

## Clinical Policy: Infertility and Fertility Preservation

Reference Number: CP.PHAR.131

Effective Date: 11.16.16

Last Review Date: 11.21

Line of Business: Commercial\*, HIM\*, Medicaid\*

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

- Gonadotropins requiring prior authorization:
  - Menotropins (Menopur<sup>®</sup>); follitropin alfa, recombinant (Gonal-f<sup>®</sup> multi-dose\*, Gonal-f<sup>®</sup> RFF, Gonal-f<sup>®</sup> RFF Redi-ject); follitropin beta, recombinant (Follistim<sup>®</sup> AQ); urofollitropin (Bravelle<sup>®</sup>); choriogonadotropin alfa (Ovidrel<sup>®</sup>); human chorionic gonadotropin (hCG; generic, Novarel<sup>®</sup>\*, Pregnyl<sup>®</sup>).
- Gonadotropin-releasing hormone (GnRH) antagonists requiring prior authorization:
  - Ganirelix acetate; Cetrorelix (Cetrotide<sup>®</sup>).

*\*Sections I.A., I.B., I.C., II.A., II.B.: Infertility/Fertility Preservation*

*All lines of business: pharmacy benefit coverage is required.*

*HIM line of business - pharmacy benefit coverage restrictions by state:*

*States without pharmacy benefit restriction: AR, FL, IL, IN, KS, NC, NV, SC, TN, WA*

*(Policy may be used for formulary and non-formulary drugs.)*

*States with pharmacy benefit restriction: AZ, GA, MO, MS, NH, OH, PA, TX*

*(Policy may be used for formulary drugs only; non-formulary drugs are a pharmacy benefit exclusion.)*

### FDA Approved Indication(s)

Drug Name	Drugs		Indications, Female		Indications, Male	
	Brand Name	Drug Class	OI	ART	HH	Prepubertal Cryptorchidism
Menotropin	Menopur	Gonadotropin (hMG - FSH and LH)	x	x		
Follitropin alfa, recombinant	Gonal-f	Gonadotropin (FSH)	x	x	x	
Follitropin alfa, recombinant	Gonal-f RFF	Gonadotropin (FHS)	x	x		
Follitropin alfa, recombinant	Gonal-f RFF Redi-ject	Gonadotropin (FSH)	x	x		
Follitropin beta, recombinant	Follistim-AQ	Gonadotropin (FSH)	x	x	x	
Urofollitropin	Bravelle	Gonadotropin (FSH)	x	x		
Ganirelix acetate	N/A	GnRH antagonist	x	x		
Cetrorelix	Cetrotide	GnRH antagonist	x	x		
Choriogonadotropin alfa	Ovidrel	Gonadotropin (hCG)	x	x		
Human chorionic gonadotropin	Novarel	Gonadotropin (hCG)	x	x	x	x
Human chorionic gonadotropin	Pregnyl	Gonadotropin (hCG)	x	x	x	x

*Abbreviations: ART: assisted reproductive technology; GnRH: gonadotropin-releasing hormone; HH: hypogonadotropic hypogonadism; hCG: human chorionic gonadotropin (produced by the placenta after implantation); hMG: human menopausal gonadotropin (combination of LH and FSH); OI: ovulation induction*

- Menopur is indicated for:
  - Development of multiple follicles and pregnancy in ovulatory women as part of an assisted reproductive technology (ART) cycle.
  
- Gonal-f is indicated for:
  - Induction of ovulation and pregnancy in the anovulatory infertile patient in whom the cause of infertility is functional and not due to primary ovarian failure (known as primary ovarian insufficiency; POI).
  - Development of multiple follicles in the ovulatory patient participating in an ART program.
  - 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 (i.e. primary hypogonadism).
  
- Gonal-F RFF and Gonal-f RFF Redi-ject are indicated for:
  - Induction of ovulation and pregnancy in oligo-anovulatory women in whom the cause of infertility is functional and not due to POI.
  - Development of multiple follicles in ovulatory women as part of an ART cycle/program.
  
- Follistim AQ is indicated for:
  - Induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not due to POI.
  - Pregnancy in normal ovulatory women undergoing controlled ovarian stimulation as part of an in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycle [ART cycle].
  - Induction of spermatogenesis in men with primary and secondary HH in whom the cause of infertility is not due to primary testicular failure.
  
