CareSource

PHARMACY POLICY STATEMENT
Indiana Medicaid

DRUG NAME	Lupron Depot and Lupron Depot-PED (leuprolide acetate)
BILLING CODE	J1950, J9217, J9218
BENEFIT TYPE	Medical
SITE OF SERVICE ALLOWED	Office/Outpatient
COVERAGE REQUIREMENTS	Prior Authorization Required (Preferred Product) QUANTITY LIMIT— see "**Dosage allowed**" below
LIST OF DIAGNOSES CONSIDERED **NOT** MEDICALLY NECESSARY	Click Here

Lupron Depot and Lupron Depot-PED (leuprolide acetate) is a **preferred** product and will only be considered for coverage under the **medical** benefit when the following criteria are met:

Members must be clinically diagnosed with one of the following disease states and meet their individual criteria as stated.

ADVANCED BREAST CANCER

For **initial** authorization:

1. Member is pre- OR peri-menopausal women with locally advanced, recurrent, or metastatic hormone receptor-positive breast cancer; AND
2. Member is not currently breast feeding, pregnant, or planning to become pregnant while receiving medication; AND
3. Medication must be prescribed by oncologist, gynecologist or obstetrician.
4. **Dosage allowed:** Lupron Depot 3.75 mg for 1-month or 11.25 mg for 3-month administration.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 6 months.

CENTRAL PRECOCIOUS PUBERTY (CPP)

For **initial** authorization:

1. Pubertal symptoms appeared before the age of 9 in male member or before the age of 8 in female member; AND
2. Member has confirmed diagnostic evaluation, including assessment of **one** of the following:
   a) Bone age advanced one year beyond chronological age;
   b) Pubertal response to a gonadotropin releasing hormone (GnRH) stimulation test; AND
3. Member's baseline gonadal sex steroid hormone levels, adrenal steroid levels, height and weight are submitted with chart notes; AND
4. Other diagnosis are ruled out (e.g., intracranial tumors, congenital adrenal hyperplasia, chronic gonadotropin-secreting tumor, etc.); AND
5. Female member must meet ALL of the following:

a) Breast development Tanner stage 2 or greater;
b) Menstrual bleeding or vaginal discharge;
c) No pregnancy currently;
d) No undiagnosed abnormal vaginal bleeding; OR

6. Male member must meet ALL of the following:
   a) Signs and symptoms as indicated by **one** or more of the following:
      i) Acne;
      ii) Erections;
      iii) Nocturnal emissions;
      iv) Oily skin; AND
   b) Testicular volume 4 mL or greater.
7. **Dosage allowed:** Lupron Depot-PED - Single intramuscular injection. The starting dose 7.5 mg, 11.25 mg, or 15 mg for 1-month administration is based on the child's weight. The doses are either 11.25 mg or 30 mg for 3-month administration.

Note: Discontinuation of leuprolide for central precocious puberty should be considered at age 11 for girls and age 12 for boys.

If member meets all the requirements listed above, the medication will be approved for 12 months.

For **reauthorization**:

1. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

ENDOMETRIOSIS

For **initial** authorization:

1. Member is a female of 18 years of age or older; AND
2. Member is not currently breast feeding, pregnant, or planning to become pregnant while receiving medication; AND
3. Medication must be prescribed by gynecologist or obstetrician; AND
4. Medication must be prescribed with daily norethindrone acetate 5 mg (Leuprolide Depot alone is not recommended for retreatment. If norethindrone acetate is contraindicated, then retreatment is not recommended); AND
5. Endometriosis symptoms, as indicated by **one** or more of the following:
   a) Dysmenorrhea;
   b) Dyspareunia;
   c) Pelvic pain; AND
6. Member has failed control of symptoms with ALL of the following:
   a) NSAIDs;
   b) Any contraceptives.
7. **Dosage allowed:** Lupron Depot 3.75 mg for 1-month or 11.25 mg for 3-month administration.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Leuprolide Depot alone is not recommended for retreatment. If norethindrone acetate is contraindicated, then retreatment is not recommended.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

CareSource

ADVANCED PROSTATE CANCER (Palliative Treatment)

For **initial** authorization:

