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Policy Number: C8756-A

Leuprolide long acting (Lupron Depot, Eligard, Lupron Depot Ped, Fensolvi, Camcevi)

PRODUCTS AFFECTED

Lupron Depot (leuprolide), Lupron Depot-Ped (leuprolide), Eligard (Leuprolide Acetate), Fensolvi (leuprolide acetate), Camcevi (leuprolide injection emulsion)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Advanced prostate cancer, Endometriosis, Anemia prior to uterine fibroid surgery, Precocious puberty, Premenopausal ovarian suppression in women with breast cancer, to suppress onset of puberty in transgender adolescents, Treatment of paraphilia/hypersexuality, Premenstrual dysphoric disorder, Ovarian cancer

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review.

A. ADVANCED PROSTATE CANCER (J9217, J1952):
1. Documentation of a diagnosis of prostate cancer and the utilization of a Gonadotropin-

Releasing Hormone Agonist is recommended for the members stage and disease per NCCN updated guidelines for prostate cancer

B. ENDOMETRIOSIS (J1950 only):

1. Documentation of a diagnosis of endometriosis either surgically confirmed OR Clinically diagnosed and failed a three-month trial of analgesics and/or combined oral estrogen progesterone contraceptives within the last year
   AND
2. Documentation member has tried/failed or has an absolute contraindication to ALL of the following: one formulary NSAIDs (i.e., Ibuprofen, naproxen), one formulary preferred oral estrogen-progestin contraceptive, medroxyprogesterone or norethindrone acetate
   AND
3. Member is older than 18 years of age

C. UTERINE LEIOMYOMATA (FIBROIDS) (J1950 only):

1. Documentation of uterine leiomyomas confirmed with pelvic imaging
   AND
2. Documentation member is symptomatic: Heavy or prolonged menstrual bleeding, Bulk- related symptoms, such as pelvic pressure and pain or Reproductive dysfunction (i.e., infertility or obstetric complications)
   AND
3. Documentation therapy is being used:
   a) As preoperative therapy 3-6 months prior to surgery for ONE of the following reasons: member has a contraindication to oral iron supplementation to facilitate the procedure and anemia correction is necessary OR volume reduction is necessary prior to procedure
   OR
   b) As transitional therapy for members in late perimenopause as they move to menopause AND
4. Member is older than 18 years of age

D. CENTRAL PRECOCIOUS PUBERTY (J1950, J1951):

1. Diagnosis of central precocious puberty and member is currently less than 13 years old
   AND
2. Documentation of an onset of secondary sexual characteristics with one of the following: Females </= 8 years of age OR Males < / = 9 years of age
   AND
3. Confirmation of diagnosis as defined by ONE of the following: (a) Pubertal basal level of luteinizing hormone (based on laboratory reference ranges) OR (b) Pubertal luteinizing hormone in response to a GnRH stimulation test OR (c) Bone age advanced one year beyond chronological age

E. BREAST CANCER (J9217 or J1950):

1. Documentation of a diagnosis of (i) breast cancer in a pre-menopausal or peri-menopausal woman at diagnosis requiring ovarian suppression therapy OR (ii) diagnosis of breast cancer in men requiring adjuvant endocrine therapy

F. PREVENTION OF CHEMOTHERAPY–INDUCED PREMATURE OVARIAN INSUFFICIENCY Ref (5-12)

1. Documentation of post puberty and premenopausal gonadotoxic therapy or gonadotoxic surgery AND
2. Prescriber attests member is not a candidate for cryopreservation or is not eligible for cryopreservation [see other considerations- ASCO recommendations]

G. OVARIAN CANCER: Refer to Standard Oncology Criteria

H. TRANSGENDER HEALTH: Refer to Gender Dysphoria Hormone Therapy

CONTINUATION OF THERAPY:

A. CENTRAL PRECOCIOUS PUBERTY:
1. Documentation of disease response as indicated by lack of progression or stabilization of secondary sexual characteristics, decrease in height velocity, and improvement in final height prediction
   AND
2. Prescriber attestation of an absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include convulsions, development or worsening of psychiatric symptoms, etc.
   AND
3. Documentation that member is not currently older than age 12 OR prescriber has provided contributing factors that may include, bone age and height age, predicted height, and planned discontinuation plan or date.

B. ALL OTHER INDICATIONS:
1. Prescriber attestation of absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include tumor flare, hyperglycemia/diabetes, cardiovascular disease (myocardial infarction, sudden cardiac death, stroke), QT/QTc prolongation, convulsions, etc.
   AND
2. Documentation of improvement and/or stabilization of disease due to long-acting leuprolide therapy
   AND
3. For Endometriosis or Uterine Fibroids: Documentation that member's treatment has not exceeded the lifetime maximum of 6 months.