- Bravelle is indicated for:
  - Induction of ovulation in women who have previously received pituitary suppression.
  - Development of multiple follicles as part of an ART cycle in ovulatory women who have previously received pituitary suppression.
  
- Ganirelix is indicated for:
  - Inhibition of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian hyperstimulation (COH).
  
- Cetrotide is indicated for:
  - The inhibition of premature LH surges in women undergoing COH.

- Ovidrel is indicated for:
  - Induction of final follicular maturation and early luteinization in infertile women who have undergone pituitary desensitization and who have been appropriately pretreated with follicle-stimulating hormones (FSH) as part of an ART program such as IVF and embryo transfer.
  - Induction of ovulation and pregnancy in anovulatory infertile patients in whom the cause of infertility is functional and not due to POI.
- Novarel and Pregnyl are indicated for:
  - Prepubertal cryptorchidism not due to anatomic obstruction.
  - Selected cases of HH 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 POI, and who has been appropriately pretreated with human menopausal gonadotropins.

### **Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Menopur, Gonal-f, Gonal-f RFF, Gonal f RFF Redi-ject, Follistim-AQ, Bravelle, ganirelix acetate, Cetrotide, Ovidrel, Novarel, and Pregnyl are **medically necessary** when the following criteria are met:

### **I. Initial Approval Criteria**

#### **A. Infertility, Female (must meet all):**

1. Member must have infertility/fertility preservation coverage (optional pharmacy benefit);
2. Diagnosis of infertility;
3. Age  $\geq$  18 years;
4. Prescribed by or in consultation with a reproductive endocrinologist;
5. The requested drug(s) is for one of the following (a or b):
  - a. OI, and both of the following (i and ii):
    - i. Member has been diagnosed with an ovulatory disorder;
    - ii. If the ovulatory disorder is secondary to hyperprolactinemia, failure of dopamine agonist treatment, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
  - b. ART, and both of the following (i and ii):
    - i. If infertility is secondary to an ovulatory disorder, member has failed OI or is not a candidate for OI (e.g., member has been diagnosed with tubal blockage, uterine cavity abnormality, diminished ovarian reserve; member's partner has been diagnosed with severe male factor infertility).
    - ii. If unexplained infertility, failure of at least 3 cycles of clomiphene citrate or letrozole (*see Appendix B*) combined with intrauterine insemination, unless contraindicated or clinically significant adverse effects are experienced;
6. Member does not have POI.

**Approval duration: 30 days or up to specified trial duration if available**

**B. Fertility Preservation, Female (must meet all):**

1. Member must have infertility/fertility preservation coverage (optional pharmacy benefit);
2. Request is for fertility preservation (embryo or oocyte cryopreservation) secondary to planned gonadotoxic therapy or gonadectomy;
3. Member meets one of the following (a or b):
  - a. Age  $\geq$  18 years and (i and ii):
    - i. Member has received fertility preservation counseling (documented);
    - ii. Member has executed an informed consent;
  - b. Of reproductive age (peri/postpubertal - off-label use) and member meets both of the following (i and ii):
    - i. All consent/assent signees have received fertility preservation counseling (documented);
    - ii. Parent(s)/guardian(s) and member have executed informed consents and assents respectively;
4. Prescribed by or in consultation with a reproductive endocrinologist;
5. Member does not have POI.

**Approval duration: 30 days or up to specified trial duration if available**

**C. Infertility, Male (must meet all):**

1. Member must have infertility/fertility preservation coverage (optional pharmacy benefit);
2. Request is for Gonal-f, Follistim-AQ, Novarel or Pregnyl;
3. Diagnosis of infertility due to HH;
4. Prescribed by or in consultation with a reproductive endocrinologist or urologist;
5. Age  $\geq$  18 years;
6. Product(s) are requested in one of the following ways (a or b):
  - a. Novarel or Pregnyl as single-agent therapy to increase testosterone to the normal range (400 to 800 ng/dL);
  - b. Gonal-f or Follistim-AQ in combination with either Novarel or Pregnyl to induce spermatogenesis once serum testosterone is within the normal range;
7. Testosterone therapy is not prescribed concomitantly;
8. Member does not have primary testicular failure.

