GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST

Generic	Brand	HICL	GCN	Exception/Other
LEUPROLIDE ACETATE	ELIGARD		17377 18155 19219 24301	
LEUPROLIDE ACETATE (GENERIC)	LEUPROLIDE ACETATE		84597	
NAFARELIN ACETATE	SYNAREL		84354	

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Is the requested medication being used for gender dysphoria?

   If yes, **approve for 12 months for the requested agent and strength by GPID and override quantity limits.**
   If no, continue to #2.

2. Is the request for Eligard or Leuprolide (generic) for a patient who has a diagnosis of advanced prostate cancer?

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Eligard 7.5mg (GPID 17377): #1 injection per 28 days (every month).**
   - **Eligard 22.5mg (GPID 18155): #1 injection per 84 days (every 3 months).**
   - **Eligard 30mg (GPID 19219): #1 injection per 112 days (every 4 months).**
   - **Eligard 45mg (GPID 24301): #1 injection per 168 days (every 6 months).**
   - **Leuprolide (generic) (GPID 84597): #1 kit per 14 days (every 2 weeks).**

   If no, continue to #3.

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GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST

INITIAL CRITERIA (CONTINUED)

3. Is the request for Synarel for a patient who has a diagnosis of moderate to severe pain associated with endometriosis **AND** meet **ALL** of the following criteria?
   - The patient is 18 years of age or older
   - The requested medication is prescribed by or in consultation with an obstetrician/gynecologist
   - The patient had a previous trial of or contraindication to a nonsteroidal anti-inflammatory drug (NSAID) **AND** a progestin-containing contraceptive preparation (e.g., combination hormonal contraceptive preparation, progestin-only contraceptive preparation)

   If yes, **approve for 6 months with the following quantity limits:**
   - **Synarel 2mg/mL (GPID 84354): #96mL per 180 days (#12 bottles).**

   If no, continue to #4.

4. Is the request for Synarel or Leuprolide (generic) for a female patient who has a diagnosis of central precocious puberty (CPP) **AND** meets **ALL** of the following criteria?
   - The patient is at least 2 years of age
   - The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
   - Patient has elevated levels of follicle-stimulating hormone (FSH) (level >4.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
   - Patient is younger than 8 years of age at the onset of CPP
   - Documentation of pubertal staging using the Tanner scale for:
     - Breast development (stage 2 or above) **AND**
     - Pubic hair growth (stage 2 or above)

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Synarel 2mg/mL (GPID 84354): #32mL per 30 days (#4 bottles).**
   - **Leuprolide (generic) 1mg/0.2 mL (GPID 84597): approve with no quantity limit.**

   APPROVAL TEXT: Renewal requires physician attestation that Tanner scale staging at initial diagnosis of CPP has become stable or regresses at three separate medical visits in previous year and that patient has not reached actual age which corresponds to current pubertal age.

   If no, continue to #5.

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GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST

INITIAL CRITERIA (CONTINUED)

5. Is the request for Synarel or Leuprolide (generic) for a male patient who has a diagnosis of central precocious puberty (CPP) **AND** meets **ALL** of the following criteria?
   - The patient is at least 2 years of age
   - The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
   - Patient has elevated levels of follicle-stimulating hormone (FSH) (level >5.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
   - Patient is younger than 9 years of age at the onset of CPP
   - Documentation of pubertal staging using the Tanner scale for:
     - o Genital development (stage 2 or above) **AND**
     - o Pubic hair growth (stage 2 or above)

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Synarel 2 mg/mL (GPID 84354): #32mL per 30 days (#4 bottles).**
   - **Leuprolide (generic) 1mg/0.2 mL (GPID 84597): approve with no quantity limit.**

   APPROVAL TEXT: Renewal requires physician attestation that Tanner scale staging at initial diagnosis of CPP has become stable or regresses at three separate medical visits in previous year and that patient has not reached actual age which corresponds to current pubertal age.

