CLINICAL MEDICATION POLICY	
Policy Name:	Lupron Depot® and Lupron Depot-PED® (leuprolide acetate)
Policy Number:	MP-046-MD-DE
Responsible Department(s):	Medical Management; Clinical Pharmacy
Provider Notice Date:	01/15/2018
Issue Date:	02/15/2018
Effective Date:	02/15/2018
Annual Approval Date:	12/15/2018
Revision Date:	N/A
Products:	Highmark Health Options Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 9

DISCLAIMER

Highmark Health Options medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Highmark Health Options may provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary intramuscular injection of Lupron depot and Lupron depot-PED (leuprolide acetate).

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Delaware Department of Health and Social Services (DHSS) and all applicable state and federal regulations.

DEFINITIONS

Lupron Depot and Lupron Depot-PED (leuprolide acetate) – A drug that is a manufactured version of a hormone. It is a hormone-releasing hormone agonist which is a synthetic analog of naturally occurring gonadotropin-releasing hormone (GnRH) possessing greater potency than the natural hormone. Lupron Depot is indicated for several conditions, including prostate cancer, endometriosis, and uterine leiomyomas. Lupron Depot-PED is indicated in the treatment of children with central precocious puberty (CPP).

Endometriosis – The abnormal growth of endometrial cells similar to those that form on the inside of the uterus, but in a location outside of the uterus. Endometriosis is most commonly found on other organs of the pelvis. The condition is common in women who are experiencing infertility.

Add-back therapy – When Lupron Depot is used alone, bone thinning and hot flashes can occur. The therapy adds back a small amount of the hormone progestin, which can help the patient manage side effects, without interfering with the Lupron depot injection.

Uterine leiomyomas (fibroid tumors) – Benign tumors that arise from the overgrowth of smooth muscle and connective tissue in the uterus.

Central precocious puberty (CPP) – A condition where a child goes through puberty sooner than normal. CPP is triggered when the brain tells the pituitary gland to release puberty hormones called gonadotropin-releasing hormone (GnRH) agonist too soon. When a child's body is ready to begin puberty, the hypothalamus releases the GnRH causing the pituitary gland to release two other hormones: luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH and FSH stimulate the ovaries to produce estrogen or the testicles to produce testosterone.

Transsexualism (per ICD-10): the desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone replacement therapy.

Gender Dysphoria (per DSM-V): is the distress and unease experienced if gender identity and sex are not completely congruent.

Real-Life Experience (per WPATH): adopting a new or evolving gender role or gender presentation in everyday life. This experience tests the person's resolve, capacity to function fully as the desired gender prior to seeking semi-reversible or totally irreversible treatment.

PROCEDURES

1. Lupron Depot and Lupron Depot-PED is considered medically necessary as an intramuscular injection when the member meets the following criteria:

    A. **Palliative treatment of advanced prostate cancer**
        i. The prescribing physician must be a Hematologist or Oncologist; AND
        ii. The member is receiving palliative treatment for advanced prostatic cancer; AND

iii. The disease must be locally advanced, recurrent, or metastatic;

OR

B. **Endometriosis**

1) The member is aged 18 years or older; AND
2) There is a confirmed diagnosis of Endometriosis by laparoscopy resistant to conventional treatment (e.g. oral contraceptives, NSAIDS); OR
3) There is endometriosis not confirmed by laparoscopy; AND
    a) An evaluation to exclude other causes of pelvic pain, such as irritable bowel syndrome (IBS), interstitial cystitis, fibromyalgia and musculoskeletal disorders (e.g. trigger point pain and pelvic floor dysfunction) should be pursued prior to therapy for endometriosis; AND
    b) Abnormalities of the urinary, gastrointestinal, neurologic and musculoskeletal systems as well as manifestations of psychological or psychiatric disorders have been ruled out as sources of pelvic pain; AND
4) Add back therapy with norethindrone acetate 5mg while on Lupron to help prevent bone density loss and/or hot flash side effects will be recommended; AND
5) For reauthorization:
    a) There is documentation of the reason for retreatment when a second course of treatment is requested;

OR

C. **Uterine leiomyomata (fibroids)**

1) The member is aged 18 years or older; AND
2) The member is a female; AND
3) The member's uterine leiomyomata(s) is(are) resistant to conventional treatment; AND
4) This drug is being used preoperatively to shrink fibroid(s) and to allow for a less invasive surgical approach other than abdominal hysterectomy; AND
5) The member has failed a one month trial of iron therapy if anemia is present; AND
6) Coverage will be approved for 3 months (one treatment course) when criteria is met; AND
7) For reauthorization:
    a) If a second course of treatment is requested, documentation of the reason for delay in surgery is required;

OR

D. **Central precocious puberty (CPP)**

Prior to initiation of treatment, a clinical diagnosis of CPP should be confirmed by:

