Clinical Policy: Leuprolide Acetate (Eligard, Fensolvi, Lupaneta Pack, Lupron Depot, Lupron Depot-Ped)
Reference Number: CP.PHAR.173
Effective Date: 10.01.16
Last Review Date: 08.20
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Leuprolide acetate (Eligard®, Fensolvi®, Lupaneta Pack® [with norethindrone acetate tablets], Lupron Depot®, Lupron Depot-Ped®) is a gonadotropin-releasing hormone (GnRH) receptor agonist.

FDA Approved Indication(s)
Leuprolide acetate is indicated for:
- Palliative treatment of advanced prostate cancer:
  - Leuprolide acetate injection
  - Eligard
  - Lupron Depot (7.5, 22.5, 30, 45)
- Management of endometriosis, including pain relief and reduction of endometriotic lesions:
  - Lupron Depot (3.75, 11.25)
  - Lupaneta Pack (3.75, 11.25)
  Limitation(s) of use: Initial treatment course is limited to 6 months and use is not recommended longer than a total of 12 months due to concerns about adverse impact on bone mineral density.
- Preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata [fibroids] administered concomitantly with iron therapy:
  - Lupron Depot (3.75, 11.25)
  Limitation of use: the recommended treatment is limited to one injection (3 months)
- Treatment of children with central precocious puberty (CPP):
  - Fensolvi
  - Leuprolide acetate
  - Lupron Depot-Ped (7.5, 11.25, 15, 30)

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that leuprolide acetate, Eligard, Fensolvi, Lupaneta Pack, Lupron Depot, and Lupron Depot-Ped are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Prostate Cancer (must meet all):
CLINICAL POLICY
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1. Diagnosis of prostate cancer;
2. Request is for one of the following (a, b, or c):
   a. Leuprolide acetate injection;
   b. Eligard;
   c. Lupron Depot (7.5 mg, 22.5 mg, 30 mg, 45 mg);
3. Prescribed by or in consultation with an oncologist or urologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a, b, or c):*
   a. Leuprolide acetate injection (SC): Dose does not exceed 1 mg per day;
   b. Eligard (SC)/Lupron Depot (IM): Dose does not exceed 7.5 mg per month, 22.5 mg per 3 months, 30 mg per 4 months, 45 mg per 6 months;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration: 12 months

B. Endometriosis (must meet all):
1. Diagnosis of endometriosis;
2. Request is for one of the following (a or b):
   a. Lupron Depot;
   b. Lupaneta Pack (3.75 mg, 11.25 mg);
3. Prescribed by or in consultation with a gynecologist;
4. Age ≥ 18 years;
5. Endometriosis as a cause of pain is one of the following (a or b):
   a. Surgically confirmed;
   b. Clinically suspected and member has failed a 3-month trial of one of the following agents within the last year or has a documented intolerance or contraindication to the agent (i, ii or iii):
      i. A nonsteroidal anti-inflammatory drug;
      ii. An oral or injectable depot contraceptive;
      iii. A progestin;
6. Dose does not exceed 3.75 mg per month or 11.25 mg per 3 months.

Approval duration: 6 months
Total duration of therapy should not exceed 12 months.

C. Uterine Fibroids (must meet all):
1. Diagnosis of anemia secondary to uterine leiomyomata (fibroids) confirmed by ultrasound;
2. Request is for Lupron Depot (3.75 mg, 11.25 mg);
3. Prescribed by or in consultation with gynecologist;
4. Age ≥ 18 years;
5. Prescribed preoperatively to reduce fibroid size and improve hematologic control;
6. Dose does not exceed 3.75 mg per month or 11.25 mg per 3 months.

Approval duration: 3 months
Total duration of therapy should not exceed 6 months.
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D. Central Precocious Puberty (must meet all):
   1. Diagnosis of CPP confirmed by all of the following (a, b, and c):
      a. Elevated basal luteinizing hormone (LH) level > 0.2 - 0.3 mIU/L (dependent on type of assay used) and/or elevated leuprolide-stimulated LH level > 3.3 - 5 IU/L (dependent on type of assay used);
      b. Difference between bone age and chronological age was > 1 year (bone age-chronological age);
      c. Age at onset of secondary sex characteristics is < 8 years if female, or < 9 years if male;
   2. Request is for one of the following (a, b, or c):
      a. Fensolvi;
      b. Leuprolide acetate;
      c. Lupron Depot Ped: 7.5 mg, 11.25 mg, 15 mg, 30 mg;
   3. Prescribed by or in consultation with a pediatric endocrinologist;
   4. Member meets one of the following age requirements (a or b):
      a. Female: 2 - 11 years;
      b. Male: 2 - 12 years;
   5. Dose does not exceed the following (a, b, c, or d):
      a. Diagnostic use: Leuprolide acetate: 20 mcg/kg or as needed;
      b. Therapeutic use: Fensolvi: 45 mg per 6 months;
      c. Therapeutic use: Leuprolide acetate (SC): Initial: 50 mcg/kg per day; titrate dose upward by 10 mcg/kg per day if down-regulation is not achieved (higher mg/kg doses may be required in younger children).
      d. Therapeutic use: Lupron Depot-Ped (IM): 15 mg per month (1-month formulation) or 30 mg per 3 months (3-month formulation) (dosing is weight-based).