1. Member has signs and symptoms of symptomatic locally advanced, recurrent, or metastatic disease; AND
2. Member has intermediate to high risk of disease recurrence in clinically localized prostate cancer, as indicated by **one** or more of the following:
   a) Intermediate risk of recurrence:
      i) T2a or lower, an aggressive histologic pattern (i.e., Gleason score of 7);
      ii) T2a or lower, and PSA 10 to 20mg/mL (mcg/L);
      iii) T2b or T2c;
   b) High risk of recurrence:
      i) T2c or lower, and aggressive histologic pattern (i.e., Gleason score of 8 to 10);
      ii) T2c or lower, and PSA greater than 20 ng/mL (mcg/L);
      iii) T3a; AND
3. Medication must be prescribed by urologist or oncologist.
4. **Dosage allowed:** Lupron Depot 7.5 mg for 1-month administration, given as a single intramuscular injection every 4 weeks. Lupron Depot 22.5 mg for 3-month administration, given as a single intramuscular injection every 12 weeks. Lupron Depot 30 mg for 4-month administration, given as a single intramuscular injection every 16 weeks. Lupron Depot 45 mg for 6-month administration, given as a single intramuscular injection every 24 weeks.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease or member did not get any worse.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 6 months.

UTERINE LEIOMYOMAS (FIBROIDS)

For **initial** authorization:

1. Member is a female of 18 years of age or older; AND
2. Member is not currently breast feeding, pregnant, or planning to become pregnant while receiving medication; AND
3. Medication must be prescribed by gynecologist or obstetrician; AND
4. Proposed date of planned fibroid surgery submitted with chart notes; AND
5. Leiomyoma symptoms, as indicated by **one** or more of the following:
   a) Abnormal uterine bleeding;
   b) Bulk-related symptoms (e.g., pelvic pain or pressure, dyspareunia, urinary symptoms);
   c) Iron deficiency anemia;
   d) Other causes of symptoms or bleeding ruled out (e.g., by endometrial biopsy).
6. **Dosage allowed:** Lupron Depot 3.75 mg for 1-month and 11.25 mg for 3-month administration with iron therapy are prescription medications used before fibroid surgery to improve anemia due to vaginal bleeding from fibroids.

Note: Treatment beyond total of 3 months is considered unproven, therefore second reauthorization would not be allowed.

If member meets all the requirements listed above, the medication will be approved for 3 months.

CareSource considers Lupron Depot and Lupron Depot-PED (leuprolide acetate) not medically necessary for the treatment of the following disease

states based on a lack of robust clinical controlled trials showing superior efficacy compared to currently available treatments:

- Dysfunctional Uterine Bleeding

DATE	ACTION/DESCRIPTION
10/09/2018	New policy for Lupron created. Age requirement for Central Precocious Puberty and diagnostic evaluation assessment were revised. Coverage for Advanced Breast Cancer is specified for hormone receptor-positive breast cancer. "Proposed date of planned fibroid surgery" criterion was added to diagnosis of Uterine Leiomyomas. Diagnosis of Dysfunctional uterine bleeding was removed. The requirement for increased uterine volume from the female criteria in CPP was removed.

References:

