector (Gonal-f RFF Rediject Subcutaneous)

300UNT/0.48ML (per 0.48 mL): $1,159.25

450 units (per 0.72 mL): $1,738.87

900UNT/1.44ML (per mL): $2,415.10

Disclaimer: A representative AWP (Average Wholesale Price) price or price range is provided as reference price only. A range is provided when more than one manufacturer's AWP price is available

and uses the low and high price reported by the manufacturers to determine the range. The pricing data should be used for benchmarking purposes only, and as such should not be used alone to set or adjudicate any prices for reimbursement or purchasing functions or considered to be an exact price for a single product and/or manufacturer. Medi-Span expressly disclaims all warranties of any kind or nature, whether express or implied, and assumes no liability with respect to accuracy of price or price range data published in its solutions. In no event shall Medi-Span be liable for special, indirect, incidental, or consequential damages arising from use of price or price range data. Pricing data is updated monthly.

Dosage Forms: Canada

Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Solution Pen-injector, Subcutaneous:

Gonal-f Pen: 300 units/0.5 mL (0.5 mL); 450 units/0.75 mL (0.75 mL); 900 units/1.5 mL (1.5 mL) [contains metacresol]

Solution Reconstituted, Subcutaneous:

Gonal-f: 37.5 units (1 ea); 75 units ([DSC]); 150 units (1 ea)

Administration: Adult

SubQ: Administer SubQ in the abdomen, upper arm, or upper leg. Contents of multidose vials (Gonal-f or Gonal-f RFF) should be administered using the calibrated syringes provided by the manufacturer. Do not shake solution; allow any bubbles to settle prior to administration. Allow Gonal-f RFF Rediject to warm to room temperature for at least 30 minutes prior to administration to avoid discomfort from cold injection. Do not mix other medications inside of the Gonal-f RFF Rediject device.

Use: Labeled Indications

Multifollicular development during assisted reproductive technology: To stimulate the development of multiple follicles with assisted reproductive technology.

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

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

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program)

There are no known significant interactions.

Reproductive Considerations

When needed for ovulation induction or as part of an assisted reproductive technology cycle, should only be used by providers with expertise in managing infertility; exclude pregnancy prior to use. Multiple births may result from use of this medication; a low dose step-up protocol is recommended to increase the chance of monofollicular development. Gonadotropins are an alternative option for ovulation induction in patients with polycystic ovary syndrome with anovulatory infertility and no other infertility factors (Teede 2023).

When used for the induction of spermatogenesis, exclude primary testicular failure and normalize testosterone levels prior to treatment. Evaluate fertility status of the female partner prior to induction of spermatogenesis when treating males with hypogonadotropic hypogonadism (AACE [Petak 2002]).

Pregnancy Considerations

Follitropin alfa is used in the management of patients who wish to become pregnant; use is not indicated for patients who are already pregnant.

Ectopic pregnancy, congenital abnormalities, spontaneous abortion, and multiple births have been reported. The incidence of congenital abnormality may be slightly higher after in vitro fertilization or intracytoplasmic sperm injection than with spontaneous conception. The higher incidence of congenital abnormalities and spontaneous abortion may be related to parenteral characteristics (maternal age, sperm characteristics) and not specifically associated with gonadotropin use.

Breastfeeding Considerations

It is not known if follitropin alfa is present in breast milk.

Prolactin secretion during lactation may lead to inadequate ovarian stimulation; therefore, breastfeeding is not recommended by the manufacturer.

Monitoring Parameters

Monitor follicular growth by transvaginal ultrasound to determine adequate ovarian response and timing of human chorionic gonadotropin (hCG) administration. Concurrent measurement of estradiol levels may also be useful.

Monitor for signs and symptoms of ovarian hyperstimulation syndrome (OHSS) for at least 2 weeks following hCG administration. Initial symptoms of moderate to severe OHSS may include a sensation of bloating, abdominal pain, rapid weight gain, and decreased urine output (Shmorgun 2017).

OHSS: Monitoring of hospitalized patients should include albumin, degree of ascites, cardiorespiratory status, electrolytes, fluid balance, hematocrit, hemoglobin, hydration, serum creatinine, urine output, urine-specific gravity, signs of thromboembolism, vital signs, weight (daily or as necessary), and liver enzymes (weekly) (Shmorgun 2017).

Spermatogenesis: Monitor serum testosterone levels, sperm count.

Mechanism of Action

Follitropin alfa is a human FSH preparation 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.