Approval duration: 12 months

E. Breast and Ovarian Cancer (off-label) (must meet all):
   1. Diagnosis of breast or ovarian cancer (including fallopian tube and primary peritoneal cancer);
   2. Request is for one of the following (a or b)
      a. Breast cancer: Lupron Depot 3.75 mg;
      b. Ovarian cancer: Lupron Depot 3.75 mg or 11.25 mg;
   3. Prescribed by or in consultation with an oncologist;
   4. Age ≥ 18 years;
   5. Request meets one of the following (a, b, or c):*
      a. Breast or ovarian cancer: Dose does not exceed 3.75 mg per month;
      b. Ovarian cancer: Dose does not exceed 11.25 mg per 3 months;
      c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration: 12 months
F. **Gender Dysphoria (off-label)** (must meet all):
1. Diagnosis of gender dysphoria;
2. Request is not for Lupaneta Pack;
3. Prescribed by or in consultation with an endocrinologist and an expert in gender dysphoria and transgender medicine (e.g., mental health professional such as psychologist, psychiatrist);
4. Age and pubertal development - meets (a or b):
   a. Member has reached or passed through Tanner Stage 2* and is < 18 years of age;
   
   *Age ranges approximating Tanner Stage 2 pubertal development extend from 8 to 13 years of age in girls and 9 to 14 years of age in boys.
   b. Member is ≥ 18 years of age and has failed to achieve physiologic hormone levels with gender-affirming hormonal therapy (e.g., estrogen, testosterone) unless contraindicated or clinically significant adverse effects are experienced;
5. Member demonstrates understanding of expected GnRH analogue treatment outcomes and has given consent for such treatment;
6. If member has a psychiatric comorbidity, member is followed by mental health provider;
7. Psychosocial support will be provided during treatment;
8. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval duration: 12 months**

G. **Salivary Gland Tumors (off-label)** (must meet all):
1. Diagnosis of salivary gland tumors;
2. Disease is androgen receptor positive and recurrent, unresectable, or metastatic;
3. Prescribed by or in consultation with an oncologist;
4. Request is for one of the following (a or b):
   a. Eligard;
   b. Lupron Depot (7.5 mg, 22.5 mg)
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration: Duration of request or through the end of the contract year, whichever is less**

H. **Other diagnoses/indications**
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.
II. Continued Therapy

A. Prostate Cancer (must meet all):
   1. Currently receiving medication via Centene benefit, or documentation supports that the member is currently receiving leuprolide acetate injection, Eligard, or Lupron Depot for prostate cancer and has received this medication for at least 30 days;
   2. Request is for one of the following (a, b, or c):
      a. Leuprolide acetate injection;
      b. Eligard;
      c. Lupron Depot (7.5 mg, 22.5 mg, 30 mg, 45 mg);
   3. Member is responding positively to therapy;
   4. If request is for a dose increase, request meets one of the following (a, b, or c):*
      a. Leuprolide acetate injection (SC): New dose does not exceed 1 mg per day;
      b. Eligard (SC)/Lupron Depot (IM): New dose does not exceed 7.5 mg per month, 22.5 mg per 3 months, 30 mg per 4 months, 45 mg per 6 months;
      c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   *Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration: 12 months

B. Endometriosis (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   2. Request is for Lupron Depot/Lupaneta Pack (3.75 mg, 11.25 mg);
   3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: improvement in dysmenorrhea, dyspareunia, pelvic pain/induration/tenderness, or size of endometrial lesions;
   4. If request is for a dose increase, new dose does not exceed 3.75 mg per month or 11.25 mg per 3 months.

Approval duration: 6 months

Total duration of therapy should not exceed 12 months.

