Pharmacy Medical Necessity Guidelines: Leuprolide Acetate

Effective: July 10, 2018

<table>
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<tr>
<th>Prior Authorization Required</th>
<th>✓</th>
<th>Type of Review – Care Management</th>
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<tr>
<td>Not Covered</td>
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<td>Type of Review – Clinical Review ✓</td>
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<tr>
<th>Pharmacy (RX) or Medical (MED) Benefit</th>
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<th>Department to Review</th>
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This Pharmacy Medical Necessity Guideline applies to the following:

**Tufts Health Plan Commercial Plans**
- Tufts Health Plan Commercial Plans – large group plans
- Tufts Health Plan Commercial Plans – small group and individual plans

**Tufts Health Public Plans**
- Tufts Health Direct – Health Connector
- Tufts Health Together – A MassHealth Plan
- Tufts Health RITogether – A RItte Care + Rhody Health Partners Plan

**Tufts Health Freedom Plan products**
- Tufts Health Freedom Plan - large group plans
- Tufts Health Freedom Plan - small group plans

**Fax Numbers:**
- MM: 888.415.9055

**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 Injection (leuprolide acetate) 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 and limitations do not apply:

**Central Precocious Puberty (Lupron Depot-Ped)**
1. The Member is a female less than 11 years of age or a male less than 12 years of age

**Endometriosis (leuprolide acetate injection, Lupron Depot)**
1. 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
OR

2. Member is new to the plan and was stabilized on leuprolide for endometriosis prior to enrollment

Uterine Leiomyomata (leuprolide acetate, Lupron Depot)
1. Member has diagnosis of uterine leiomyomata

Oncology Indications (Eligard, leuprolide acetate, Lupron Depot)
1. Member has a diagnosis of prostate cancer

OR

2. Member has another form of cancer and treatment guidelines (see below) support the use of leuprolide for the condition

Transgender Dysphoria or Status-post Transgender Surgery
1. Member has a diagnosis of transgender dysphoria or status-post transgender surgery

Blockade of puberty
1. Member is a transgender adolescent

AND

2. 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
• Annals of Oncology
• Annals of Surgical Oncology
• Biology of Blood and Marrow Transplantation
• Blood
• Bone Marrow Transplantation
• British Journal of Cancer
• British Journal of Hematology
• British Medical Journal
• Cancer
• Clinical Cancer Research
• Drugs
• European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology)
• Gynecologic Oncology
• International Journal of Radiation, Oncology, Biology, and Physics
• The Journal of the American Medical Association
• Journal of Clinical Oncology
• Journal of the National Cancer Institute
• Journal of the National Comprehensive Cancer Network (NCCN)
• Journal of Urology
• Lancet
• Lancet Oncology
• Leukemia
• The New England Journal of 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

1. Initial requests will be approved for the following durations:
   a. Endometriosis: 6 months
   b. Precocious Puberty: Until the age of 11 if female or the age of 12 if male
   c. Uterine Fibroid Tumors: 3 months
   d. Prostate cancer or other forms of cancer: life of plan

2. Subsequent authorizations for endometriosis may be given in 12 month intervals when the Member meets the following criteria:
   a. Member has been on leuprolide therapy for less than 12 months
      AND
   b. Member is concurrently receiving leuprolide with add-back progestin therapy, or add-back estrogen-progestin therapy
      OR
   c. Provider indicates clinical inappropriateness to hormonal therapy and alternative regimens (i.e. low dose leuprolide or longer dosing intervals) or alternative agents being prescribed to address leuprolide’s hypoestrogenic (bone density) effects, or is BMD closely monitored.
      OR
   d. Member has been on leuprolide therapy for 12 months or greater
      AND
   e. Member has tried and failed surgical interventions, or did the provider indicate surgical interventions are not indicated for this patient
      AND
   f. Member is concurrently receiving leuprolide with add-back progestin therapy, or add-back estrogen-progestin therapy
      OR
   g. Provider indicates clinical inappropriateness to hormonal therapy and alternative regimens (i.e. low dose leuprolide or longer dosing intervals) or alternative agents being prescribed to address leuprolide’s hypoestrogenic (bone density) effects, or is BMD closely monitored.

3. Subsequent authorizations for endometriosis may be given up to 3 months when the Member meets the following criteria:
   a. Member has been on leuprolide therapy for 12 months or greater
      AND
   b. Member has not tried and failed surgical interventions, or did the provider indicate surgical interventions are not indicated for this patient
      AND
   c. Member has related surgery in the near future.
4. Subsequent authorizations for uterine fibroid tumors may be given in 12 month intervals when the Member meets the following criteria:
   a. Member has tried and failed surgical interventions, or did the provider indicate surgical interventions are not indicated for this patient
      \[ \text{AND} \]
   b. Member is concurrently receiving leuprolide with add-back progestin therapy, or add-back estrogen-progestin therapy
      \[ \text{OR} \]
   c. Provider indicates clinical inappropriateness to hormonal therapy and alternative regimens (i.e. low dose leuprolide or longer dosing intervals) or alternative agents being prescribed to address leuprolide's hypoestrogenic (bone density) effects, or is BMD closely monitored.
5. Subsequent authorizations for endometriosis may be given up to 3 months when the Member meets the following criteria:
   a. Member has not tried and failed surgical interventions, or did the provider indicate surgical interventions are not indicated for this patient
      \[ \text{AND} \]
   b. Member has related surgery in the near future.

**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

**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. They are used in conjunction with a Member’s benefit document and in coordination with the Member’s physician(s). 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.

This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan Members or to certain delegated service arrangements. Unless otherwise noted in the Member’s benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity Guidelines do not apply to CareLinkSM Members. For self-insured plans, drug coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. Applicable state or federal mandates will take precedence.

For Tufts Health Plan Medicare Preferred, please refer to Tufts Health Plan Medicare Preferred Prior Authorization Criteria.

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.