RATIONALE FOR INCLUSION IN PA PROGRAM

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-dependent 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).

**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**