C. Uterine Fibroids (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   2. Request is for Lupron Depot (3.75 mg, 11.25 mg);
   3. Member is responding positively to therapy;
   4. If request is for a dose increase, new dose does not exceed 3.75 mg per month or 11.25 mg per 3 months.

Approval duration: 3 months

Total duration of therapy should not exceed 6 months.

D. Central Precocious Puberty (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
   2. Request is for one of the following (a, b, or c):
a. Fensolvi;  
b. Leuprolide acetate;  
c. Lupron Depot Ped: 7.5 mg, 11.25 mg, 15 mg, 30 mg;

3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: decreased growth velocity, cessation of menses, softening of breast tissue or testes, arrested pubertal progression;

4. Member meets one of the following age requirements (a or b):
   a. Female: ≤ 11 years;  
   b. Male: ≤ 12 years;

5. If request is for a dose increase, new dose does not exceed one of the following (a, b or c):
   a. Leuprolide acetate (SC): Initial: 50 mcg/kg per day; titrate dose upward by 10 mcg/kg per day if down-regulation is not achieved (higher mg/kg doses may be required in younger children);
   b. Lupron Depot-Ped (IM): 15 mg per month (1-month formulation) or 30 mg per 3 months (3-month formulation) (dosing is weight-based);
   c. Fensolvi: 45 mg per 6 months.

Approval duration: 12 months

E. Breast and Ovarian Cancer (off-label) (must meet all):
   1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Lupron Depot for breast cancer or ovarian cancer and has received this medication for at least 30 days;
   2. Request is for one of the following (a or b):
      a. Breast cancer: Lupron Depot 3.75 mg;  
      b. Ovarian cancer: Lupron Depot 3.75 mg or 11.25 mg;
   3. Member is responding positively to therapy;
   4. If request is for a dose increase, request meets one of the following (a, b, or c):*
      a. Breast or ovarian cancer: New dose does not exceed 3.75 mg per month;  
      b. Ovarian cancer: New dose does not exceed 11.25 mg per 3 months;  
      c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration: 12 months

F. Gender Dysphoria (off-label) (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;  
   2. Member is responding positively to therapy;  
   3. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months
G. Salivary Gland Tumors (off-label) (must meet all):
   1. Currently receiving medication via Centene benefit or member has previously met
      initial approval criteria;
   2. Request is for one of the following (a or b):
      a. Eligard;
      b. Lupron Depot (7.5 mg, 22.5 mg);
   3. Member is responding positively to therapy;
   4. If request is for a dose increase, new dose is within FDA maximum limit for any
      FDA-approved indication or is supported by practice guidelines or peer-reviewed
      literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

H. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports
      positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT
      specifically listed under section III (Diagnoses/Indications for which coverage is
      NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance
      marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is
      sufficient documentation of efficacy and safety according to the off label use policies –
      CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and
      CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   CPP: central precocious puberty
   DSM-5: Diagnostic and Statistical
   Manual of Mental Disorders, 5th edition
   FDA: Food and Drug Administration
   GnRH: gonadotropin-releasing hormone
   LH: luteinizing hormone
   NCCN: National Comprehensive Cancer Network

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval
   criteria. The drugs listed here may not be a formulary agent for all relevant lines of business
   and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs*: ibuprofen, naproxen, fenoprofen, ketoprofen, mefenamic acid, meclofenamate, indomethacin, tolmetin, diclofenac, etodolac, diflunisal, meloxicam, piroxicam</td>
<td>Endometriosis Varies – refer to specific prescribing information</td>
<td>Varies – refer to specific prescribing information</td>
</tr>
</tbody>
</table>
Leuprolide Acetate

### Drug Name

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined oral estrogen-progesterone contraceptives: ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone, norgestimate, or norgestrel); estradiol valerate + dienogest; mestranol + norethindrone</td>
<td>Endometriosis 1 tablet PO QD (may vary per specific prescribing information)</td>
<td>1 tablet per day (may vary per specific prescribing information)</td>
</tr>
<tr>
<td>Progestin-only oral contraceptives: norethindrone</td>
<td>Endometriosis 0.35 mg PO QD</td>
<td>0.35 mg per day</td>
</tr>
<tr>
<td>Depot injection progestin contraceptives: medroxyprogesterone acetate</td>
<td>Endometriosis IM: 150 mg per 3 months (every 13 weeks) SC: 104 mg per 3 months (every 12 to 14 weeks)</td>
<td>See regimen</td>
</tr>
</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Examples provided may not be all-inclusive

### Appendix C: Contraindications/Boxed Warnings

- **Contraindication(s):**
  - Known hypersensitivity to GnRH, GnRH agonist analogs or any of the components of the individual products (all leuprolide products);
  - Pregnancy (all leuprolide products except Eligard);
  - Lupron 3.75 mg/11.25 mg and Lupaneta Pack:
    - Undiagnosed abnormal vaginal bleeding;
    - Breast-feeding;
    - If used with norethindrone acetate:
      - Thrombophlebitis, thromboembolic disorders, cerebral apoplexy, or a past history of these conditions;
      - Markedly impaired liver function or liver disease;
      - Known or suspected carcinoma of the breast.