1. Lupron Depot [package insert]. North Chicago, IL: AbbVie Inc.; June, 2016.
2. Lupron Depot – PED [package insert]. North Chicago, IL: AbbVie Inc.; May, 2017.
3. Burstein HJ, Lacchetti C, Anderson H, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American society of clinical oncology clinical practice guideline update on ovarian suppression. *J Clin Oncol*. 2016;34(14):1689-701.
4. Dowsett M, Mehta A, Mansi J, Smith IE. A dose-comparative endocrine-clinical study of leuprorelin in premenopausal breast cancer patients. Br J Cancer. 1990;62(5):834-837.
5. Dowsett M, Jacobs S, Aherne J, Smith IE. Clinical and endocrine effects on leuprorelin acetate in pre- and postmenopausal patients with advanced breast cancer. *Clin Ther*. 1992;14(suppl A):97-103.
6. Gradishar WJ, Anderson BO, Blair SL, et al, and the National Comprehensive Cancer Network Breast Cancer Panel. Breast cancer version 3.2014. J Natl Compr Canc Netw. 2014;12(4):542-590.
7. Kurebayashi J, Toyama T, Sumino S, Miyajima E, Fujimoto T. Efficacy and safety of leuprorelin acetate 6-month depot, TAP-144-SR (6M), in combination with tamoxifen in postoperative, premenopausal patients with hormone receptor-positive breast cancer: A phase III, randomized, open-label, parallel-group comparative study. *Breast Cancer*. 2017;24(1):161-170.
8. Recchia F, Candeloro G, Necozione S, et al. Premenopausal hormone-responsive breast cancer with extensive axillary nodes involvement: total estrogen blockade and chemotherapy. *Anticancer Res*. 2011;31:671-676.
9. Schmid P, Untch M, Kossé V, et al. Leuprorelin acetate every-3-months depot versus cyclophosphamide, methotrexate, and fluorouracil as adjuvant treatment in premenopausal patients with node-positive breast cancer: the TABLE study. *J Clin Oncol*. 2007;25(18):2509-2515.
10. Shiba E, Yamashita H, Kurebayashi J, et al. A randomized controlled study evaluating safety and efficacy of leuprorelin acetate every-3-months depot for 2 versus 3 or more years with tamoxifen for 5 years as adjuvant treatment in premenopausal patients with endocrine-responsive breast cancer. *Breast Cancer*. 2016;23(3):499-509.
11. Untch M, Fuchs W, Kreienberg R. Clinical efficacy of leuprorelin acetate monthly depot in premenopausal patients with metastatic breast cancer. *Oncol Rep*. 1997;4(4):717-721.
12. Watanabe T, Adachi I, Taguchi T, et al; with members of the TAP-144-SR Breast Cancer Study Group. Phase II trial of TAP-144-SR (leuprorelin sustained release formulation) in premenopausal patients with metastatic breast cancer (MBC) [abstract]. Breast Cancer Res Treat. 1996;37(suppl 1):74. Abstract 233.
13. Jasonni VM, D'Anna R, Mancuso A, Caruso C, Corrado F, Leonardi I. Randomized double-blind study evaluating the efficacy on uterine fibroids shrinkage and on intra-operative blood loss of different length of leuprolide acetate depot treatment before myomectomy. *Acta Obstet Gynecol Scand*. 2001;80(10):956-958.
14. Palomba S, Orio Jr. F, Russo T, et al. Long-term effectiveness and safety of GnRH agonist plus raloxifene administration in women with uterine leiomyomas. *Human Reproduction*. 2004;19(6):1308-1314.
15. Schlaff WD, Zerhouni EA, Huth JAM, Chen J, Damewood MD, Rock JA. A placebo-controlled trial of a depot gonadotropin-releasing hormone analogue (leuprolide) in the treatment of uterine leiomyomata. *Obstet Gynecol*. 1989;74(6):856-862.
16. Vavalà V, Lanzone A, Monaco A, Scribanti A, Guida C, Mancuso S. Postoperative GnRH analog treatment for the prevention of recurrences of uterine myomas after myomectomy. A pilot study. Gynecol Obstet Invest. 1997;43(4):251-254.
17. Stovall TG, Muneyyirci-Delale O, Summitt RL Jr, Scialli AR; Leuprolide Acetate Study Group. GnRH agonist and iron versus placebo and iron in the anemic patient before surgery for leiomyomas: a randomized controlled trial. *Obstet Gynecol*. 1995;86(1):65-71.

18. Donnez J, Tomaszewski J, Vazquez F, et al; for the PEARL II Study Group. Ulipristal acetate versus leuprolide acetate for uterine fibroids. *N Eng J Med.* 2012;366(5):421-432.
19. Mitwally MFM, Gotlieb L, Casper RF. Prevention of bone loss and hypoestrogenic symptoms by estrogen and interrupted progestogen add-back in long-term GnRH-agonist down-regulated patients with endometriosis and premenstrual syndrome. Menopause. 2002;9(4):236-241.
20. Bedaiwy MA, Casper RF. Treatment with leuprolide acetate and hormonal add-back for up to 10 years in stage IV endometriosis patients with chronic pelvic pain [letter]. Fertil Steril. 2006;86(1):220-222.
21. Eksioglu AS, et al. Value of pelvic sonography in the diagnosis of various forms of precocious puberty in girls. J *Clin Ultrasound*. 2013 Feb;41(2):84-93.
22. Sathasivam A, et al. Pelvic ultrasonography in the evaluation of central precocious puberty: comparison with leuprolide stimulation test. *J Pediatr*. 2011 Sep;159(3):490-5.

Effective date: 10/26/2018
Revised date: 10/09/2018