**Approval duration: 6 months**

**D. Prepubertal Cryptorchidism (undescended testes) (must meet all):**

1. Request is for Novarel or Pregnyl;
2. Diagnosis of prepubertal cryptorchidism;
3. Prescribed by or in consultation with a pediatric specialist in one of the following areas: endocrinology, urology, genetics, surgery;
4. Age  $\leq$  9 years;
5. One of the following (a or b):
  - a. Member is not a candidate for corrective surgery;
  - b. hCG will be used in coordination with surgery.

**Approval duration: 3 months**

**E. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Infertility and Fertility Preservation, Female (must meet all):**

1. Member must have infertility/fertility preservation coverage (optional pharmacy benefit);
2. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
3. Member is responding positively to therapy;
4. Request is for an OI or ART cycle currently underway.

**Approval duration: 30 days or up to specified trial duration if available**

*(For additional reproductive attempts please refer to the initial criteria.)*

**B. Infertility, Male (must meet all):**

1. Member must have infertility/fertility preservation coverage (optional pharmacy benefit);
2. Request is for Gonal-f, Follistim-AQ, Novarel or Pregnyl;
3. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
4. Member is responding positively to therapy;
5. If request is for Novarel or Pregnyl (a or b):
  - a. Pregnancy has not yet been achieved;
  - b. Pregnancy has been achieved, and another pregnancy is being considered;
6. If request is for Gonal-f or Follistim-AQ (a and b):
  - a. Prescribed in combination with Novarel or Pregnyl;
  - b. Current reproductive attempt has not yet achieved pregnancy (*if pregnancy has been achieved, refer to initial criteria for subsequent Gonal-F or Follistim-AQ requests*).

**Approval duration: 6 months**

**C. Prepubertal Cryptorchidism (undescended testes) (must meet all):**

1. Request is for Novarel or Pregnyl;
2. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
3. Member is responding positively to therapy.

**Approval duration: 3 months**

*(Treatment for this indication should not exceed a total of 3 months.)*

**D. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

- Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;
- B. Treatment of obesity.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

ART: assisted reproductive technology	hMG: human menopausal gonadotropin
ASCO: American Society of Clinical Oncology	ICSI: intracytoplasmic sperm injection
AYA: adolescent and young adult	IVF: in vitro fertilization
COH: controlled ovarian hyperstimulation	LH: luteinizing hormone
FDA: Food and Drug Administration	NCCN: National Comprehensive Cancer Network
FSH: follicle-stimulating hormone	POI: primary ovarian insufficiency, primary ovarian failure
hCG: human chorionic gonadotropin	
HH: hypogonadotropic hypogonadism	

*Appendix B: Therapeutic Alternatives*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
cabergoline	<b>Hyperprolactinemia (labeled):</b> Initial: 0.25 mg PO twice weekly; may increase by 0.25 mg twice weekly (no more often than every 4 weeks) up to a maximum of 1 mg twice weekly according to the patient’s serum prolactin level.	1 mg twice weekly
bromocriptine (Parlodel <sup>®</sup> )	<b>Hyperprolactinemia (labeled):</b> Initial: 1.25 to 2.5 mg PO daily; may be increased by 2.5 mg daily as tolerated every 2 to 7 days until optimal response (range: 2.5 to 15 mg/day).	15 mg/day
clomiphene citrate	<b>Treatment of ovulatory dysfunction in women desiring pregnancy (labeled):</b> Initial: 50 mg PO once daily for 5 days. Begin on or about the fifth day of cycle if progestin-induced bleeding is scheduled or spontaneous uterine bleeding occurs prior to therapy. Therapy may be initiated at any time in patients with no recent uterine bleeding. Subsequent doses may be increased to 100 mg once daily for 5 days only if ovulation does not occur at the	150 mg/day per expert review  Durations: 5 to 7 days per expert review

