Medical Policy:
LHRH Agonists/Antagonists (Camcevi, Firmagon, Lupron Depot, Lupron Depot-Ped, Trelstar, Zoladex)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.360	June 12, 2023	August 11, 2022

Definitions

Camcevi™ (leuprolide subcutaneous injection – Accord BioPharma), **Trelstar®** (triptorelin pamoate intramuscular injection – Verity Pharmaceuticals), and **Firmagon®** (degarelix subcutaneous injection – Ferring Pharmaceuticals) are all indicated for the treatment of advanced prostate cancer. Camcevi and Trelstar are gonadotropin-releasing hormone (GnRH) agonists, whereas Firmagon is a GnRH antagonist.

Lupron Depot (3.75 mg intramuscular (IM) injection every month, 11.25 mg IM injection every 3 months) is indicated for the preoperative hematologic improvement of women with anemia caused by uterine leiomyomata (fibroids) for whom 3 months of hormonal suppression is deemed necessary. (Lupron Depot in combination with iron therapy), Endometriosis, including pain relief and reduction of endometriotic lesions (Lupron Depot monotherapy), and Endometriosis, initial management of the painful symptoms of endometriosis and management of recurrence of symptoms (Lupron Depot in combination with norethindrone acetate 5 mg daily).

Lupron Depot (7.5 mg IM injection every month, 22.5 mg IM injection every 3 months, 30 mg IM injection every 4 months, and 45 mg IM injection every 6 months) is indicated for the palliative treatment of advanced prostate cancer.

Lupron Depot-Ped is indicated for the treatment of pediatric patients with central precocious puberty and is used off-label for the treatment of gender-dysphoric/gender-incongruent persons to suppress physical changes of puberty and gonadal function.
Zoladex® (goserelin acetate subcutaneous implant – TerSera Therapeutics) is approved for abnormal uterine bleeding, use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding, Breast cancer, palliative treatment of advanced breast cancer in pre- and perimenopausal women., Endometriosis, including pain relief and reduction of endometriotic lesions for the duration of therapy, and Prostate cancer: In combination with flutamide for the management of locally confined Stage T2b-T4 (Stage B2-C) or as advanced carcinoma or palliative treatment.
NOTE: Zoladex 10.8 mg (equivalent to 11.3 mg goserelin acetate) is only indicated for prostate cancer.

Dosing Limits [Medical Benefit]

Drug	Route of Administration	Dose and Frequency
Camcevi	Subcutaneous	• 42 mg every 6 months
Zoladex	Subcutaneous	All indications • 3.6 mg SQ every 28 days Prostate Cancer ONLY • 10.8mg
Lupron Depot	Intramuscular	**Endometriosis**: For the first 6 months of treatment, Lupron Depot may be used as monotherapy or in combination with norethindrone acetate. If retreatment is needed, Lupron Depot must be used in combination with norethindrone acetate (for 6 months). Total duration of treatment is limited to 12 months. • 3.75 mg every month • 11.25mg every 3 months **Prostate Cancer** • 7.5 mg every month • 22.5 mg every 3 months • 30mg every 4 months • 45mg every 6 months
Lupron Depot-Ped	Intramuscular	• 7.5mg every month or 3 months • 11.25mg every month or 3 months • 15 mg every month or 3 months
Firmagon	Subcutaneous	• Starting dose of 240 mg given as two injections of 120 mg • First maintenance dose given 28 days after the starting dose • Maintenance dose of 80 mg as one injection given every 28 days
Trelstar	Intramuscular	• 3.75 mg every 4 weeks • 11.25 mg every 12 weeks • 22.5 mg every 24 weeks

Guideline

1. **Prostate Cancer.** Approve Camcevi, Lupron, Zoladex, Firmagon, or Trelstar for 1 year if the following criteria are met.
   A. Medication is prescribed by or in consultation with an oncologist or urologist; **AND**
   B. Patient has advanced disease

2. **Abnormal Uterine Bleeding.** Approve Zoladex 3.6 mg for 2 months if the patient meets the following conditions (A and B):
   A. Zoladex is used as an endometrial-thinning agent prior to endometrial ablation; **AND**
   B. The medication is prescribed by or in consultation with an obstetrician-gynecologist or a healthcare practitioner who specializes in the treatment of women's health.

