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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	January 1, 2011
Subject:	ART Drugs	**Page:**	1 of 8

Last Review Date: June 16, 2022

ART Drugs

Description

Bravelle (urofollitropin)
Cetrotide (cetrorelix)
Clomiphene citrate, Clomiphene powder
Crinone, Endometrin, Progesterone in oil, Progesterone powder, Prometrium (progesterone)
Follistim AQ (follitropin beta)
Fyremadel/Ganirelix (ganirelix)
Gonal-F, Gonal-F RFF (follitropin alfa)
Menopur (menotropins)
Milprosa* (progesterone)

*This medication is included in this policy but is not available on the market as of yet

Background
Assisted reproductive technologies (ART) represent a group of non-coital manipulations and processes that manipulate ova and/or sperm to achieve a pregnancy. The most well-known examples are ovulation induction, intrauterine insemination and in-vitro fertilization. ART and infertility drugs used in conjunction with ART procedures or for erectile or sexual dysfunction, weight loss, performance (athletic) enhancement and anti-aging are not covered by the Plan. The diagnosis of hypogonadotropic hypogonadism is an off-label indication for these medications.

A variety of drugs are used to manipulate the hypothalamic-pituitary-gonadal axis in order to induce ovulation in females known as controlled ovarian hyperstimulation (COH). Some of these pharmacologic agents are used for additional clinical care indications.

Drugs Included in Infertility Drugs / ART Criteria

- Bravelle (urofollitropin) – ovulation induction and multiple follicle development during ART
- Clomiphene citrate – ovulation induction
- Clomiphene powder – ovulation induction
- Crinone (progesterone) – progesterone supplementation during ART
- Endometrin (progesterone) – progesterone supplementation during ART
- Follistim AQ (follitropin beta) – ovulation induction and multiple follicle development during ART
- Fyremadel/Ganirelix (ganirelix) – inhibition of premature LH surges in women undergoing COH
- Gonal-F (follitropin alfa) – ovulation induction, and multiple follicle development during ART
- Gonal-F RFF (follitropin alfa) – ovulation induction and multiple follicle development during ART
- HCG powder (human chorionic gonadotropin)- ovulation induction, spermatogenesis induction – separate policy
- Menopur (menotropins) – multiple follicle development during ART
- Milprosa (progesterone) – progesterone supplementation during ART
- Novarel (chorionic gonadotropin) – ovulation induction – separate policy
- Ovidrel (choriogonadotropin) – ovulation induction and stimulation of final follicle maturation and early luteinization for ART – separate policy
- Pregnyl (chorionic gonadotropin) – ovulation induction – separate policy
- Progesterone in oil (progesterone) – progesterone supplementation during ART
- Progesterone powder (progesterone) – progesterone supplementation during ART
- Prometrium (progesterone) – progesterone supplementation during ART

Drugs Excluded from Infertility Drugs / ART Criteria

- Arimidex (anastrozole) – limited use in ART and used to treat breast cancer
- Aromasin (exemestane) – limited use in ART and used to treat breast cancer
- Femara (letrozole) – limited use in ART and used to treat breast cancer
- Tamoxifen – limited use in ART and used to treat breast cancer

Regulatory Status

The drugs addressed by this policy are FDA-approved for use in one or more of a variety of conditions.

Related policies
HCG, Synarel

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

The drugs addressed by this policy may be considered **medically necessary** for all indications considered a covered benefit, and if the conditions indicated below are met.

The drugs addressed by this policy are **not covered** by the Plan if used for erectile/sexual dysfunction, weight loss, performance (athletic) enhancement, anti-aging, or in conjunction with ART procedures.

Prior-Approval Requirements

The drugs addressed by this policy are covered without a Prior Authorization (PA) for all female patients over 50 years of age.

Diagnoses

Female

ALL diagnoses are covered **EXCEPT:**

Patients must **NOT** use for the following indication:

1. Used in conjunction with assisted reproductive technology (ART) procedures, which include but are not limited to:
    a. Artificial insemination (AI)
    b. In vitro fertilization (IVF)
    c. Embryo transfer and gamete intrafallopian transfer (GIFT)
    d. Zygote intrafallopian transfer (ZIFT)
    e. Intravaginal insemination (IVI)
    f. Intracervical insemination (ICI)
    g. Intracytoplasmic sperm injection (ICSI)
    h. Intrauterine insemination (IUI)

Male

ALL diagnoses are covered **EXCEPT:**

For the following indication patient must have:

1. Hypogonadism with **ALL** of the following:

a. Hypogonadotropic hypogonadism
b. **NOT** caused by primary testicular failure
c. Patient has low pretreatment testosterone levels
d. Patient has low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels
e. Used for spermatogenesis

AND NOT used for the following for both males and females:

1. Weight loss
2. Anti-aging effects
3. Performance (athletic) enhancement
4. Erectile or sexual dysfunction

Diagnosis

The patient must have the following:

Gender Dysphoria (GD)

1. Prescribed by an endocrinologist or transgender specialist
2. Patient has met the DSM V criteria for GD

Prior – Approval *Renewal* Requirements

The drugs addressed by this policy are covered without a Prior Authorization (PA) for all female patients over 50 years of age.