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	initial dose. If needed, the 5-day cycle may be repeated as early as 30 days after the previous one. Exclude the presence of pregnancy. The lowest effective dose should be used. Maximum dose: 100 mg once daily for 5 days for up to 6 cycles.	
letrozole (Femara)	<b>Infertility - ovulation stimulation in anovulatory females (off-label):</b> Initial: 2.5 mg PO once daily for 5 days, starting on day 3, 4, or 5 following menses or progestin induced bleed; may increase to 5 mg/day for 5 days in subsequent cycles if ovulation does not occur.	7.5 mg/day  Durations: 5 to 7 days per expert review

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): pregnancy; for additional contraindications, please refer to the product package inserts
- Boxed warning(s): none reported

*Appendix D: General Information*

- Female Infertility
  - OI refers to pharmacological treatment of anovulation with fertility medications to induce ovulation. OI is used in conjunction with intercourse or intrauterine insemination.
  - ART procedures include but are not limited to 1) in vitro fertilization (IVF), 2) intracytoplasmic sperm injection (ICSI), and 3) assisted reproductive hatching. IVF is the most common type of ART. An IVF interval generally is two weeks in length and includes 1) ovarian stimulation with fertility medications to induce development of multiple ovarian follicles/oocytes (i.e., COH), 2) aspiration and fertilization of oocyte(s) in the laboratory setting ("in vitro"), and then 3) transfer of the embryo(s) into the uterine cavity.
- Male Infertility
  - Male infertility secondary to HH is amendable to treatment with fertility drugs. Once reproductive attempts are complete, transition to testosterone replacement therapy is an option if needed for long-term treatment.
- Prepubertal Males: cryptorchidism
  - Corrective surgery for cryptorchidism (orchidopexy) is considered first-line therapy. Surgery and/or gonadotropin therapy typically would be completed by 24 months of age to avoid potential negative fertility and cancer risk sequelae.
- Fertility Medications
  - Fertility medications are used together in coordinated individualized regimens. The regimens in Section V: Dosage and Administration are presented as general guidelines drawn from FDA labels and expert input. Care should be taken not to interrupt a reproductive attempt currently underway.

- Fertility Preservation
  - For females, ART may be preferable to OI in cases of fertility preservation (embryo or oocyte cryopreservation) secondary to planned gonadotoxic therapy or gonadectomy.  
*\*Gonadotoxic therapies or gonadectomy may be undertaken as treatment for cancer as well as benign autoimmune or hematologic conditions such as systemic lupus erythematosus, multiple sclerosis, autoimmune thrombocytopenia, rheumatoid arthritis, Wegener's granulomatosis and Behçet's disease.*
  - For males, various fertility preservation strategies are available but do not typically involve the medications central to the present policy.\*  
*\*See Practice Committee of the American Society for Reproductive Medicine. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril, 2019;112:1022-33, for more information in this regard.*
  - The American Society of Clinical Oncology (ASCO, 2018), American Society for Reproductive Medicine (ASRM, 2018/2019), Society for Assisted Reproductive Technology (SART)/ASRM (2007), and National Comprehensive Cancer Network (NCCN, 2020) provide guidance for fertility preservation prior to gonadotoxic medical treatment for patients of reproductive age as well as prepubertal patients. Selected ASCO recommendations are listed below:
    - Adult women
      - Recommendation 3.1. Embryo cryopreservation is an established fertility preservation method, and it has routinely been used for storing surplus embryos after in vitro fertilization.
      - Recommendation 3.2. Cryopreservation of unfertilized oocytes is an option, and may be especially well suited to women who do not have a male partner, do not wish to use donor sperm, or have religious or ethical objections to embryo freezing.
      - Recommendation 3.5 (updated). There is conflicting evidence to recommend GnRH agonists and other means of ovarian suppression for fertility preservation. The Panel recognizes that, when proven fertility preservation methods such as oocyte, embryo, or ovarian tissue cryopreservation are not feasible, and in the setting of young women with breast cancer, GnRH agonists may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency. However, GnRH agonists should not be used in place of proven fertility preservation methods.
      - Recommendation 3.6 (updated). Ovarian tissue cryopreservation for the purpose of future transplantation does not require ovarian stimulation and can be performed immediately. In addition, it does not require sexual maturity and hence may be the only method available in children. Finally, this method may also restore global ovarian function. However, it should be noted further investigation is needed to confirm whether it is safe in patients with leukemias.
    - Adult men
      - Recommendation 2.1. Sperm cryopreservation is effective, and health care providers should discuss sperm banking with postpubertal males receiving cancer treatment.
      - Recommendation 2.2. Hormonal gonadoprotection: Hormonal therapy in men is not successful in preserving fertility. It is not recommended.

