1. **Background:**

Leuprolide acetate is a synthetic nonapeptide analog of naturally occurring gonadotropin releasing hormone (GnRH) or luteinizing hormone-releasing hormone (LH-RH) which acts as a potent inhibitor of gonadotropin secretion when given continuously in therapeutic doses. Consequently, tissues and functions that depend on gonadal steroids for their maintenance become quiescent. \(^{10}\)

Subcutaneously (SC) administered leuprolide acetate (Eligard and generics) is FDA-labeled for the palliative treatment of advanced prostate cancer. \(^1,2\)

In addition to prostate cancer, The National Cancer Comprehensive Network (NCCN) recommends leuprolide acetate for the treatment of breast cancer and ovarian cancer. \(^3\) However, the NCCN recommendations for these cancers are for the depot formulations of leuprolide, which are covered under the medical benefit.

While a depot formulation of leuprolide (Lupron Depot-Ped) is FDA labeled for the treatment of central precocious puberty (CPP), \(^4\) clinical evidence supports the use of daily SC administered leuprolide acetate for the same indication. \(^5\) CPP is defined as early onset of secondary sexual characteristics, generally earlier than 8 years of age in girls and 9 years of age in boys, associated with pubertal pituitary gonadotropin activation. Leuprolide prescribing information states that prior to initiation of treatment, a clinical diagnosis of CPP should be confirmed by blood concentration of luteinizing hormone (LH) (basal or stimulated with a GnRH analog) and assessment of bone age versus chronological age. \(^4\) Once therapy is initiated, CPP patients should be evaluated every 3 to 6 months for pubertal development and growth, and bone age should be measured radiographically every 6 to 12 months. \(^5\)

Clinical evidence also supports the use of leuprolide as part of an assisted reproductive technology (ART) protocol in the treatment of infertility. ‘Long protocols’ most commonly utilized in ART include leuprolide initiation on day 21-24 of the menstrual cycle that occurs prior to the planned ovarian stimulation cycle. Leuprolide administration (in combination with FSH) then continues during oocyte stimulation until sufficient follicular development is attained. \(^6-8,11\)

2. **Coverage Criteria:**

This criteria provides parameters for coverage of oncology indications based upon the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium. TM The Compendium lists the appropriate drugs and biologics for specific cancers using US Food and Drug Administration
(FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

UnitedHealthcare recognizes indications and uses of leuprolide acetate listed in the NCCN Drugs and Biologics Compendium with Categories of Evidence and Consensus of 1, 2A, and 2B as proven and Categories of Evidence and Consensus of 3 as unproven.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

A. Patients less than 19 years of age

1. Initial Authorization
   a. Eligard, leuprolide acetate bulk powder®, or generic leuprolide acetate 1 mg/0.2 mL injection kit will be approved based on both of the following criteria:
      (1) Patient has an oncology diagnosis
      -AND-
      (2) Patient is less than 19 years of age

   Authorization will be issued for 12 months.

2. Reauthorization
   a. Eligard, leuprolide acetate bulk powder®, or generic leuprolide acetate 1 mg/0.2 mL injection kit will be approved based on the following criterion:
      (1) Patient does not show evidence of progressive disease while on therapy

   Authorization will be issued for 12 months.

B. Treatment of Prostate Cancer

1. Initial Authorization
   a. Eligard, leuprolide acetate bulk powder®, or generic leuprolide acetate 1 mg/0.2 mL injection kit will be approved based on the following criteria:
      (1) For the palliative treatment of advanced prostate cancer

   Authorization will be issued for 12 months.

2. Reauthorization
   a. Eligard, leuprolide acetate bulk powder®, or generic leuprolide acetate 1 mg/0.2 mL injection kit will be approved based on the following criterion:
      (1) Patient does not show evidence of progressive disease while on therapy

   Authorization will be issued for 12 months.
mL injection kit will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on therapy

Authorization will be issued for 12 months.

C. Treatment of Central Precocious Puberty (CPP) [off-label]

1. Initial Authorization

a. Generic leuprolide acetate 1 mg/0.2 mL injection kit or leuprolide bulk powder
   will be approved based on all of the following criteria:

   (1) Diagnosis of central precocious puberty (idiopathic or neurogenic)

   -AND-

   (2) Onset of secondary sexual characteristics in one of the following:

      (a) Females ≤ 8 years of age
      (b) Males ≤ 9 years of age

   -AND-

   (3) Confirmation of diagnosis as defined by one of the following:

      (a) A pubertal luteinizing hormone response to a GnRH stimulation test
      (b) Bone age advanced one year beyond the chronological age

   Authorization will be issued for 12 months.

2. Reauthorization

a. Generic leuprolide acetate 1 mg/0.2 mL injection kit or leuprolide acetate bulk
   powder
   will be approved based on the following criterion:

   (1) Documentation of bone age monitoring (e.g., radiographic imaging)

   Authorization will be issued for 12 months.

D. Treatment of Infertility [off-label]*

1. Generic leuprolide acetate 1 mg/0.2 mL injection kit or leuprolide bulk powder
   will be approved based on both of the following criteria*:

   a. Diagnosis of infertility

   -AND-
b. Used as part of an assisted reproductive technology (ART) protocol

Authorization will be issued for 2 months.

3. Additional Clinical Rules:

Supply limitations may be in place.

*Infertility is typically excluded from coverage for UnitedHealthcare. Please refer to member’s specific benefits for coverage determination.

ǂLeuprolide bulk powder is also subject to Compounds and Bulk Powders Notification criteria.

4. References:

<table>
<thead>
<tr>
<th>Program</th>
<th>Prior Authorization/Notification - leuprolide acetate (bulk powder, 1 mg/0.2 mL injection, Eligard)</th>
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**Change Control**

<table>
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<tr>
<th>Date</th>
<th>Description</th>
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<tbody>
<tr>
<td>7/2014</td>
<td>Annual review. Revised age criterion for CPP to ≤ 8 years of age in females and ≤ 9 years of age in males. Simplified criteria for leuprolide bulk powder and added note that Compounds and Bulk Powders Notification criteria apply as well.</td>
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<tr>
<td>7/2015</td>
<td>Annual review. Revised criterion for CPP with no change to clinical intent. Updated references.</td>
</tr>
<tr>
<td>6/2016</td>
<td>Annual review. No changes to criteria. Updated references.</td>
</tr>
<tr>
<td>6/2017</td>
<td>Annual review. No changes to criteria. Updated references.</td>
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