Pharmacokinetics (Adult Data Unless Noted)

Onset of action: Peak effect:

Spermatogenesis, median: 6.8-12.4 months (range 2.7-18.1 months)

Follicle development: Within cycle

Absorption: SubQ: Absorption rate is slower than the elimination rate

Distribution: Mean V_d: 0.7 L with *in vitro* fertilization/embryo transfer patients

Bioavailability: ~66% to 76% in healthy female volunteers; 10% in *in vitro* fertilization/embryo transfer patients

Half-life elimination:

SubQ: 24-53 hours in healthy female volunteers; 32-41 hours in healthy male volunteers

Time to peak: In healthy volunteers:

Females: SubQ: 8-16 hours

Males: SubQ: 11-20 hours

Excretion: Clearance: IV: 0.6 L/hour in healthy female volunteers

Brand Names: International

International Brand Names by Country

For country code abbreviations (show table)

(AE) United Arab Emirates: Bemfola | Gonal f; (AR) Argentina: Gonal f; (AT) Austria: Bemfola | Gonal f; (AU) Australia: Bemfola | Gonal f; (BE) Belgium: Bemfola | Gonal f; (BG) Bulgaria: Bemfola | Gonal f; (BR) Brazil: Gonal f; (CH) Switzerland: Gonal f; (CI) Côte d'Ivoire: Gonal f; (CL) Chile: Bemfola; (CN) China: Gonal f; (CO) Colombia: Bemfola | Gonal f; (CR) Costa

Rica: Gonal f; (CZ) Czech Republic: Bemfola | Gonal f; (DE) Germany: Bemfola | Gonal f | Gonal-f; (DO) Dominican Republic: Gonal f; (EC) Ecuador: Bemfola | Gonal f; (EE) Estonia: Bemfola | Gonal f; (EG) Egypt: Gonal f | Gonapure; (ES) Spain: Bemfola | Gonal f; (FI) Finland: Bemfola | Gonal f; (FR) France: Bemfola | Gonal f; (GB) United Kingdom: Bemfola | Gonal f; (GR) Greece: Bemfola | Gonal f; (HK) Hong Kong: Gonal f; (HR) Croatia: Gonal f; (HU) Hungary: Bemfola | Gonal f; (ID) Indonesia: Gonal f; (IE) Ireland: Bemfola | Gonal f; (IL) Israel: Gonal f; (IN) India: Folisurge | Gonal f; (IQ) Iraq: Cinnal f; (IT) Italy: Bemfola | Gonal f; (JO) Jordan: Gonal f; (JP) Japan: Gonalef; (KE) Kenya: Folisurge | Gonal f; (KR) Korea, Republic of: Follitrope | Gonal f; (KW) Kuwait: Bemfola | Gonal f; (LB) Lebanon: Gonadopin | Gonal f; (LI) Liechtenstein: Bemfola; (LT) Lithuania: Bemfola | Gonal f; (LU) Luxembourg: Bemfola | Gonal f; (LV) Latvia: Bemfola | Gonal f; (MA) Morocco: Gonal f; (MX) Mexico: Corneumon | Gonal f | Zimfola; (MY) Malaysia: Gonal f; (NL) Netherlands: Bemfola | Gonal f; (NO) Norway: Bemfola | Gonal f; (NZ) New Zealand: Bemfola | Gonal f; (PA) Panama: Gonal f; (PE) Peru: Bemfola | Gonal f; (PH) Philippines: Gonal f; (PK) Pakistan: Gonadopin | Gonal f; (PL) Poland: Bemfola | Gonal f; (PT) Portugal: Bemfola | Gonal f; (QA) Qatar: Gonal-F; (RO) Romania: Bemfola | Gonal f; (RU) Russian Federation: Follitrop | Gonal f | Gonal-e | Primapur; (SA) Saudi Arabia: Gonal f; (SE) Sweden: Bemfola | Gonal f; (SG) Singapore: Gonal f; (SI) Slovenia: Bemfola | Gonal f; (SK) Slovakia: Bemfola | Gonal f; (TH) Thailand: Follitrope | Gonal f; (TN) Tunisia: Gonal f; (TR) Turkey: Gonal f; (TW) Taiwan: Gonal f; (UA) Ukraine: Bemfola | Gonal f; (UG) Uganda: Folisurge | Gonal f; (UY) Uruguay: Gonal f; (VE) Venezuela, Bolivarian Republic of: Gonal f; (ZA) South Africa: Gonal f

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