**Pharmacy Medical Necessity Guidelines: Leuprolide Acetate**

*Effective: May 13, 2019*

<table>
<thead>
<tr>
<th>Prior Authorization Required</th>
<th>Type of Review – Care Management</th>
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<td>Type of Review – Care Management</td>
<td>MED</td>
<td>Department to Review</td>
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These pharmacy medical necessity guidelines apply to the following:

**Commercial Products**
- Tufts Health Plan Commercial products – large group plans
- Tufts Health Plan Commercial products – small group and individual plans
- Tufts Health Freedom Plan products – large group plans
- Tufts Health Freedom Plan products – small group plans
- CareLink<sup>SM</sup> – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

**Tufts Health Public Plans Products**
- Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
- Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
- Tufts Health RITogether – A Rhode Island Medicaid Plan

**Fax Numbers:**
- MM: 888.415.9055

**Note:** This guideline does not apply to Medicare Members (includes dual eligible Members).

**OVERVIEW**

**FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS**

**Eligard** (leuprolide acetate) Kit for Subcutaneous Use is indicated for the palliative treatment of advanced prostate cancer.

**Leuprolide** (leuprolide acetate) injection is indicated in the palliative treatment of advanced prostatic cancer.

**Lupron Depot** (leuprolide acetate for depot suspension) 7.5 mg for 1-month administration, 22.5 mg for 3-month administration, 30 mg for 4-month administration, and 45 mg for 6-month administration are indicated in the palliative treatment of advanced prostatic cancer.

**Lupron Depot** (leuprolide acetate for depot suspension) 3.75 mg for 3-month administration is indicated
- For management of endometriosis, including pain relief and reduction of endometriotic lesions. Duration of initial treatment or retreatment should be limited to 6 months.
- Concomitantly with iron therapy for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata. The clinician may wish to consider a one-month trial period on iron alone inasmuch as some of the patients will respond to iron alone. Lupron Depot may be added if the response to iron alone is considered inadequate. Experience with Lupron Depot in females has been limited to women 18 years of age and older.

**Lupron Depot** (leuprolide acetate for depot suspension) 11.25 mg for 3-month administration is indicated
- For management of endometriosis, including pain relief and reduction of endometriotic lesions. Duration of initial treatment or retreatment should be limited to 6 months.
- Concomitantly with iron therapy for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata. The clinician may wish to consider a one-month trial period on iron alone inasmuch as some of the patients will respond to iron alone. Lupron Depot may be added if the response to iron alone is considered inadequate. Experience with Lupron Depot–3 Month 11.25 mg in females has been limited to women 18 years of age and older treated for no more than 6 months.

**Lupron Depot-Ped** (leuprolide acetate for depot suspension) is indicated in the treatment of children with central precocious puberty.
**COVERAGE GUIDELINES**

The plan may authorize coverage of leuprolide acetate injection, Lupron Depot, Lupron Depot-Ped or Eligard for Members when all the following criteria are met:

**Central Precocious Puberty (Lupron Depot-Ped)**
1. Documented diagnosis of central precocious puberty
2. The Member is ≤18 years of age

**Endometriosis (leuprolide acetate injection, Lupron Depot)**
1. Documented diagnosis of endometriosis
2. Documentation of one of the following:
   a) The Member has tried and failed therapy with, or there is a contraindication or intolerance to, hormonal therapy with one of the following: Oral contraceptives, progestins, or androgens
   b) Member is new to the plan and was stabilized on leuprolide acetate for endometriosis prior to enrollment

**Uterine Leiomyomata (leuprolide acetate, Lupron Depot)**
1. Documented diagnosis of uterine leiomyomata

**Oncology Indications (Eligard, leuprolide acetate, Lupron Depot)**
1. Documented diagnosis of prostate cancer

**Transgender Dysphoria or Status-post Transgender Surgery**
1. Documentation of one of the following:
   a) Diagnosis of transgender dysphoria
   b) Status-post transgender surgery

**Blockade of puberty**
1. Documented use for blockade of puberty
2. The Member is a transgender adolescent
3. The prescriber is an endocrinologist

**Off-label Use Coverage for Other Cancer Diagnoses**
Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia, or in the medical literature, or by the Massachusetts commissioner of Insurance (commissioner) under the provisions of the "Sullivan Law": (M.G.L. c.175, s.47K).

The plan may authorize coverage for use for other cancer diagnoses provided effective treatment with such drug is recognized as a "Medically Accepted Indication" according to the National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium as indicated by a Category 1 or 2A for quality of evidence and level of consensus.

**Note:** The plan requires prescribers to submit clinical documentation supporting the drug’s effectiveness in treating the intended malignancy, including the applicable NCCN guideline(s).

In cases where the requested off-label use for the diagnosis is not recognized by the NCCN Drugs and Biologics Compendium, the plan will follow the Centers for Medicare and Medicaid Services (CMS) guidance, unless otherwise directed by the commissioner, and accept clinical documentation referenced in one of the other "Standard Reference Compendia" noted below or supported by clinical research that appears in a regular edition of a "Peer-Reviewed Medical Literature" noted below.

