I. Medication Description

Leuprolide is part of a class of medications called gonadotropin-releasing hormone (GnRH) agonists. It is used to decrease levels of certain hormones (testosterone or estrogen) that affect the behavior of certain cells within the body. Leuprolide is used to treat specific conditions in women, men and children such as uterine fibroids, endometriosis, prostate cancer, and precocious puberty.

II. Position Statement

- Requests for use of J1950, J9217, and J9218 with certain diagnostic codes do not require prior authorization and supporting clinical documentation. See Addendum.
- Coverage is determined through a prior authorization process with supporting clinical documentation for all other requests (coverage for indications related to infertility are addressed in the Drug Therapy Guideline for Injectable Fertility Medications).

III. Policy

- Coverage for Eligard® is provided for treatment of Prostate Cancer.
- Coverage for Lupron Depot®/Lupron Depot Ped® is provided for treatment of the following conditions:
  - Prostate Cancer
  - Central Precocious Puberty (idiopathic or neurogenic):
    - Coverage is requested by an endocrinologist AND
    - Patient is less than 11 years old for females or 12 years old for males
      - If age is greater than the above, clear medical necessity of further treatment must be outlined with physician statement an supported by patient chart/progress notes
  - Breast cancer:
    - In men or in premenopausal women with hormone receptor-positive disease AND
    - In combination with appropriate endocrine therapy for recurrent or metastatic disease
  - Ovarian cancer:
    - As a single agent for persistent or recurrent disease OR
    - For clinical relapse in patients with stage II – IV granulosa cell tumors
  - Endometriosis
  - For the preoperative treatment of anemia due to uterine leiomyomata (fibroids)
  - Gender dysphoria
The diagnosis of gender dysphoria and the referral for hormone therapy have been made by a mental health professional in accordance with the WPATH criteria **AND**

- The patient must be followed by an endocrinologist **AND**
- If used for suppression of puberty, therapy should not be started earlier than Tanner stage 2

- **Coverage for Lupaneta®** is provided for the treatment of endometriosis.
- **Coverage for leuprolide injection** is provided for the treatment of the following conditions:
  - Prostate cancer
  - Central precocious puberty (idiopathic or neurogenic):
    - Treatment is requested by an endocrinologist **AND**
    - Patient is less than 11 years old for females or 12 years old for males
    - If age is greater than the above, clear medical necessity of further treatment must be outlined with physician statement and supported by patient chart/progress notes

### IV. Quantity Limitations

- **Eligard®**: 45mg every 6 months
- **Lupron Depot®/Lupron Depot Ped®**:
  - Prostate cancer: 45mg every 6 months
  - Central precocious puberty: 15mg every month (180mg every 12 months)
  - All other indications: 11.25mg every 3 months (22.5mg every 6 months)
- **Lupron®**: to allow for desired response within FDA-dosing guidelines
- **Lupaneta**:
  - Leuprolide: 11.25mg every 3 months
  - Norethindrone 5mg tablets: 90 every 3 months

### V. Coverage Duration

Coverage will be provided as follows:

- Prostate cancer: indefinite approval
- Central Precocious Puberty:
  - Until female patient reaches 11 years of age
  - Until male patient reaches 12 years of age
- Endometriosis, Breast Cancer, Ovarian Cancer: 6 months and may be renewed
- Uterine Fibroids: 3 months and may be renewed
- Gender dysphoria: 12 months and may be renewed

### VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Prostate Cancer: n/a
• Breast Cancer, Ovarian Cancer:
  o Tumor response with stabilization of disease or decrease in size of tumor or tumor spread AND
  o Absence of unacceptable toxicity from the drug

• Central Precocious Puberty:
  o Absence of unacceptable toxicity from the drug AND
  o One of the following is true:
    ▪ Patient’s age is less than 11 years for females and 12 years for males OR
    ▪ If age is greater than the above, clear medical necessity of further treatment is outlined with physician statement and supported by patient chart/progress notes