DURATION OF APPROVAL:

ADVANCED PROSTATE CANCER, BREAST CANCER AND CENTERAL PRECOCIOUS PUBERTY: Initial authorization: 6 months, Continuation of Therapy: 12 months

ENDOMETRIOSIS & UTERINE FIBROIDS: Initial authorization: 3 months, Continuation of Therapy: 3 months--Lifetime maximum: 6 months

PREVENTION OF CHEMOTHERAPY–INDUCED PREMATURE OVARIAN INSUFFICIENCY: Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Endometriosis, Uterine Fibroids: Prescribed by or in consultation with a gynecologist or specialist in women's health.

Precocious Puberty: Prescribed by or in consultation with a Pediatrician or Pediatric Endocrinologist.

Oncology conditions: Prescribed by or in consultation with an Oncologist or specialist in cancer treatment.

If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests.

AGE RESTRICTIONS:

Central Precocious Puberty- 2 years of age and older (LUPRON DEPO-PED, FENSOLVI)

PREVENTION OF CHEMOTHERAPY–INDUCED PREMATURE OVARIAN INSUFFICIENCY- patient must be post-puberty

All other indications: 18 years of age and older

QUANTITY:
Lupron Depot 1-Month 3.75 mg 1 injection 28 days
Lupron Depot 1-Month 7.5 mg 1 injection 28 days
Lupron Depot 3-Month 11.25 mg 1 injection 84 days
Lupron Depot 3-Month 22.5 mg 1 injection 84 days
Lupron Depot 4-Month 30 mg 1 injection 112 days
Lupron Depot 6-Month 45 mg 1 injection 168 days
Lupron Depot-Ped 7.5 mg 1 injection 28 days
Lupron Depot-Ped 11.25 mg 1 injection 28 days
Lupron Depot-Ped 3-Month 11.25 mg 1 injection 84 days
Lupron Depot-Ped 15 mg 1 injection 28 days
Lupron Depot-Ped 3-Month 30 mg 1 injection 84 days
Eligard 7.5 mg 1 injection 28 days
Eligard 22.5 mg 1 injection 84 days
Eligard 30 mg 1 injection 112 days
Eligard 45 mg 1 injection 168 days
Fensolvi 45mg 1 injection 168 days
Camcevi 42 mg 1 subcutaneous injection 168 days

Maximum Quantity Limits – Per FDA labeling for products.

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous and intramuscular injectable products be administered in a place of service that is a non-hospital facility-based location.

RECOMMEND USE OF J9217 FOR ONCOLOGY INDICATIONS, RECOMMEND USE OF J1950 FOR WOMEN'S HEALTH AND CPP INDICATIONS

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intramuscular Administration, Subcutaneous Injection

DRUG CLASS:
Antineoplastic Agent, Gonadotropin-Releasing Hormone Agonist; Gonadotropin Releasing Hormone Agonist

FDA-APPROVED USES:
Advanced prostate cancer, Endometriosis and Uterine leiomyomata fibroids, Central precocious puberty

COMPENDIAL APPROVED OFF-LABELED USES:
Breast cancer, premenopausal ovarian suppression

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Leuprolide is a synthetic nonapeptide analog of naturally occurring gonadotropin-releasing hormone or leutinizing hormone-releasing hormone (GnRH or LHRH), which possesses greater potency compared with the natural hormone (generally considered a GnRH agonist). It acts as a potent inhibitor of gonadotropin secretion when administered continuously in therapeutic doses. Following initial stimulation of gonadotropins, chronic administration of leuprolide leads to suppression of ovarian and testicular steroidogenesis. These effects are reversible after drug discontinuation.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Leuprolide long acting (Lupron Depot, Eligard, Lupaneta, Lupron Depot Ped) are considered experimental/ investigational and therefore, will follow Molina's Off-Label policy. Other exclusions include: Women who are pregnant or those who may become pregnant or breastfeeding, Undiagnosed abnormal vaginal bleeding, OR used for In vitro fertilization or infertility, Hirsutism or Menstrual Migraine

OTHER SPECIAL CONSIDERATIONS:

FERTILITY PRESERVATION:

Fertility Preservation in Patients with Cancer: American Society of Clinical Oncology Clinical P Adult Women Recommendation 3.1 Embryo cryopreservation: Embryo cryopreservation is an established fertility preservation method, and it has routinely been used for storing surplus embryos after in vitro fertilization.

Recommendation 3.2. Cryopreservation of unfertilized oocytes: Cryopreservation of unfertilized oocytes is an option and may be especially well suited to women who do not have a male partner, do not wish to use donor sperm, or have religious or ethical objections to embryo freezing. Oocyte cryopreservation should be performed in centers with the necessary expertise. As of October 2012, the American Society for Reproductive Medicine no longer deems this procedure experimental.
Qualifying statement. More flexible ovarian stimulation protocols for oocyte collection are now available. Timing of this procedure no longer depends on the menstrual cycle in most cases, and stimulation can be initiated with less delay compared with old protocols. Thus, oocyte harvesting for the purpose of oocyte or embryo cryopreservation is now possible on a cycle day–independent schedule. Of special concern in estrogen-sensitive breast and gynecologic malignancies is the possibility that these fertility preservation interventions (e.g., ovarian stimulation regimens that increase estrogen levels) and/or subsequent pregnancy may increase the risk of cancer recurrence. Aromatase inhibitor–based stimulation protocols are now well established and may ameliorate this concern. Studies do not indicate increased cancer recurrence risk as a result of aromatase inhibitor– supplemented ovarian stimulation and subsequent pregnancy.