- Recommendation 2.3. Other methods, such as testicular tissue cryopreservation and reimplantation or grafting of human testicular tissue, should be performed only as part of clinical trials or approved experimental protocols.
- Special Considerations: Children:
  - Recommendation 5.1. Suggest established methods of fertility preservation (eg, semen or oocyte cryopreservation) for postpubertal children, with patient assent and parent or guardian consent. For prepubertal children, the only fertility preservation options are ovarian and testicular cryopreservation, which are investigational.

**V. Dosage and Administration**

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Maximum Dose</b>
<i>Infertility, Female</i>		
<b><i>Follicle stimulating agents</i></b>		
Menopur (menotropins)	Up to 450 IU SC per day	<ul style="list-style-type: none"> <li>• Doses are individualized.</li> <li>• Duration typically would not exceed one month per reproductive attempt; there may be exceptions.</li> </ul>
Bravelle (urofollitropin)	Up to 450 IU IM or SC per day	
Gonal-f, Gonal-f RFF, Gonal-f RFF Redi-ject (follitropin alpha, recombinant)	Up to 450 SC IU per day	
Follistim-AQ (follitropin beta, recombinant)	Up to 500 IU SC per day	
<b><i>Pituitary suppression agents</i></b>		
Ganirelix acetate	250 mcg SC per day	<ul style="list-style-type: none"> <li>• Doses and durations as noted above.</li> </ul>
Cetrotide (cetorelix)	0.25 mg SC per day	
<b><i>Ovulatory “trigger” agents</i></b>		
Ovidrel (choriogonadotropin alfa; recombinant hCG)	250 mcg SC once	<ul style="list-style-type: none"> <li>• Doses are individualized.</li> <li>• An agent from this category is typically given once per reproductive attempt.</li> </ul>
hCG (Novarel, Pregnyl; urinary hCG)	5,000 to 10,000 USP Units IM once	
<i>Infertility, Male: Due to hypogonadotropic hypogonadism</i>		
Novarel, Pregnyl (hCG)	Dosing may range from 500 to 4,000 USP Units IM on BIW/TIW schedules for up to 12 months to achieve/maintain normal testosterone levels.	Regimens and maximum doses/durations vary; single agent hCG therapy followed by follitropin/hCG combination therapy may extend up to 24 months or at times longer.
Gonal-f (follitropin alfa, recombinant)	150 to 300 IU SC TIW up to 18 months in combination with hCG at the dose required to maintain normal testosterone levels.	
Follistim-AQ (follitropin beta, recombinant)	150 to 225 IU SC on BIW/TIW schedules up to 12 months in	

Drug Name	Dosing Regimen	Maximum Dose
	combination with hCG at the dose required to maintain normal testosterone levels.	
<i>Prepubertal Cryptorchidism</i>		
Novarel, Pregnyl (hCG)	Dosing may range from 500 to 5,000 IM USP Units with varying schedules (e.g., every 2nd/3rd day, TIW) with prn repeat courses up to 3 months.	Regimens and maximum doses vary. Maximum duration: 3 months.

## VI. Product Availability

Drug Name	Availability
Menopur	Injection: 75 U FSH and 75 U LH/vial
Bravelle	Injection: 75 U FSH/vial
Gonal-F multi dose vial	Injection: 450 U/vial; 1,050 U/vial
Gonal-F RFF single dose vial:	Injection: 75 U/vial
Gonal-F RFF Redi-ject	Prefilled auto-injection device: 300 U/0.5 mL, 450 U/0.75 mL, 900 U/1.5 mL
Follistim-AQ	Injection cartridge: 150 U, 300 U, 600 U, 900 U
Ganirelix acetate	Prefilled syringe: 250 mcg/0.5 mL
Cetrotide	Injection: 0.25 mg/vial
Ovidrel	Prefilled syringe: 250 mcg/0.5 mL
Novarel	Injection: 5,000 U/vial, 10,000 U/vial
Pregnyl	Injection: 10,000 U/vial
Chorionic gonadotropin (hCG)	Injection: 10,000 U/vial