• Uterine fibroids/Endometriosis:
  o Renewal is dependent on recurrence of symptoms AND
  o There is an absence of unacceptable toxicity from the drug AND
  o Documentation of why member cannot undergo surgical intervention is provided AND
  o If used longer than 12 months, appropriate periodic bone mineral density assessment is ensured

• Gender dysphoria:
  o Absence of unacceptable toxicity from the drug AND
  o Chart notes assessing pubertal development, height, weight, BMI, bone age, bone mineral density AND
  o Physician statement outlining medical necessity and treatment plan

VII. Billing/Coding Information

• Eligard®
  o Available as 7.5mg, 22.5mg, 30mg, and 45mg suspension
  o J9217 - 1 billable unit equals 7.5mg
  o Available as a medical benefit

• Lupron Depot®/Lupron Depot Ped®
  o Available as 3.75mg, 7.5mg, 11.25mg, 15mg, 22.5mg, 30mg, 45mg powder for suspension
  o J1950 - 1 billable unit equals 3.75 mg
  o J9217 – 1 billable unit equals 7.5 mg
  o Available as a medical benefit

• Leuprolide injection
  o Available as 1mg/0.2ml solution
  o J9218 - 1 billable unit equals 1 mg
  o Available as a medical benefit and a pharmacy benefit

• Lupaneta®
  o Available as a 1-month kit containing 3.75mg leuprolide acetate for suspension with 30 count bottle of 5mg norethindrone oral tablets and 3-month kit containing 11.25mg leuprolide acetate for suspension with 90 count bottle of 5mg norethindone oral tablets
  o J3490
  o Available as a medical benefit
• Pertinent diagnoses:
  o Breast cancer: C50.019, C50.029, C50.119, C50.219, C50.319, C50.419, C50.519, C50.619, C50.819, C50.919, C50.929, Z85.3
  o Central Precocious Puberty: E30.1, E30.8
  o Endometriosis: N80.0, N80.1, N80.2, N80.3, N80.4, N80.5, N80.6, N80.8, N80.9
  o Ovarian Cancer: C48.1, C48.2, C48.8, C56.9, C57.00, C57.01, C57.20, C57.3, C57.4, Z85.43
  o Prostate Cancer: C61, Z85.46
  o Uterine Fibroids: D25.0, D25.1, D25.2, D25.9
  o Gender identity disorder: F64.1, F64.2

VIII. Summary of Policy Changes

• 1/1/12
  o Requirement of iron usage timeframes added for anemia secondary to uterine leiomyomata
  o Quantity allowances and coverage duration revised
  o Removal of diagnosis 198.82 from autopay, will be reviewed
  o Central precocious puberty (259.1) no longer autopay diagnosis, will be reviewed
    ▪ Coverage criteria outlined
    ▪ Renewal criteria outlined
  o Clarification of pharmacy benefit vs. medical benefit made
  o Coverage criteria for breast and ovarian cancers included

• 12/15/12
  o Removal of trial of iron supplementation required for fibroid treatment
  o Addition of monitoring for bone density to warnings
  o Addition of renewal criteria for uterine fibroids/endometriosis to address surgical intervention

• 6/2013: added Lupaneta to policy

• 12/15/13:
  o Change in criteria for ovarian cancer and uterine fibroids
  o Clarified Lupron Depot is not covered under the pharmacy benefit

• 1/1/15:
  o Updated breast cancer coverage criteria to mirror current NCCN treatment guidelines
  o Added quantity limits to Lupaneta
  o Added requirement for periodic bone mineral density screening when treating endometriosis or fibroids for over 12 months

• 3/15/15: Addition of coverage criteria in the setting of gender dysphoria

• 7/1/15: formulary distinctions made

• 10/1/15: ICD9 references omitted

• 6/15/16: no policy changes

• 4/5/17: removed requirement for obtaining documentation of informed consent and laboratory testing when requested for the treatment of gender dysphoria
IX. References

1. UpToDate Online, retrieved March 2011.

Addendum:

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<thead>
<tr>
<th>ICD10</th>
<th>Description</th>
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<tbody>
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<td>C61</td>
<td>Malignant neoplasm of prostate</td>
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The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary agent will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.