**"Standard Reference Compendia"**
1. American Hospital Formulary Service – Drug Information (AHFS-DI)
2. Thomson Micromedex DrugDex
3. Clinical Pharmacology (Gold Standard)
4. Wolters Kluwer Lexi-Drugs

**"Peer Reviewed Medical Literature"**
- American Journal of Medicine
- Annals of Internal Medicine
When the plan evaluates the evidence in published, peer-reviewed medical literature, consideration will be given to the following:

1. Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients.
4. Whether the study is appropriate to address the clinical question.
   a) whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover.);
   b) that non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs; and,
   c) that case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

**LIMITATIONS**

- The plan does not provide coverage for Lupron Depot for the treatment of idiopathic short stature.
- Initial requests will be approved for the following durations:
  - Central precocious puberty: Until the age of 18 years
  - Endometriosis: 6 months
  - Uterine leiomyomata: 3 months
- Subsequent authorizations for endometriosis may be given when the following criteria are met:
  - For Members who have been on leuprolide acetate therapy for <12 months – 12 months
    - Documentation of one of the following:
      - The Member is concurrently receiving leuprolide acetate therapy with add-back progestin or estrogen-progestin therapy
      - Provider documents clinical inappropriateness to hormonal therapy and at least one of the following is occurring:
        - Alternative leuprolide regimens (i.e., low dose, longer dosing intervals)
        - Alternative agents are prescribed to address leuprolide acetate's hypoestrogenic (bone density) effects
        - Bone mineral density is closely monitored
  - For Members who have been on leuprolide acetate therapy >12 months – 12 months
    - Documentation the Member has tried and failed surgical interventions, or the provider has documented surgical interventions are not indicated
    - Documentation of one of the following:
      - The Member is concurrently receiving leuprolide acetate therapy with add-back progestin or estrogen-progestin therapy
• Provider documents clinical inappropriateness to hormonal therapy and at least one of the following is occurring:
  o Alternative leuprolide regimens (i.e., low dose, longer dosing intervals)
  o Alternative agents are prescribed to address leuprolide acetate’s hypoestrogenic (bone density) effects
  o Bone mineral density is closely monitored
  o For Members who have been on leuprolide therapy ≥12 months with a surgery in the near future – up to 3 months
    ▪ Documentation the Member has tried and failed surgical interventions, or the provider has documented surgical interventions are not indicated
    AND
    ▪ Documentation the Member has related surgery in the near future

• Subsequent authorizations for uterine leiomyomata may be given in 12 months intervals for Members, when the following criteria are met:
  o Documentation the Member has tried and failed surgical interventions, or the provider has documented surgical interventions are not indicated
  AND
  o Documentation the Member is concurrently receiving leuprolide acetate therapy with add-back progestin or estrogen-progestin therapy
  AND
  o Provider documents clinical inappropriateness to hormonal therapy and at least one of the following is occurring:
    ▪ Alternative leuprolide regimens (i.e., low dose, longer dosing intervals)
    ▪ Alternative agents are prescribed to address leuprolide acetate’s hypoestrogenic (bone density) effects
    ▪ Bone mineral density is closely monitored

CODES
The following HCPCS/CPT code(s) are:

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<th>Code</th>
<th>Description</th>
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<tr>
<td>J1950</td>
<td>Injection, leuprolide acetate (for depot suspension), per 3.75 mg</td>
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<tr>
<td>J9217</td>
<td>Leuprolide acetate (for depot suspension), 7.5 mg</td>
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<tr>
<td>J9218</td>
<td>Leuprolide acetate, per 1 mg</td>
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REFERENCES
11. Lupron Depot (leuprolide acetate for depot suspension 7.5 mg, 22.5 mg, 30 mg, 45 mg) [package insert]. North Chicago, IL: AbbVie Inc.; June 2014.
12. Lupron Depot-Ped (leuprolide acetate for depot suspension 7.5 mg, 11.25 mg, 15 mg, 30 mg) [package insert]. North Chicago, IL: Abbott Laboratories; June 2013.

**APPROVAL HISTORY**

October 2006: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

- August 12, 2014: No Changes
- November 10, 2015: Changed title from Leuprolide, Lupron, Lupron-Depot®, Lupron Depot-Ped®, Eligard® (leuprolide) to Leuprolide Acetate. Removed Lupron, product has been discontinued.
- January 1, 2016: Administrative change to rebranded template.
- May 10, 2016: Added indication of blockade of puberty for adolescent members who are transgender. Removed infertility indication as this coverage is only applicable to Commercial plans.
- April 11, 2017: Administrative update, adding Tufts Health RITogether to the template.
- July 11, 2017: No changes
- July 10, 2018: No changes
- May 7, 2019: Effective May 13, 2019, the Medical Necessity Guideline applies to Tufts Health RITogether. Updated coverage criteria for central precocious puberty to all for coverage until the age of 18 years of age for both males and females. Added the following limitation “The plan does not provide coverage for Lupron Depot for the treatment of idiopathic short stature.”

**BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION**

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member’s health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern.
Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.