Diagnoses

Female

ALL diagnoses are covered **EXCEPT:**

Patients must **NOT** use for the following indication:

1. Use in conjunction with assisted reproductive technology (ART) procedures, which include but are not limited to:
   a. Artificial insemination (AI)
   b. In vitro fertilization (IVF)
   c. Embryo transfer and gamete intrafallopian transfer (GIFT)
   d. Zygote intrafallopian transfer (ZIFT)
   e. Intravaginal insemination (IVI)

f. Intracervical insemination (ICI)
g. Intracytoplasmic sperm injection (ICSI)
h. Intrauterine insemination (IUI)

Male

ALL diagnoses are covered **EXCEPT:**

For the following indication patient must have:

1. Hypogonadism with **ALL** of the following:
    a. Hypogonadotropic hypogonadism
    b. **NOT** caused by primary testicular failure
    c. Patient has low pretreatment testosterone levels
    d. Patient has low or low-normal follicle stimulating hormone (FSH) or luteinizing hormone (LH) levels
    e. Used for spermatogenesis

AND NOT used for the following for both males and females:

1. Weight loss
2. Anti-aging effects
3. Performance (athletic) enhancement
4. Erectile or sexual dysfunction

Diagnosis

The patient must have the following:

Gender Dysphoria (GD)

1. Prescribed by an endocrinologist or transgender specialist

Policy Guidelines

Pre - PA Allowance

The drugs addressed by this policy are covered without a Prior Authorization (PA) for all female patients over 50 years of age.

Prior - Approval Limits

Duration	Females	6 months
	Males	12 months
	GD	2 years

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Assisted reproductive technologies (ART) represent a group of non-coital manipulations and processes that manipulate ova and/or sperm to achieve a pregnancy. ART and infertility drugs used in conjunction with ART procedures, or for erectile/sexual dysfunction, weight loss, performance (athletic) enhancement or anti-aging are not covered by the Plan.

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of drugs used for ART and GD while maintaining optimal therapeutic outcomes.

References

1. Esteves, Sandro C, Humaidan, Peter, Roque, Matheus, Agarwal, Ashok. Female fertility and assisted reproductive technology. Panminerval Medica 2019, March; 61 (1): 1-2. doi: 10.23736/S0031-0808.18.03553-X
2. Chehab M, Madala A, Trussell JC. On-label and off-label drugs used in the treatment of male infertility. Fertil Steril. 2015 Mar;103(3):595-604. doi: 10.1016/j.fertnstert.2014.12.122. Epub 2015 Feb 3. PMID: 25660648.
3. Hembree, WC, Cohen-Kettenis, P, et al. Endocrine Treatment of Transsexual Persons: AAn Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.*. 2009; 94(9):3132-3154.

Policy History

Date	Action
March 2011	Adding human chorionic gonadotropin (HCG) powder to the list of drugs used in infertility and ART; HCG is used to induce ovulation and spermatogenesis.

August 2011	Removing HCG POWDER (human chorionic gonadotropin) NOVAREL / PREGNYL (chorionic gonadotropin) and OVIDREL (choriogonadotropin) from this criterion; these agents will be on their own criterion to exclude use for weight loss, performance enhancement, and anti-aging effects.
December 2012	Annual editorial review and reference update
July 2013	Removal of Prochieve due to withdrawal from the market
February 2013	Addition of Leuprolide powder
September 2014	Annual review Addition of Gender Identity Disorder (and other conditions associated with sex transformations), erectile or sexual dysfunction, weight loss, performance enhancing or anti-aging as a non-covered benefit Addition of hypogonadism as a non-covered off label use Removal of Standard Allowance for men under 50
September 2015	Annual editorial review and reference update
December 2015	Annual review Addition of Gender Dysphoria (GD) use and duration
September 2016	Annual editorial review Addition of or transgender specialist to GD Addition of these drugs are covered for only female members greater than 50 years of age
January 2017	Removal of First – Progesterone VGS and the GD age requirement
March 2017	Annual review
July 2017	Removal of primary hypogonadism as a non-covered off label use and the addition of the hypogonadism requirements
September 2017	Annual review
April 2018	Removal of Leuprolide powder
June 2018	Annual review
December 2019	Annual editorial review. Changed approval duration for gender dysphoria from lifetime to 2 years
March 2020	Added requirement of no erectile or sexual dysfunction for female patients
May 2020	Removal of leuprolide drugs to their own policy
June 2020	Annual review
September 2020	Annual review
March 2021	Annual review and reference update
April 2021	Addition of Milprosa
June 2021	Annual review

September 2021	Annual review
March 2022	Annual review
April 2022	Addition of branded generic Fyremadel (ganirelix) to policy. Removed discontinued brand names from policy (Antagon, Clomid and Serophene).
June 2022	Annual review. Revised hypogonadism requirements to clarify that hypogonadism must be hypogonadotropic to meet criteria

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.