## VII. References

1. Menopur Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; May 2018. Available at <http://www.ferringusa.com/wp-content/uploads/2018/03/Menopur-PI-Rev.-08.2017.pdf>. Accessed July 21, 2021.
2. Bravelle Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; February 2014. Available at <http://www.ferringusa.com/wp-content/uploads/2016/02/BravellePI-2.2014.pdf>. Accessed July 21, 2021.
3. Gonal-f Multi-Dose Prescribing Information. Rockland, MA: EMD Serono; December 2020. Available at <https://www.emdserono.com/us-en/expertise/fertility.html>. Accessed July 21, 2021.
4. Gonal-f RFF Prescribing Information. Rockland, MA: EMD Serono; December 2020. Available at <https://www.emdserono.com/us-en/expertise/fertility.html>. Accessed July 21, 2021.
5. Gonal-f RFF Redi-ject Prescribing Information. Rockland, MA: EMD Serono; February 2020. Available at <https://www.emdserono.com/us-en/expertise/fertility.html>. Accessed July 21, 2021.

6. Follistim AQ Prescribing Information. Ravensburg, Germany: Vetter Pharma-Fertigung GmbH and Co. KG; June 2020. Available at [https://www.merck.com/product/usa/pi\\_circulars/f/follistim\\_aq\\_cartridge/follistim\\_cartridge\\_pi.pdf](https://www.merck.com/product/usa/pi_circulars/f/follistim_aq_cartridge/follistim_cartridge_pi.pdf). Accessed July 21, 2021.
7. Ganirelix acetate Prescribing Information. Ravensburg, Germany: Vetter Pharma-Fertigung GmbH and Co. KG; June 2021. Available at [https://www.merck.com/product/usa/pi\\_circulars/g/ganirelix/ganirelix\\_pi.pdf](https://www.merck.com/product/usa/pi_circulars/g/ganirelix/ganirelix_pi.pdf). Accessed July 21, 2021.
8. Cetrotide Prescribing Information. Rockland, MA: EMD Serono; May 2018. Available at <https://www.emdserono.com/us-en/expertise/fertility.html>. Accessed July 21, 2021.
9. Ovidrel Prescribing Information. Rockland, MA: EMD Serono; June 2018. Available at <https://www.emdserono.com/us-en/expertise/fertility.html>. Accessed July 21, 2021.
10. Novarel Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; May 2018. Available at <http://www.ferringusa.com/wp-content/uploads/2017/01/NovarelPI-9.2016.pdf>. Accessed July 21, 2021.
11. Pregnyl Prescribing Information. Halle, Germany: Baxter Oncology GmbH; January 2015. Available at [https://www.merck.com/product/usa/pi\\_circulars/p/pregnyl/pregnyl\\_pi.pdf](https://www.merck.com/product/usa/pi_circulars/p/pregnyl/pregnyl_pi.pdf). Accessed July 21, 2021.

Infertility Definition

12. Practice Committee of the American Society of Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. *Fertil Steril*. June 2020; 113: 533-5.

Infertility, Female

13. Practice Committee of the American Society of Reproductive Medicine. Diagnostic evaluation of the infertile female: a committee opinion. *Fertil Steril*. June 2015; 103(6): e44-e50.
14. Practice Committee of American Society for Reproductive Medicine in collaboration with Society for Reproductive Endocrinology and Infertility. Optimizing natural fertility. *Fertil Steril*. November 2017; 107: 52-8.
15. Practice Committee of the American Society of Reproductive Medicine. Use of exogenous gonadotropins for ovulation induction in anovulatory women: a committee opinion. *Fertil Steril*, 2019;90:S712.
16. Practice Committee of the American Society for Reproductive Medicine. Evidence-based treatments for couples with unexplained infertility: a guideline. *Fertil Steril*. February 2020; 113(2): 305-322.