3. **Breast Cancer.** Approve Zoladex 3.6 mg for 1 year if the patient meets the following conditions (A and B):
   A. Zoladex is used in a premenopausal or perimenopausal woman; **AND**
   B. The medication is prescribed by or in consultation with an oncologist.

4. **Endometriosis**.
   Approve Zoladex 3.6 mg for 6 months if the patient meets the following conditions (A and B):
   A. Patient is ≥ 18 years of age; **AND**
   B. The medication is prescribed by or in consultation with an obstetrician-gynecologist or a healthcare practitioner who specializes in the treatment of women's health.
   Approve Lupron Depot (3.75 mg or 11.25 mg) for 1 year if the patient has tried one of the following (A, B, or C):
   A. A contraceptive (e.g., combination oral contraceptives, levonorgestrel-releasing intrauterine systems [e.g., Mirena, Liletta]), **OR**
   B. An oral progesterone (e.g., norethindrone tablets), **OR**
   C. A depo-medroxyprogesterone injection, unless contraindicated.

5. **Uterine Leiomyomata (fibroids)** Approve for 3 months if the following criteria is met.
   A. Lupron Depot 3.75 mg or 11.25 mg

6. **Central Precocious Puberty**.
   A. Approve Lupron Depot-Ped for 1 year.

5. **Head and Neck Cancer – Salivary Gland Tumors** **
   *Approve Camcevi for 1 year if the patient meets the following criteria (A, B, **and** C):*
   A. Patient has distant metastases; **AND**
   B. Patient has androgen receptor-positive disease; **AND**
   C. The medication is prescribed by or in consultation with an oncologist.
   *Approve Lupron Depot 7.5 mg or 22.5 mg for 1 year if the patient meets the following criteria (A, B, **and** C):*
   A. Patient has advanced salivary gland tumors with distant metastases; **AND**
   B. Patient has androgen receptor (AR)-positive disease; **AND**
   C. The medication is prescribed by or in consultation with an oncologist.

6. **Abnormal Uterine Bleeding**** Approve for 6 months if the following criteria is met.
   A. Dose of Lupron Depot is 3.75mg or 11.25mg

7. **Breast Cancer**** Approve for 1 year if the following criteria are met
   A. Lupron Depot (3.75mg or 11.25mg) is prescribed by or in consultation with an oncologist.

8. **Gender Dysphoric/Gender-Incongruent Person; Person Undergoing Gender Reassignment (Female-To-Male [FTM] or Male-To-Female [MTF])**** Approve for 1 year if the following criteria are met.
   A. Lupron Depot is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender patients.

9. **Ovarian Cancer**** Approve for 1 year if the following criteria are met.
   A. Lupron Depot (3.75 mg, 7.5 mg, 11.25 mg, or 22.5 mg) is prescribed by or in consultation with an oncologist.

10. **Preservation of Ovarian Function/Fertility in Patients Undergoing Chemotherapy**** Approve for 1 year if the following criteria are met.
    A. Patient is premenopausal; **AND**
    B. Patient is receiving treatment with cytotoxic chemotherapy with the potential to cause ovarian damage/toxicity (e.g., cyclophosphamide, melphalan, procarbazine vinblastine,imatinib, etc.) **AND**
    C. Lupron Depot (3.75 mg or 11.25 mg) is prescribed by or in consultation with an oncologist.

11. **Prophylaxis or Treatment of Uterine Bleeding or Menstrual Suppression in Patients with Hematologic Malignancy, or Undergoing Cancer Treatment, or Prior to Bone Marrow/Stem Cell Transplantation (BMT/SCT)**** Approve for 1 year if the following criteria are met.
    A. Lupron Depot (3.75 mg or 11.25 mg) is prescribed by or in consultation with an oncologist.

