Clinical Policy: Infertility and Fertility Preservation

Reference Number: CP.PHAR.131
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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 are: menotropins (Menopur®); follitropin alfa, recombinant (Gonal-f® multi-dose*, Gonal-f® RFF, Gonal-f® RFF Redi-ject); follitropin beta, recombinant (Follistim® AQ); choriogonadotropin alfa (Ovidrel®); human chorionic gonadotropin (hCG; generic, Pregnyl®).

Gonadotropin-releasing hormone (GnRH) antagonists requiring prior authorization are: ganirelix acetate; Cetrorelix (Cetrotide®).

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**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

- ***AR**: In vitro fertilization are covered when: 1) The patient is the policyholder or the spouse of the policyholder and a covered dependent member under the policy, and the member's oocytes are fertilized with the sperm of the patient's spouse, and the patient and the patient's spouse have a history of unexplained infertility of at least two years' duration; OR 2) The infertility is associated with one or more of the following medical conditions: endometriosis; exposure in utero to diethylstilbestrol, commonly known as DES; Blockage of or removal of one or both fallopian tubes (lateral or bilateral salpingectomy) not a result of voluntary sterilization; or abnormal male factors contributing to the infertility.*
- ***AZ**: Infertility - limited to diagnostic rendered for infertility evaluation; Fertility Preservation - medically necessary services and supplies for standard fertility preservation treatments are covered when a cancer treatment may directly or indirectly cause iatrogenic infertility. Iatrogenic infertility is infertility that is caused by a medical intervention, including reactions from prescribed drugs or from medical or surgical procedures that may be provided for cancer treatment.*
- ***CA**: Fertility Preservation – covers medically necessary services and supplies for established fertility preservation treatments in connection with iatrogenic Infertility; Infertility - with the exception of covered fertility preservation services, services or supplies that are intended to impregnate a woman are not covered. Excluded procedures include, but are not limited to:*
  - *Conception by medical procedures, such as artificial insemination, in-vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), or any process that involves harvesting, transplanting, or manipulating a human ovum. Also not covered are services and supplies (including injections and injectable medications) which prepare the covered person to receive these services;*
  - *Services and supplies for the purpose of diagnosing the cause of infertility.*
- ***DE:** Fertility/Infertility Preservation - For individuals who qualify under Delaware law, covered services include fertility care services, including in vitro fertilization services, identified in 18 Del. C. § 3342 for individuals who suffer from a disease or condition that results in the inability to procreate or to carry a pregnancy to live birth and standard fertility preservation services for individuals who must undergo medically necessary treatment that may cause iatrogenic infertility. Experimental fertility care services, monetary payments to gestational carriers or surrogates, and reversals of voluntary sterilization are not covered services.*
- ***GA:** Chapter 24 of Title 33 of the Official Code of Georgia:"Every health benefit policy renewed or issued after January 1, 2026, shall include coverage for expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility in any covered person.*

Such coverage shall include evaluation expenses, laboratory assessments, medications, and treatments associated with standard fertility preservation services, including storage of gametes for up to one year."