1) Baseline LH and FSH measurements in the pubertal response to a GnRH/ LUPRON DEPOT stimulation test performed (defined as >/=2 standard deviations above the gender/age related mean); AND
2) The prescribing physician must be a Pediatric Endocrinologist; AND
3) The member receives a baseline evaluation including height, weight, sex steroid levels, and adrenal steroid levels; AND
4) Neuro-imaging (CT or MRI) of the brain and pituitary/hypothalamic area to rule out CNS lesions; AND
5) If a male child, beta human chorionic gonadotropin level to rule out a chorionic gonadotropin secreting tumor; AND
6) There is documentation of the age of onset of secondary sexual characteristics occurred (Females: ≤ 8 years of age OR Males: ≤ 9 years of age); OR

7) There is documentation of current age (Females: < 11 years of age OR Males: < 12 years of age); AND
8) Coverage will be approved for 12 months when criteria is met;
9) For reauthorization:
    a) There is documentation that the member has had a physical exam in the prescribing physician's office within the past year; AND
    b) There is documentation of current age (Females: <11 years of age OR Males: <12 years of age) and evaluation of pubertal development and bone age;

OR

E. Puberty suppression therapy for gender dysphoria

Prior to treatment initiation, adolescents must meet the following criteria:

1) The member has experienced puberty to Tanner stage 2; AND
2) The member fulfills DSM-V and/or ICD-10 criteria for gender dysphoria (formally known as; gender Identity disorder) by a mental health professional with the appropriate expertise in the treatment of children and adolescents with gender dysphoria (See Appendix A or B for age appropriate applicability); OR
3) The member is diagnosed with transsexualism by a mental health professional with the appropriate expertise in the treatment of children and adolescents with transsexualism (See Appendix A or B for age appropriate applicability); AND
4) The adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed); AND
5) Gender dysphoria emerged or worsened with the onset of puberty; AND
6) Any co-existing psychological, medical, or social problems that could interfere with treatment have been addressed, such that the adolescent's situation and function are stable enough to start treatment; AND
7) The adolescent has given informed consent and, particularly when the adolescent has not reached the age of medical consent, the parents, other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process; AND
    a) When parental consent cannot be obtained, exceptions will be reviewed on a case by case basis and in conjunction with the behavioral health provider.
8) The member does not suffer from comorbid psychiatric illnesses that would interfere with treatment; AND
9) Puberty suppressing hormones that are deemed necessary for treatment are prescribed by or in consultation with a provider that is experienced and specialized in pediatric physical and psychological development. LUPRON DEPT must be prescribed in a manner consistent with the current World Professional Association for Transgender Health (WPATH) standards of care for the health of transsexual, transgender and gender nonconforming people. Appropriate providers may include:
    a) Mental health professional(s) specializing in pediatrics OR
    b) Pediatric endocrinologist OR
    c) Adolescent medicine specialist OR
    d) Medical provider with experience and/or training in transgender medicine;

AND

10) The documentation of clinical and laboratory monitoring every 6 months; AND
11) **For reauthorization**:

a) There is documentation indicating stability or improvement in gender dysphoria; AND
b) There is documentation of continued need to delay puberty (until the age of 18 years old).

2. Contraindications
   LUPRON DEPOT is contraindicated in individuals with known hypersensitivity to GnRH agonists or any of the excipients in LUPRON DEPOT.

   LUPRON DEPOT is contraindicated for pregnant women because the drug may cause fetal harm. Expected hormonal changes that occur with LUPRON DEPOT treatment increase the risk for pregnancy loss and fetal harm when administered to a pregnant women. LUPRON DEPOT is also contraindicated in women who may become pregnant while taking the drug.

   Patients should not receive add-back therapy plus LUPRON DEPOT if the patient has a clotting disorder, heart disease, stroke, impaired liver function or liver disease, or breast cancer.

3. When the LUPRON DEPOT services are not covered
   LUPRON DEPOT is not covered for any condition not listed above because the scientific evidence has not been established.

   Coverage may be provided for any non-FDA labeled indication or a medically accepted indication that is supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis for which it is prescribed and will be reviewed on a case-by-case basis to determine medical necessity.

   When non-formulary criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

4. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Health Options at any time pursuant to the terms of your provider agreement.

5. Place of Service
   The place of service for the administration of LUPRON DEPOT is outpatient.

GOVERNING BODIES APPROVAL

In January 1996, the FDA approved a 3-month therapy of LUPRON DEPOT for the treatment of advanced-stage prostate cancer. In July 1997, the drug was approved for a 4-month therapy in the palliative treatment of advanced prostate cancer.

In June 1999, the FDA approved LUPRON DEPOT for the treatment of endometriosis and uterine fibroids for a 3-month depot formulation.

On August 17, 2011, the FDA approved LUPRON DEPOT-PED for the treatment of central precocious puberty within children. The drug helps to arrest pubertal development until a more appropriate time.