   If no, do not approve.
   INITIAL DENIAL TEXT: The guideline named **GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST** requires that the patient has gender dysphoria or a diagnosis of advanced prostate cancer, moderate to severe pain associated with endometriosis, or central precocious puberty (CPP). In addition, the following criteria must also be met for the requested diagnosis:

   Patients diagnosed with moderate to severe pain associated with endometriosis, approval requires:
   - The request is for Synarel
   - The patient is 18 years of age or older
   - The requested medication is prescribed by or in consultation with an obstetrician/gynecologist
   - The patient had a previous trial of or contraindication to a nonsteroidal anti-inflammatory drug (NSAID) **AND** a progestin-containing contraceptive preparation (e.g., combination hormonal contraceptive preparation, progestin-only contraceptive preparation)

   (Initial denial text continued on next page)

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GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST

INITIAL CRITERIA (CONTINUED)

Female patients diagnosed with CPP, approval requires:

- The request is for Synarel or Leuprolide (generic)
- The patient is at least 2 years of age
- The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
- Patient has elevated levels of follicle-stimulating hormone (FSH) (level >4.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
- Patient is younger than 8 years of age at the onset of CPP
- Documentation of pubertal staging using the Tanner scale for:
  - Breast development (stage 2 or above) **AND**
  - Pubic hair growth (stage 2 or above)

Male patients diagnosed with CPP, approval requires:

- The request is for Synarel or Leuprolide (generic)
- The patient is at least 2 years of age
- The requested medication is prescribed by or given in consultation with a pediatric endocrinologist
- Patient has elevated levels of follicle-stimulating hormone (FSH) (level >5.0 mIU/ml) and luteinizing hormone (LH) (level > 0.2 to 0.3 mIU/L) at diagnosis
- Patient is younger than 9 years of age at the onset of CPP
- Documentation of pubertal staging using the Tanner scale for:
  - Genital development (stage 2 or above) **AND**
  - Pubic hair growth (stage 2 or above)

Requests for Eligard or Leuprolide (generic) for patients with advanced prostate cancer will be approved without requiring additional criteria.

Requests for patients with gender dysphoria will be approved without requiring additional criteria.

RENEWAL CRITERIA

1. Is the requested medication being used for gender dysphoria?

   If yes, **approve for 12 months for the requested agent and strength by GPID.**
   If no, continue to #2.

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GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST

RENEWAL CRITERIA (CONTINUED)

2. Is the request for Eligard or Leuprolide (generic) for a patient who has a diagnosis of advanced prostate cancer?

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Eligard 7.5mg (GPID 17377): #1 injection per 28 days (every month).**
   - **Eligard 22.5mg (GPID 18155): #1 injection per 84 days (every 3 months).**
   - **Eligard 30mg (GPID 19219): #1 injection per 112 days (every 4 months).**
   - **Eligard 45mg (GPID 24301): #1 injection per 168 days (every 6 months).**
   - **Leuprolide (generic) (GPID 84597): #1 kit per 14 days (every 2 weeks)**

   If no, continue to #3.

3. Is the request for Synarel for a patient who has a diagnosis of moderate to severe pain associated with endometriosis **AND** meet **ALL** of the following criteria?
   - Physician attestation of improvement of pain related to endometriosis while on therapy
   - The patient is receiving concomitant add-back therapy (e.g., combination estrogen-progestin or progestin-only contraceptive preparation)
   - The patient has **NOT** received a total course of Synarel therapy exceeding 12 months

   If yes, **approve for 6 months with the following quantity limits:**
   - **Synarel 2mg/mL (GPID 84354): #96mL per 180 days (#12 bottles).**

   If no, continue to #4.

4. Is the request for Synarel or Leuprolide (generic) for a patient who has a diagnosis of central precocious puberty (CPP) **AND** meet **ALL** of the following criteria?
   - Physician attestation for **ALL** of the following:
     - Tanner scale staging at initial diagnosis of CPP has stabilized or regressed during three separate medical visits in the previous year
     - Patient has not reached actual age which corresponds to current pubertal age

   If yes, **approve for 12 months for the requested agent and strength with the following quantity limits:**
   - **Synarel 2mg/mL (GPID 84354): #32mL per 30 days (#4 bottles).**
   - **Leuprolide 1mg/0.2mL (generic) (GPID 84597): approve with no quantity limit.**

   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

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GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST

RENEWAL CRITERIA (CONTINUED)

RENEWAL DENIAL TEXT: The guideline named **GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST** requires that the patient has gender dysphoria or a diagnosis of advanced prostate cancer, moderate to severe pain associated with endometriosis, or central precocious puberty (CPP). In addition, the following criteria must also be met for the requested diagnosis:

Patients diagnosed with moderate to severe pain associated with endometriosis, approval requires:

- The request is for Synarel
- Physician attestation of improvement of pain related to endometriosis while on therapy
- The patient is receiving concomitant add-back therapy (e.g., combination estrogen-progestin or progestin-only contraceptive preparation)
- The patient has **NOT** received a total course of Synarel therapy exceeding 12 months

Patients diagnosed with CPP, approval requires:

- The request is for Synarel or Leuprolide (generic) with physician attestation of all of the following:
  - Tanner scale staging at initial diagnosis of CPP has stabilized or regressed during three separate medical visits in the previous year
  - Patient has not reached actual age which corresponds to current pubertal age

Requests for Eligard or Leuprolide (generic) for patients with advanced prostate cancer will be approved without additional criteria.

Requests for patients with gender dysphoria will be approved without requiring additional criteria.

RATIONALE

Promote appropriate utilization of **GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST** (Eligard, Leuprolide acetate [generic], and Synarel) based on FDA approved indications and dosing.

FDA APPROVED INDICATIONS

Eligard is a GnRH agonist indicated for the palliative treatment of advanced prostate cancer.

Leuprolide acetate is a GnRH agonist indicated for the palliative treatment of advanced prostate cancer and treatment of children with central precocious puberty.

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GONADOTROPIN RELEASING HORMONE (GNRH) AGONIST

FDA APPROVED INDICATIONS (CONTINUED)

Synarel is a GnRH agonist indicated for the 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.

Synarel is indicated for the treatment of central precocious puberty (gonadotropin-dependent precocious puberty) in children of both sexes.

DOSAGE AND ADMINISTRATION

Eligard:
Eligard is administered subcutaneously as follows: 7.5 mg every month, 22.5 mg every 3 months, 30 mg every 4 months, and 45 mg every 6 months.

Leuprolide acetate:

	Indication	Dosing
Leuprolide acetate	Prostate cancer	1 mg subcutaneously daily
	Central precocious puberty	Initial: 50 mcg/kg/day given subcutaneously; titrate dose upward by 10 mcg/kg/day if down-regulation is not achieved. Higher mg/kg doses may be required in younger children.

Synarel:
For the management of endometriosis, the recommended daily dose of Synarel is 400 µg. This is achieved by one spray (200 µg) into one nostril in the morning and one spray into the other nostril in the evening. Treatment should be started between days 2 and 4 of the menstrual cycle. Occasionally, the 400 µg daily dose may not produce amenorrhea. For these patients with persistent regular menstruation after 2 months of treatment, the dose of Synarel may be increased to 800 µg daily. The 800 µg dose is administered as one spray into each nostril in the morning (a total of two sprays) and again in the evening.

For the management of CPP, the recommended daily dose of Synarel is 1600 µg. The dose can be increased to 1800 µg daily if adequate suppression cannot be achieved at 1600 µg/day. The 1600 µg dose is achieved by two sprays (400 µg) into each nostril in the morning (4 sprays) and two sprays into each nostril in the evening (4 sprays), a total of 8 sprays per day. The 1800 µg dose is achieved by 3 sprays (600 µg) into alternating nostrils three times a day, a total of 9 sprays per day. The patient's head should be tilted back slightly, and 30 seconds should elapse between sprays.

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REFERENCES

- Eligard [Prescribing Information]. Tolmar Pharmaceuticals, Inc. Fort Collins, CO. Nov 2017.
- Leuprolide acetate [Prescribing Information]. Sandoz Inc. Princeton, NJ. Aug 2017.
- Synarel [Prescribing Information]. Pfizer Inc. New York, NY. Dec 2017.

Library	Commercial	NSA
Yes	Yes	No

Part D Effective: N/A
Commercial Effective: 10/01/18
Created: 09/18
Client Approval: 09/18
P&T Approval: 07/18