Infertility, Male

17. Practice Committee of American Society for Reproductive Medicine. Management of nonobstructive azoospermia: a committee opinion. *Fertil Steril*. December 2018; 110(7): 0015-0282.
18. Mulhall JP, Trost LW, Brannigan RE et al. Evaluation and management of testosterone deficiency: American Urological Association guideline. *J Urol*. 2018 Aug;200(2):423-432. doi: 10.1016/j.juro.2018.03.115. Epub 2018 Mar 28.
19. Practice Committee of the American Society of Reproductive Medicine. Diagnostic evaluation of the infertile male: a committee opinion. *Fertil Steril*. Mar 2015; 103(3): e18-25.

20. Boehm U, Bouloux PM, Dattani MT, et al. European Consensus Statement on congenital hypogonadotropic hypogonadism pathogenesis, diagnosis and treatment Nat. Rev. Endocrinol. 11, 547564 (2015); published online 21 July 2015; doi:10.1038/nrendo.2015.112
21. Petak SM, Nankin HR, Spark RF et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients - 2002 update. Endocrine Practice. November/December 2002; 8(6): 439-56.

*Prepubertal Cryptorchidism*

22. Kolon TF, Herndon CDA, Baker LA, et al. Evaluation and treatment of cryptorchidism: AUA guideline. J Urol. 2014;192(2):337. Epub 2014 May 20.
23. Braga LH, Lorenzo AJ, Romao RLP. Canadian Urological Association-Pediatric Urologists of Canada (CUA-PUC) guideline for the diagnosis, management, and followup of cryptorchidism. Can Urol Assoc J 2017;11(7):E251-60. <http://dx.doi.org/10.5489/cuaj.4585>

*Fertility Preservation*

24. Oktay K, Harvey BE, Partridge AH, et al. Fertility preservation for patients with cancer: American Society of Clinical Oncology (ASCO) clinical practice guideline update. Journal of Clinical Oncology. July 1, 2018; 36(19): 1994-2001.
25. National Comprehensive Cancer Network (NCCN). Adolescent and young adult (AYA) oncology. Version 1.2020. Accessed August 3, 2020.
26. Practice Committee of the American Society for Reproductive Medicine. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril, 2019;112:1022-33.
27. Practice Committee of the American Society for Reproductive Medicine. Fertility preservation and reproduction in patients facing gonadotoxic therapies: an ethics opinion. Fertil Steril, 2018;110:380-6.
28. Practice Committee of the Society for Assisted Reproductive Technology, Practice Committee of the American Society for Reproductive Medicine. Essential elements of informed consent for elective oocyte cryopreservation: a Practice Committee opinion. Fertil Steril. 2007;88(6):1495. Epub 2007 Oct 17.
29. Fertility preservation in patients with non-oncological conditions. Reproductive BioMedicine Online, Vol 16. No 6. 2008 792-800.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<b>HCPCS Codes</b>	<b>Description</b>
S0122	Injection, menotropins, 75 iu
S0126	Injection, follitropin alfa, 75 iu
S0128	Injection, follitropin beta, 75 iu
J3355	Injection, urofollitropin, 75 iu
S0132	Injection, ganirelix acetate, 250 mcg
J0725	Injection, chorionic gonadotropin, per 1,000 usp units

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: policy adapted from previously approved CP.CPA.26 and HIM.PA.148 policies; HIM-Medical Benefit and Medicaid lines of business added; two additional products added - Gonal-f and Gonal-f RFF Redi-ject; criteria updated and organized around three criteria sets for female infertility (includes fertility preservation), male fertility, and prepubertal cryptorchidism; policy name changed from Infertility Therapy to Infertility and Fertility Preservation; references reviewed and updated.	08.21.18	11.18
4Q 2019 annual review: HIM-MB added; HIM pharmacy nonformulary status added for two products; references reviewed and updated.	09.03.19	11.19
HIM line of business applied to all agents; infertility/fertility preservation benefit exclusion added for HIM line of business except for HIM Illinois; infertility/fertility preservation pharmacy benefit requirement added for all lines of business.	05.12.20	08.20
4Q 2020 annual review: step therapies added to OI and ART; 150 unit cartridge added to Follistim-AQ; exclusion added for use of policy drugs as treatment for obesity; general information appendix and references reviewed and updated.	09.01.20	11.20
4Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	07.21.21	11.21

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene<sup>®</sup> and Centene Corporation<sup>®</sup> are registered trademarks exclusively owned by Centene Corporation.