CODING REQUIREMENTS

Covered Procedure Codes

HCPCS Codes	Description
J1950	Leuprolide acetate injection (for depot suspension), per 3.75mg
J9217	Leuprolide acetate (for depot suspension), per 7.5mg
J9218	Leuprolide acetate, per 1 mg
J9219	Leuprolide acetate, 65 mg

Covered Diagnosis Codes

ICD-10 Codes	Description
Prostate Cancer	
C61	Malignant neoplasm of prostate
C68.0	Malignant Neoplasm of urethra
C79.11	Secondary malignant neoplasm of bladder
C79.19	Secondary malignant neoplasm of other urinary organs
C79.82	Secondary malignant neoplasm of genital organs
D07.5	Carcinoma in situ of prostate
D09.10	Carcinoma in situ of unspecified urinary organ
D09.19	Carcinoma in situ of other urinary organs
Z85.46	Personal history of malignant neoplasm of prostate
Uterine Leiomyomata (fibroids)	
D25	Leiomyoma of uterus
D25.0	Submucous leiomyoma of uterus
D25.1	Intramural leiomyoma of uterus
D25.2	Subserosal leiomyoma of uterus
D25.9	Leiomyoma of uterus, unspecified
Central Precocious Puberty	
E30.1	Precocious puberty
E30.8	Other disorders of puberty
E22.8	Other hyperfunction of pituitary gland (central precocious puberty diagnosis)
Endometriosis	
N80.0	Endometriosis of uterus
N80.1	Endometriosis of ovary
N80.2	Endometriosis of fallopian tube
N80.3	Endometriosis of pelvic peritoneum
N80.4	Endometriosis of rectovaginal septum and vagina
N80.5	Endometriosis of intestine
N80.6	Endometriosis in cutaneous scar

N80.8	Other endometriosis
N80.9	Endometriosis, unspecified
N97.0	Female infertility of associated with anovulation
N97.1	Female infertility of uterine origin
N97.2	Female infertility of other origin
N97.8	Female infertility of other origin
N97.9	Female infertility, unspecified
Z31.62	Encounter for fertility preservation counseling
Z31.84	Encounter for fertility preservation procedure
Z51.11	Encounter for antineoplastic chemotherapy
Z92.21	Personal history of antineoplastic chemotherapy
Gender dysphoria	
F64.0	Transsexualism, Gender identity disorder in adolescence and adulthood, Gender dysphoria in adolescents and adults
F64.1	Gender identity disorder of childhood, Gender dysphoria in children

Dosing Recommendations Based on Body Weight for LUPRON DEPOT-PED® 1-Month Formulations	
Body Weight	Recommended Dose
≤ 25 kg	7.5 mg
> 25-37.5 kg	11.25 mg
> 37.5 kg	15 mg

Diagnostic Statistical Manual of Mental Disorders (DSM-5) Criteria for Gender Dysphoria

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested by **two or more** of the following:

Adults and Adolescents

1) A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or, in young adolescents, the anticipated secondary sex characteristics); OR
2) A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or, in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics); OR
3) A strong desire for the primary and/or secondary sex characteristics of the other gender; OR
4) A strong desire to be of the other gender (or some alternative gender different from one's assigned gender); OR
5) A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender); OR

6) A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender); AND

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Children

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months duration, as manifested **by six or more of the following** (one of which must be criterion A.1.:
   1) A strong desire to be of the other gender or an insistence that one is the other gender (or some alternative gender, different from one's assigned gender); OR
   2) In boys (assigned gender), a strong preference for cross dressing or simulating female attire; or in girls (assigned gender), a strong preference for wearing only typical masculine clothing and a strong resistance to wearing of typical feminine clothing; OR
   3) A strong preference for cross-gender roles in make-believe play or fantasy play; OR
   4) A strong preference for toys, games, or activities stereotypically used or engaged in by the other gender; OR
   5) A strong preference for playmates of the other gender; OR
   6) In boys (assigned gender), a strong rejection of typically masculine toys, games and activities and a strong avoidance of rough and tumble play; or in girls (assigned gender), a strong rejection of typically feminine toys, games and activities; OR
   7) A strong dislike of one's sexual anatomy; OR
   8) A strong dislike for the primary and/or secondary sex characteristics that match one's experienced gender.

B. The condition is associated with clinically significant distress or impairment in social, school, or other important areas of functioning.

REIMBURSEMENT

Participating facilities will be reimbursed per their Highmark Health Options contract.

POLICY SOURCE(S)

LUPRON DEPOT® (leuprolide acetate) [package insert]. North Chicago, IL: AbbVie Inc. 2016. Accessed on January 6, 2017 and available at: http://www.lupron.com/.

Lee, P., Neely, K., et al. Efficacy of Leuprolide Acetate 1-Month Depot for Central Precocious Puberty (CPP): Growth Outcomes during a Prospective, Longitudinal Study. BioMed Central Ltd.; 2011; Accessed on January 9, 2017 and available at: http://ijpeonline.biomedcentral.com/articles/10.1186/1687-9856-2011-7.

N National Comprehensive Cancer Network® NCCN Clinical Practice Guidelines in Oncology™. Accessed on December 28, 2016 and available at: http://www.nccn.org/index.asp.

Policy History

Date	Activity
01/07/2017	Initial policy developed
12/12/2017	QI/UM committee approval
02/15/2018	Provider effective date