Synarel

Description

Assisted Reproductive Technology (ART) / Infertility / Synarel (nafarelin)

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 are not a covered benefit (1).

A variety of drugs are used to manipulate the hypothalamic-pituitary-gonadal axis in order to induce ovulation in females. Some of these pharmacologic agents are used for additional clinical care indications (1).

Synarel (nafarelin acetate nasal solution) is a potent agonistic analog of gonadotropin-releasing hormone (GnRH). At the onset of administration, nafarelin stimulates the release of the pituitary gonadotropins, LH and FSH, resulting in a temporary increase of ovarian steroidogenesis (1).

These effects on ovarian steroid hormone production have been utilized in the treatment of infertility.

Regulatory Status

FDA-approved indications: Synarel (nafarelin acetate nasal solution) has two FDA approved indications: (2)

1. Nafarelin is indicated for treatment of central precocious puberty (CPP) (gonadotropin-independent precocious puberty) in children of both sexes. The diagnosis of central precocious puberty (CPP) is suspected when premature development of secondary
sexual characteristics occurs at or before the age of 8 years in girls and 9 years in boys, and is accompanied by significant advancement of bone age and/or a poor adult height prediction. The diagnosis should be confirmed by pubertal gonadal sex steroid levels and a pubertal LH response to stimulation by native GnRH.

2. Nafarelin is indicated for management of endometriosis, including pain relief and reduction of endometriotic lesions. Experience with Synarel for the management of endometriosis has been limited to women 18 years of age and older treated for 6 months. When used regularly at the recommended dose, the drug usually inhibits ovulation and stops menstruation.

**Off-Label Use:**
Nafarelin can be used in the treatment of Gender Dysphoria (GD) and should only be started once a diagnosis of GD or transsexualism has been made per the DSM V or ICD-10 criteria (4).

**Related policies**
ART Infertility Drugs

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

Synarel may be considered medically necessary if the conditions below are met for all indications other than those that are considered to be assisted reproductive technology (ART) or weight loss, performance enhancement, anti-aging, and erectile or sexual dysfunction are non-covered benefits.

Synarel may be considered medically necessary in patients with Gender Dysphoria (GD) and must be prescribed by an endocrinologist; patient has met the DSM V criteria for GD.

Synarel may be considered investigational if the criteria for medical necessity are not met.

**Prior-Approval Requirements**

**Diagnoses**

**Female**

ALL diagnoses are covered EXCEPT:

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

Male patients must NOT use for the following indication:

1. Erectile or sexual dysfunction

AND NOT for the following for both males and females:

1. Weight loss
2. Anti-aging effects
3. Performance enhancement

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

Diagnoses

Female

ALL diagnoses are covered EXCEPT:

Patients must NOT use for the following indications:

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)
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Male

ALL diagnoses are covered EXCEPT:

For the following indication patient must have:

1. Hypogonadotrophic hypogonadism with ALL of the following:
   a. NOT caused by primary testicular failure
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   d. Used for spermatogenesis

Male patients must NOT use for the following indication:

1. Erectile or sexual dysfunction

AND NOT for the following for both males and females:

a. Weight loss
b. Anti-aging effects

c. Performance enhancement

Policy Guidelines

Pre - PA Allowance

Synarel is a covered benefit for female members greater than 50 years of age.

Prior - Approval Limits

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<th>Duration</th>
<th>Females</th>
<th>Males</th>
<th>GD</th>
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<tbody>
<tr>
<td></td>
<td>6 months</td>
<td>12 months</td>
<td>Lifetime</td>
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Prior – Approval Renewal Limits

<table>
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Rationale

Summary

ART is not a covered benefit. The primary pharmacologic treatments used to induce ovulation in coital reproduction and for controlled ovarian hyperstimulation (COH) in ART are generally the same (1-2).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Synarel while maintaining optimal therapeutic outcomes.

References

**5.30.03**

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<thead>
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<th>Section:</th>
<th>Prescription Drugs</th>
<th>Effective Date:</th>
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<td>Endocrine and Metabolic Drugs</td>
<td>Original Policy Date:</td>
<td>January 1, 2011</td>
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### Policy History

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<tr>
<td>December 2012</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>September 2014</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>September 2015</td>
<td>Annual editorial review and reference update. Addition 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</td>
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<td>December 2015</td>
<td>Annual review</td>
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<tr>
<td>September 2016</td>
<td>Annual editorial review and reference update. Addition of Artificial insemination (AI) to the list of non-covered diagnoses and to GD a transgender specialist Policy number change from 5.08.03 to 5.30.03</td>
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<td>Removal of GD age requirements</td>
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<td>March 2017</td>
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<td>July 2017</td>
<td>Removal of primary hypogonadism as a non-covered off label use and the addition of the hypogonadism requirements</td>
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<td>Annual review</td>
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### Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 15, 2017 and is effective on October 1, 2017.