- ***IL:*** *Fertility Preservation Services – Coverage for medically necessary expenses for standard fertility preservation services when a necessary medical treatment may directly or indirectly cause iatrogenic infertility to a member; Infertility Expense Benefits – Infertility coverage for the diagnosis and treatment of infertility including, but not limited to, in vitro fertilization, uterine embryo lavage, embryo transfer, artificial insemination, gamete intrafallopian tube transfer, zygote intrafallopian tube transfer, low tubal ovum transfer, oocyte retrieval and intracytoplasmic sperm injection, to the extent the treatment is legal under applicable law.*
- ***IN:*** *Infertility Services - Covered services under this benefit are limited to medically necessary diagnostic tests to determine infertility and treatment of the underlying medical conditions that may cause infertility (e.g., endometriosis, obstructed fallopian tubes and hormone deficiency).*
- ***KS:*** *Infertility Services - Covered services for infertility treatment are limited to diagnostic testing to find the cause of infertility, such as diagnostic laparoscopy, endometrial biopsy, and semen analysis. Benefits are included to treat the underlying medical conditions that cause infertility (such as endometriosis, obstructed fallopian tubes and hormone deficiency).*
- ***KY:*** *Infertility Benefits - Covered services under this benefit are provided for medically necessary diagnostic and exploratory procedures to determine infertility including surgical procedures to correct a medically diagnosed disease or condition of the reproductive organs including, but not limited to, treatment of the following:1. Endometriosis;2. Collapsed/clogged fallopian tubes; or 3. Testicular failure.*
- ***LA****: Fertility Preservation – Medically necessary fertility preservation services for enrollees when a medical treatment will directly or indirectly result in "iatrogenic infertility," which is an impairment of fertility by surgery, radiation, chemotherapy, or other medical treatment affecting reproductive organs or processes. Cost-sharing such as deductibles, copayments, and coinsurance may be imposed on fertility preservation services if the cost-sharing is consistent with other benefits in the contract and place of service. Services include the collecting, freezing, preserving of ova or sperm, and other standard services that are not experimental or investigational. Coverage includes up to three (3) years of storage costs associated with oocytes and sperm during the enrollee's membership. Infertility – Covered services under this benefit are provided for medically necessary diagnostic and exploratory procedures to determine infertility and surgical procedures to correct a medically diagnosed disease or condition of the reproductive organs including, but not limited to, treatment of the following: 1. Endometriosis; 2. Collapsed/clogged fallopian tubes; or 3. Testicular failure.*
- ***MI****: Infertility Services - Covered service expenses under this benefit are provided for medically necessary diagnostic and exploratory procedures to determine infertility, including surgical procedures and prescription drugs, to correct a medically diagnosed disease or condition of the reproductive organs including, but not limited to, treatment of the following: 1. Endometriosis; 2. Collapsed/clogged fallopian tubes; or 3. Testicular failure*
- ***MO:*** *Infertility Services - Covered services for infertility treatment are limited to diagnostic testing to find the cause of infertility, such as diagnostic laparoscopy, endometrial biopsy, and semen analysis. Benefits are included to treat the underlying medical conditions that cause infertility (such as endometriosis, obstructed fallopian tubes and hormone deficiency).*
- ***NE:*** *For the treatment of infertility. Note: Coverage is available for diagnosis and services required to correct underlying medical causes of infertility.*
- ***NV:*** *Limited diagnostic and therapeutic infertility services determined to be medically necessary and requires prior authorization. Covered services do not include those services specifically excluded herein, but do include limited: a. Laboratory studies; b. Diagnostic procedures; and c. Artificial insemination services, up to six (6) cycles per member per lifetime.*
- ***NJ****: Subject to pre-approval, covered charges include: artificial insemination; and standard dosages, lengths of treatment and cycles of therapy of prescription drugs used to stimulate ovulation for artificial insemination or for unassisted conception*
- ***NC****: Limited to diagnostic testing to find the cause of infertility, such as diagnostic laparoscopy, endometrial biopsy, and semen analysis. Treatment of the underlying medical conditions that cause infertility (such as endometriosis, obstructed fallopian tubes and hormone deficiency)are considered a separate benefit. Treatment for infertility is limited to a lifetime benefit maximum, per member, of three medical ovulation induction cycles.*
- ***NY****: Infertility Treatment - We cover services for the diagnosis and treatment (surgical and medical) of infertility "Infertility" is a disease or condition characterized by the incapacity to impregnate another person or to conceive, defined by the failure to establish a clinical pregnancy after 12 months of regular, unprotected*

sexual intercourse or therapeutic donor insemination, or after six (6) months of regular, unprotected sexual intercourse or therapeutic donor insemination for a female 35 years of age or older. Earlier evaluation and treatment may be warranted based on a Member's medical history or physical findings. Basic Infertility Services, Comprehensive Infertility Services, Fertility Preservation Services