** OFF LABEL INDICATION

Applicable Procedure Codes

Code	Description
J9217	Leuprolide acetate (for depot suspension), 7.5 mg, 22.5mg, 30mg, 45mg
J1950	Injection, leuprolide acetate (for depot suspension) (Lupron Depot-Ped), 3.75 mg, 7.5mg, 11.25, 15mg, 30mg
J9155	Injection, degarelix, 1 mg, Firmagon
J1952	Leuprolide injectable, camcevi
J9202	Goserelin acetate implant, Zoladex
J3315	Injection, triptorelin pamoate, 3.75 mg, Trelstar

Applicable NDCs

Code	Description
00074-3641-xx	Lupron Depot 1-Month 3.75 mg
00074-3642-xx	Lupron Depot 1-Month 7.5 mg
00074-3663-xx	Lupron Depot 3-Month 11.25 mg
00074-3346-xx	Lupron Depot 3-Month 22.5 mg
00074-3683-xx	Lupron Depot 4-Month 30 mg
00074-3473-xx	Lupron Depot 6-Month 45 mg
00074-2108-xx	Lupron Depot-Ped 7.5 mg
00074-2282-xx	Lupron Depot-Ped 11.25 mg
00074-3779-xx	Lupron Depot-Ped 3-Month 11.25 mg
00074-2440-xx	Lupron Depot-Ped 15 mg

00074-9694-xx	Lupron Depot-Ped 3-Month 30 mg
55566-8403-01	FIRMAGON 120MG Solution Reconstituted
55566-8303-01	FIRMAGON 80MG Solution Reconstituted
72851-0042-xx	Camcevi 42 mg
00023-5906-xx	TRELSTAR 22.5MG Suspension Reconstituted
00023-5904-xx	TRELSTAR 11.25MG Suspension Reconstituted
00023-5902-xx	TRELSTAR 3.75MG Suspension Reconstituted
70720-0950-36	ZOLADEX 3.6MG Implant
70720-0951-30	ZOLADEX 10.8MG Implant
50090-2027-00	ZOLADEX 3.6MG Implant
50090-3466-00	ZOLADEX 3.6MG Implant

ICD-10 Diagnoses

Code	Description
C07	Malignant neoplasm of parotid gland
C08.0	Malignant neoplasm of submandibular gland
C08.1	Malignant neoplasm of sublingual gland
C08.9	Malignant neoplasm of major salivary gland, unspecified
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right female breast
C50.022	Malignant neoplasm of nipple and areola, left female breast
C50.029	Malignant neoplasm of nipple and areola, unspecified female breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast

C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs

C57.9	Malignant neoplasm of female genital organ, unspecified
C61	Malignant neoplasm of prostate
D25.0	Submucous leiomyoma of uterus
D25.1	Intramural leiomyoma of uterus
D25.2	Subserosal leiomyoma of uterus
D25.9	Leiomyoma of uterus, unspecified
E30.1	Precocious puberty
E30.8	Other disorders of puberty
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
Z85.3	Personal history of malignant neoplasm of breast
Z85.43	Personal history of malignant neoplasm of ovary
Z85.46	Personal history of malignant neoplasm of prostate

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	6/12/2023	Annual Review: No criteria changes
EmblemHealth & ConnectiCare	8/11/2022	New Policy

References

1. Zoladex® 3.6 mg subcutaneous implant [prescribing information]. Lake Forest, IL: TerSera Therapeutics; December 2020.
2. Zoladex® 10.8 mg subcutaneous implant [prescribing information]. Lake Forest, IL: TerSera Therapeutics; December 2020.
3. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – December 20, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on Augest 2, 2022.
4. Lupron Depot® – 3.75 mg [prescribing information]. North Chicago, IL: AbbVie; February 2021.
5. Lupron Depot® –11.25 mg [prescribing information]. North Chicago, IL: AbbVie; March 2020.
6. Firmagon® subcutaneous injection [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals; February 2020.
7. Trelstar® intramuscular injection [prescribing information]. Wayne, PA: Verity Pharmaceuticals; May 2020.
8. Camcevi subcutaneous injection [prescribing information]. Durham, NC: Accord BioPharma; May 2021.
9. The NCCN Head and Neck Cancer Clinical Practice Guidelines in Oncology (version 1.2022 – December 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 4, 2022.
10. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version 3.2022 – January 20, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 4, 2022.