- **Boxed warning(s):** None reported

### Appendix D: Additional Information on Diagnosis-specific HCPCS Codes, Billable Units, and Day Supply

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Requested Product</th>
<th>HCPCS Code</th>
<th>Billable Units</th>
<th>Day Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate Cancer</td>
<td>Leuprolide acetate, per 1 mg</td>
<td>J9218</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Lupron Depot 1-Month &amp; Eligard 7.5 mg</td>
<td>J9217</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Lupron Depot 3-Month &amp; Eligard 22.5 mg</td>
<td></td>
<td>3</td>
<td>84</td>
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## V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuprolide acetate injection</td>
<td>Prostate cancer</td>
<td>Leuprolide acetate injection (SC): 1 mg per day</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 7.5, 22.5, 30, 45)</td>
<td></td>
<td>Lupron Depot (IM) - 7.5 mg per month; 22.5 mg per 3 months; 30 mg per 4 months; 45 mg per 6 months</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate (Eligard 7.5, 22.5, 30, 45)</td>
<td></td>
<td>Eligard (SC) - 7.5 mg per month; 22.5 mg per 3 months; 30 mg per 4 months; 45 mg per 6 months</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 3.75, 11.25)</td>
<td>Endometriosis</td>
<td>Lupron Depot/Lupaneta Pack (IM) - 3.75 mg per month; 11.25 mg per 3 months</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupaneta Pack 3.75, 11.25)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 3.75)</td>
<td>Uterine fibroids</td>
<td>Lupron Depot (IM) - 3.75 mg/month, 11.25 mg per 3 months</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate injection</td>
<td>CPP</td>
<td>Leuprolide acetate (SC):</td>
<td>See regimen</td>
</tr>
</tbody>
</table>
### CLINICAL POLICY

#### Leuprolide Acetate

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuprolide acetate (Lupron Depot-Ped 7.5, 11.25, 15 [1 mo]; 11.25, 30 [3 mo])</td>
<td>- Diagnostic: 20 mcg/kg or as needed; - Treatment: Initial: 50 mcg/kg/day; titrate dose upward by 10 mcg/kg/day if down-regulation is not achieved (higher mcg/kg doses may be required in younger children).</td>
<td>Lupron Depot-Ped (IM): Monthly administration weight-based starting dose: 7.5 mg (≤ 25 kg), 11.25 mg (&gt; 25 to 37.5 kg), 15 mg (&gt; 37.5 kg) (increase as needed to 15 mg/month); 3-month administration: 11.25 mg or 30 mg</td>
<td>See regimen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fensolvi (SC): 45 mg once every six months</td>
<td></td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 3.75)</td>
<td>Breast cancer</td>
<td>Lupron Depot (IM) 3.75 mg per month</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 3.75, 11.25)</td>
<td>Ovarian cancer</td>
<td>Lupron Depot (IM) 3.75 mg per month, 11.25 mg per 3 months</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 7.5, 22.5)</td>
<td>Salivary Gland tumors</td>
<td>Lupron Depot (IM) - 7.5 mg per month; 22.5 mg per 3 months. Eligard (SC) - 7.5 mg per month; 22.5 mg per 3 months; 30 mg per 4 months; 45 mg per 6 months</td>
<td>See regimen</td>
</tr>
<tr>
<td>Leuprolide acetate (Eligard 7.5, 22.5, 30, 45)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**VI. Product Availability**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuprolide acetate injection</td>
<td>Kit: 2.8 mL multi-dose vial (1 mg/0.2 mL)</td>
</tr>
<tr>
<td>Leuprolide acetate (Eligard)</td>
<td>Kit: 7.5 mg (1 month), 22.5 mg (3 month), 30 mg (4 month), 45 mg (6 month)</td>
</tr>
<tr>
<td>Leuprolide acetate and norethindrone tablets (Lupaneta Pack)</td>
<td>Pack: 3.75 mg leuprolide acetate syringe (1 month) with 5 mg norethindrone tablets Pack: 11.25 mg leuprolide acetate syringe (3 month) with 5 mg norethindrone tablets</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot)</td>
<td>Prefilled syringe: 7.5 mg (1 month), 22.5 mg (3 month), 30 mg (4 month), 45 mg (6 month)</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 3.75)</td>
<td>Prefilled syringe: 3.75 mg (1 month)</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Availability</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot 11.25)</td>
<td>Prefilled syringe: 11.25 mg (3 month)</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron Depot-Ped)</td>
<td>Prefilled syringe: 7.5 mg (1 month), 11.25 mg (1 month), 15 mg (1 month)</td>
</tr>
<tr>
<td></td>
<td>Prefilled syringe: 11.25 mg (3 month), 30 mg (3 month)</td>
</tr>
<tr>
<td>Leuprolide acetate (Fensolvi)</td>
<td>Kit: syringe A: prefilled with diluent for reconstitution</td>
</tr>
<tr>
<td></td>
<td>and syringe B: prefilled with 45 mg lyophilized leuprolide acetate powder</td>
</tr>
</tbody>
</table>