- ***NH**: Infertility Services - Covered services for infertility treatment are limited to diagnostic testing to find the cause of infertility, such as diagnostic laparoscopy, endometrial biopsy, and semen analysis. Benefits are included to treat the underlying medical conditions that cause infertility (such as endometriosis, obstructed fallopian tubes and hormone deficiency). Benefits are only available to the extent the covered fertility services are legal under applicable law*
- ***OH**: Infertility - Covered service expenses under this benefit are provided for medically necessary diagnostic and exploratory procedures to determine infertility including surgical procedures to correct a medically diagnosed disease or condition of the reproductive organs including, but not limited to, treatment of the following:1. Endometriosis;2. Collapsed/clogged fallopian tubes; or 3. Testicular failure. This benefit is subject to deductible and coinsurance amount/copayment. No benefits will be payable for charges related to artificial insemination services, in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), and zygote intrafallopian transfer (ZIFT).*
- ***OK**: Infertility - Covered service expenses under this benefit are provided for medically necessary diagnostic and exploratory procedures to determine infertility including surgical procedures to correct a medically diagnosed disease or condition of the reproductive organs including, but not limited to, treatment of the following:1. Endometriosis;2. Collapsed/clogged fallopian tubes; or3. Testicular failure. This benefit is subject to deductible and coinsurance amount/copayment No benefits will be payable for charges related to artificial insemination services, in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), and zygote intrafallopian transfer (ZIFT). Fertility Preservation -We cover standard medically necessary fertility preservation services for enrollees within reproductive age, diagnosed with cancer, when a medical treatment will directly or indirectly result in "iatrogenic infertility," which is an impairment of fertility by surgery, radiation, chemotherapy, or other medical treatment affecting reproductive organs or processes. Cost-sharing such as deductibles, copayments, and coinsurance may be imposed on fertility preservation services if the cost-sharing is consistent with other benefits in the contract and place of service.*
- ***PA:** Infertility - Covered services under this benefit are provided for medically necessary diagnostic and exploratory procedures to determine infertility. Coverage is also provided for artificial insemination, as well as for surgical procedures to correct a medically diagnosed disease or condition of the reproductive organs including, but not limited to, treatment of the following: 1. Endometriosis; 2. Collapsed/clogged fallopian tubes; or 3. Testicular failure. This benefit is subject to deductible and coinsurance/copayment. No benefits will be payable for charges related to in vitro fertilization (IVF), embryo transplant, gamete intrafallopian transfer (GIFT), and zygote intrafallopian transfer (ZIFT).*
- ***SC**: Infertility - Infertility treatment is limited to medical services provided to the member which are medically necessary for the diagnosis of infertility and services required to correct underlying medical conditions that may cause infertility (e.g., endometriosis). This does not include treatment for infertility, including artificial insemination, in vitro fertilization, and other types of artificial or surgical means of conception nor drugs administered in connection with these procedures*
- ***TN**: Infertility Services - Covered services for infertility treatment are limited to diagnostic testing to find the cause of infertility, such as diagnostic laparoscopy, endometrial biopsy, and semen analysis. Benefits are included to treat the underlying medical conditions that cause infertility (such as endometriosis, obstructed fallopian tubes and hormone deficiency).*
- ***TX**: Infertility - Infertility treatment is a covered service expense when medical services are provided to the enrollee which are medically necessary for the diagnosis of infertility such as diagnostic laparoscopy, endometrial biopsy, and semen analysis. Benefits are included to treat the underlying medical conditions that cause infertility (such as endometriosis, obstructed fallopian tubes and hormone deficiency). This does not cover treatment or surgical procedures for infertility including artificial insemination, in vitro fertilization, medically assisted reproduction (MAR), and other types of artificial or surgical means of contraception including drugs administered in connection with these procedures. Fertility Preservation - Medically necessary fertility preservation services for enrollees when a medical treatment will directly or indirectly result in "iatrogenic infertility," which is an impairment of fertility by surgery, radiation, chemotherapy, or other medical treatment affecting reproductive organs or processes. Cost-sharing such as deductibles, copayments, and coinsurance may be imposed on fertility preservation services if the cost-sharing is consistent with other benefits in the contract and place of service. Services include the collecting, freezing, preserving of ova or*

sperm, and other standard services that are not experimental or investigational. (Storage is an exclusion.). Coverage may be limited to in-network providers for fertility preservation services unless the issuer does not have an in-network provider with the appropriate training and expertise to meet the needs of the enrollee. Prior authorization and/or referrals may be required.

- ***All other states**: No benefits will be paid under this benefit provision for services provided or expenses incurred for infertility drugs, unless otherwise listed on the formulary.*

FDA Approved Indication(s)

Drugs			Indications, Female		Indications, Male	
Drug Name	**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 (FSH)	x	x		
Follitropin alfa, recombinant	Gonal-f RFF Redi-ject	Gonadotropin (FSH)	x	x		
Follitropin beta, recombinant	Follistim-AQ	Gonadotropin (FSH)	x	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	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 oligo-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 infertile women as part of an ART cycle/program.
  - Induction of spermatogenesis in infertile 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 infertile 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.

- 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.

- Pregnyl is 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 menotropins.

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® that Menopur, Gonal-f, Gonal-f RFF, Gonal f RFF Redi-ject, Follistim-AQ, ganirelix acetate, Cetrotide, cetrorelix, Ovidrel, 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 ≥ 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*);*
      ** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
   b. ART, and both of the following (i and ii):*
      ** For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
      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;
7. If request is for brand Cetrotide, member must use generic cetrorelix, unless contraindicated or clinically significant adverse effects are experienced.

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 ≥ 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;
6. If request is for brand Cetrotide, member must use generic cetrorelix, unless contraindicated or clinically significant adverse effects are experienced.

