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5.30.002

Section:	Prescription Drugs	**Effective Date:**	October 1, 2024
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	January 1, 2011
Subject:	ART Drugs	**Page:**	1 of 8

Last Review Date: September 6, 2024

ART Drugs

Description

Cetrotide (cetrorelix)
Clomiphene citrate
Clomiphene powder
Crinone/Endometrin/Milprosa*/Progesterone in oil/Progesterone powder/Prometrium (progesterone)
Firmagon (degarelix)
Follistim AQ (follitropin beta)
Fyremadel/Ganirelix (ganirelix)
Gonal-F/Gonal-F RFF (follitropin alfa)
Menopur (menotropins)
Supprelin LA (histrelin)
Synarel (nafarelin)
Trelstar/Triptodur (triptorelin)
Zoladex (goserelin)

*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)

- Cetrotide (cetrorelix)
- Clomiphene citrate
- Clomiphene powder
- Crinone/Endometrin/Milprosa/Progesterone in oil/Progesterone powder/Prometrium (progesterone)
- Firmagon (degarelix)
- Follistim AQ (follitropin beta)
- Fyremadel/Ganirelix (ganirelix)
- Gonal-F/Gonal-F RFF (follitropin alfa)
- Menopur (menotropins)
- Supprelin LA/Vantas (histrelin)
- Synarel (nafarelin)
- Trelstar/Triptodur (triptorelin)
- Zoladex (goserelin)

Drugs Included in Infertility Drugs (Separate Criteria)

- Camcevi (leuprolide mesylate)
- Eligard/Fensolvi/Leuprolide Acetate/Lupron Depot (leuprolide acetate)
- HCG powder (human chorionic gonadotropin)
- Novarel (chorionic gonadotropin)
- Ovidrel (choriogonadotropin)
- Pregnyl (chorionic gonadotropin)

Drugs Excluded from Infertility Drugs

- 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, Leuprolide

Policy

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

ART Drugs may be considered **medically necessary** if the conditions indicated below are met.

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.

When used for medically assisted reproduction, ART drugs are limited to 3 cycles per benefit year for *in vitro* fertilization procedures. There are no cycle limits when used for artificial insemination procedures.

Female

ALL diagnoses are covered **EXCEPT:**

For the diagnosis of Infertility:

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

AND NOT used for the following:

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

Male
ALL diagnoses are covered **EXCEPT:**

For the following diagnosis, the 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:

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

Diagnosis

Patient must have the following:

Gender Dysphoria (GD)

Prior – Approval *Renewal* Requirements

Same as above

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

When used for medically assisted reproduction, ART drugs are limited to 3 cycles per benefit year for *in vitro* fertilization procedures. There are no cycle limits when used for artificial insemination procedures.

Diagnosis	Duration
Gender Dysphoria	2 years
ART - IVF procedures	4 months
ART - AI procedures	12 months
All other indications	12 months

Prior – Approval *Renewal* Limits

Diagnosis	Duration
Gender Dysphoria	2 years
ART - IVF procedures	4 months* ***ONLY** two renewals every calendar year
ART - AI procedures	12 months
All other indications	12 months

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 ART drugs 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
September 2022	Annual review
December 2022	Annual review. Removed GD requirements of meeting DSM criteria and being prescribed by an endocrinologist or transgender specialist
March 2023	Annual review
June 2023	Annual editorial review. Removed Bravelle from policy due to being discontinued
September 2023	Annual review

January 2024	Per FEP, added infertility with ART as an approvable diagnosis with a limit of 3 cycles per year for IVF-related procedures and unlimited cycles of AI-related procedures. Combined with 5.30.003 Synarel (nafarelin) policy and 5.30.039 GnRH GD policy. Removed Bravelle from policy due to being discontinued
March 2024	Annual review
June 2024	Annual review
September 2024	Annual editorial review. Removed brand name Vantas from policy due to being discontinued

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.