VII. References

Gender Dysphoria

Coding Implications*
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>HCPSC Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J1950</td>
<td>Injection, leuprolide acetate (for depot suspension), per 3.75 mg</td>
</tr>
<tr>
<td>J9217</td>
<td>Leuprolide acetate (for depot suspension), 7.5 mg</td>
</tr>
<tr>
<td>J9218</td>
<td>Leuprolide acetate, per 1 mg</td>
</tr>
<tr>
<td>J9219</td>
<td>Leuprolide acetate implant, 65 mg</td>
</tr>
</tbody>
</table>

*See Appendix D: Additional Information on Diagnosis-specific HCPSC Codes, Billable Units, and Day Supply
<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age removed.</td>
<td>01.17</td>
<td>02.17</td>
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<tr>
<td>Formulations added.</td>
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<tr>
<td>Off-label NCCN recommended uses added (prostate and breast cancer; doses removed; 3-month injectable requirement removed).</td>
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<tr>
<td>Age and dosing added to oncology criteria; age added to gynecology criteria.</td>
<td>09.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Positive therapeutic response examples added to oncology and endometriosis criteria.</td>
<td></td>
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<tr>
<td>Oncology FDA/NCCN (categories 1 and 2A) indications listed separately.</td>
<td></td>
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<tr>
<td>Pelvic pain criteria deleted with direction to suspected endometriosis if appropriate.</td>
<td></td>
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<tr>
<td>Endometriosis step therapy edited from estrogen/progestin OC to OC or depot contraceptive or progestin.</td>
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<tr>
<td>Total approval duration increased from 6 to 12 months.</td>
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<tr>
<td>Concomitant iron therapy and specific time period within which surgery must be performed are removed from fibroid criteria. Total approval duration increased from 3 to 6 months.</td>
<td></td>
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<tr>
<td>Specialist requirement added for endometriosis, fibroids, CPP. Safety information removed with exception of pregnancy.</td>
<td></td>
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<tr>
<td>4Q 2018 annual review; policies combined for Centene Medicaid and HIM (HIM.PA.SP51); no significant changes; for oncology, summarized NCCN and FDA-approved uses for improved clarity (limited to diagnosis); specialist involvement in care and continuation of care added; references reviewed and updated.</td>
<td>08.07.18</td>
<td>11.18</td>
</tr>
<tr>
<td>Addition of gender dysphoria as off-label use.</td>
<td>07.16.19</td>
<td>08.19</td>
</tr>
<tr>
<td>4Q 2019 annual review: added Commercial and HIM-Medical Benefit line of business, added notation that Lupron Depot-Ped (3 month) 11.25 mg strength is non-formulary for HIM; for prostate cancer added urologist specialist option; references reviewed and updated.</td>
<td>08.01.19</td>
<td>11.19</td>
</tr>
<tr>
<td>3Q 2020 annual review: revised HIM-Medical Benefit to HIM line of business; added Fensolvi (new dosage form) to the policy for Central Precocious Puberty; added off-label NCCN indication and criteria for salivary gland tumor; references reviewed and updated.</td>
<td>05.07.20</td>
<td>08.20</td>
</tr>
<tr>
<td>Added Appendix D: Additional Information on Diagnosis-specific HCPCS Codes, Billable Units, and Day Supply.</td>
<td>01.25.21</td>
<td></td>
</tr>
</tbody>
</table>

**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional...
organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.