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, or Pregnyl;
3. Diagnosis of infertility due to HH;
4. Prescribed by or in consultation with a reproductive endocrinologist or urologist;
5. Age ≥ 18 years;
6. Product(s) are requested in one of the following ways (a or b):
   a. 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 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 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 ≤ 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 (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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, or Pregnyl;
3. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
4. Member is responding positively to therapy;
5. If request is for Pregnyl, one of the following (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, both of the following (a and b):
   a. Prescribed in combination with 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 Pregnyl;
2. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
3. Member is responding positively to therapy.
4. Member has not received more than 3 months of therapy;

Approval duration: 3 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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
ASCO: American Society of Clinical Oncology
AYA: adolescent and young adult
COH: controlled ovarian hyperstimulation
FDA: Food and Drug Administration
FSH: follicle-stimulating hormone
GnRH: gonadotropin-releasing hormone
hCG: human chorionic gonadotropin
HH: hypogonadotropic hypogonadism
hMG: human menopausal gonadotropin
ICSI: intracytoplasmic sperm injection
IVF: in vitro fertilization
LH: luteinizing hormone
NCCN: National Comprehenswive Cancer Network
OI: ovulation induction
POI: primary ovarian insufficiency, primary ovarian failure

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cabergoline	**Hyperprolactinemia (labeled):** Initial: 0.25 mg PO twice weekly; may increase by 0.25 mg twice weekly (no more often than every 4	1 mg twice weekly

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	weeks) up to a maximum or 1 mg twice weekly according to the patient's serum prolactin level.	
bromocriptine (Parlodel®)	**Hyperprolactinemia (labeled):** 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	**Treatment of ovulatory dysfunction in women desiring pregnancy (labeled):** 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 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.	150 mg/day per expert review Durations: 5 to 7 days per expert review
letrozole (Femara®)	**Infertility - ovulation stimulation in anovulatory females (off-label):** 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® (generic) when the drug is available by brand name only and generic (Brand name®) 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 (embyro 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, 2023) 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 gonad protection: 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 (e.g., 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

Drug Name	Dosing Regimen	Maximum Dose
Infertility, Female		
Follicle stimulating agents		
Menopur (menotropins)	Up to 450 IU SC per day	• Doses are individualized. • Duration typically would not exceed one month per reproductive attempt; there may be exceptions.
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	
Pituitary suppression agents		
Ganirelix acetate	250 mcg SC per day	• Doses and durations as noted above.
Cetrotide (cetrorelix)	0.25 mg SC per day	
Ovulatory "trigger" agents		
Ovidrel (choriogonadotropin alfa; recombinant hCG)	250 mcg SC once	• Doses are individualized.

Drug Name	Dosing Regimen	Maximum Dose
hCG (Pregnyl; urinary hCG)	5,000 to 10,000 USP Units IM once	• An agent from this category is typically given once per reproductive attempt.
Infertility, Male: Due to hypogonadotropic hypogonadism		
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 combination with hCG at the dose required to maintain normal testosterone levels.	
Prepubertal Cryptorchidism		
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
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
Pregnyl	Injection: 10,000 U/vial
Chorionic gonadotropin (hCG)	Injection: 10,000 U/vial

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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.

HCPCS Codes	Description
S0122	Injection, menotropins, 75 iu
S0126	Injection, follitropin alfa, 75 iu
S0128	Injection, follitropin beta, 75 iu
S0132	Injection, ganirelix acetate, 250 mcg
J0725	Injection, chorionic gonadotropin, per 1,000 usp units
J3490	Unclassified drug
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	07.21.21	11.21
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.16.22	11.22
4Q 2023 annual review: evidence of coverage for infertility/fertility preservation language added for HIM line of business (AZ, CA, KS, MI, NE, NJ, NM, NC, SC, and all other states); for prepubertal cryptorchidism, added criterion "member has not received more than 3 months of therapy" to continued therapy; removed references to Bravelle due to product discontinuation; references reviewed and updated.	06.29.23	11.23
4Q 2024 annual review: evidence of coverage for infertility/fertility preservation language for HIM line of business updated for the following states: add AR, IL, LA, NV and removed KS, MI, NE, NM, SC; added HCPC code [J3490, J3590]; added for brand Cetrotide requests redirection to generic cetrorelix; removed	07.16.24	11.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
references to brand Novarel due to product discontinuation; references reviewed and updated.		
4Q 2025 annual review: evidence of coverage for infertility/fertility preservation language added for HIM line of business (DE, GA, IN, KS, KY, MI, MO, NE, NY, NH, OH, OK, PA, SC, TN, TX); references reviewed and updated.	07.11.25	11.25

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.