Recommendation 3.3. Ovarian transposition: Ovarian transposition (oophoropexy) can be offered when pelvic irradiation is performed as cancer treatment. However, because of radiation scatter, ovaries are not always protected, and patients should be aware that this technique is not always successful. Because of the risk of remigration of the ovaries, this procedure should be performed as close to the time of radiation treatment as possible.

Recommendation 3.4. Conservative gynecologic surgery: It has been suggested that radical

trachelectomy (surgical removal of the uterine cervix) should be restricted to stage IA2 to IB cervical cancer with diameter, 2 cm and invasion, 10 mm. In the treatment of other gynecologic malignancies, interventions to spare fertility have generally centered on doing less radical surgery, with the intent of sparing the reproductive organs as much as possible. Ovarian cystectomy can be performed for early-stage ovarian cancer.

Recommendation 3.5 (updated). Ovarian suppression: There is conflicting evidence to recommend GnRHa and other means of ovarian suppression for fertility preservation. The Panel recognizes that, when proven fertility preservation methods such as oocyte, embryo, or ovarian tissue cryopreservation are not feasible, and in the setting of young women with breast cancer, GnRHa may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency. However, GnRHa should not be used in place of proven fertility preservation methods.

Recommendation 3.6 (updated). Ovarian tissue cryopreservation and transplantation: Ovarian tissue cryopreservation for the purpose of future transplantation does not require ovarian stimulation and can be performed immediately. In addition, it does not require sexual maturity and hence may be the only method available in children. Finally, this method may also restore global ovarian function.
However, it should be noted further investigation is needed to confirm whether it is safe in patients with leukemias. Practice Guideline Update

Special Considerations: Children
Recommendation 5.1. Suggest established methods of fertility preservation (eg, semen or oocyte cryopreservation) for post pubertal children, with patient assent and parent or guardian consent.
For prepubertal children, the only fertility preservation options are ovarian and testicular cryopreservation, which are investigational

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J9218	leuprolide acetate
J9217	leuprolide acetate depot (Eligard/Lupron Depot)
J9219	leuprolide implant (Viadur)- discontinued
J3490	leuprolide/norethindrone (Lupaneta Pack)
J1950	leuprolide depot per 3.75mg (Lupron/LupronDepot/Lupron Depot Ped)
J1951	Injection, leuprolide acetate for depot suspension (fensolvi), 0.25 mg
J1952	Leuprolide injectable, camcevi, 1 mg

AVAILABLE DOSAGE FORMS:
Prostate cancer:
Eligard KIT 7.5MG
Eligard KIT 22.5MG
Eligard KIT 30MG

Eligard KIT 45MG
Lupron Depot (1-Month) KIT 7.5MG
Lupron Depot (3-Month) KIT 22.5MG
Lupron Depot (4-Month) KIT 30MG
Lupron Depot (6-Month) KIT 45MG

RECOMMEND USE OF J9217 FOR MEDICAL BILLING

Prostate cancer:
Camcevi 42 MG
RECOMMEND USE OF J1952 FOR MEDICAL BILLING

Endometriosis and Uterine leiomyomata fibroids:
Lupron Depot (1-Month) KIT 3.75MG
Lupron Depot (3-Month) KIT 11.25MG
RECOMMEND USE OF J1950 FOR MEDICAL BILLING

Central Precocious puberty:
Lupron Depot-Ped (1-Month) KIT 11.25MG
Lupron Depot-Ped (1-Month) KIT 15MG
Lupron Depot-Ped (1-Month) KIT 7.5MG
Lupron Depot-Ped (3-Month) KIT 11.25MG (Ped)
Lupron Depot-Ped (3-Month) KIT 30MG (Ped)
RECOMMEND USE OF J1950 FOR MEDICAL BILLING

Central Precocious puberty:
Fensolvi (6 Month) KIT 45MG (Ped)
RECOMMEND USE OF J1951 FOR MEDICAL BILLING

REFERENCES

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4. Blumenfeld Z, Katz G, Evron A: 'An ounce of prevention is worth a pound of cure': The case for and against GnRH-agonist for fertility preservation. Ann Oncol 5:1719-1728, 2014
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11. National Comprehensive Cancer Network Guidelines Version 4.2018. ProstateCancer. www.nccn.org. Accessed 04/2019
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Products Affected Required Medical Information Prescriber Requirements Quantity Coding/Billing Information Available Dosage Forms References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file