
5.30.002

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

Last Review Date: March 8, 2024

ART Drugs

Description

Cetrotide (cetorelix)
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)

*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.

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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 (cetorelix)
- 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

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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)

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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
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Diagnosis

Patient must have the following:

Gender Dysphoria (GD)

Prior – Approval *Renewal* Requirements

Same as above

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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,

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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 |

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| 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 |

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| 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 |

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.