**Original Effective Date: 03/2016**
**Current Effective Date: 11/17/2022**
**Last P&T Approval/Version: 07/27/2022**
**Next Review Due By: 07/2023**
**Policy Number: C8757-A**

# Zoladex (goserelin acetate)

## PRODUCTS AFFECTED

Zoladex (goserelin acetate)

## 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:**
Prostate cancer, endometriosis, dysfunctional uterine bleeding, breast 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. PROSTATE CANCER (J9217 ONLY):
   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
      AND
   2. Documentation of trial, failure or labeled contraindication to Eligard (leuprolide acetate)

B. BREAST CANCER:
1. Diagnosis of breast cancer meeting one of the following:
(i) Female member who is pre-menopausal at diagnosis and requires ovarian suppression
OR
(ii) Male member requiring adjuvant endocrine therapy diagnosis of breast

C. ENDOMETRIOSIS/ENDOMETRIAL THINNING:
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 contraceptives, medroxyprogesterone or norethindrone acetate

D. DYSFUNCTIONAL UTERINE BLEEDING/UTERINE LEIOMYOMAS:
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 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

E. 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]

**CONTINUATION OF THERAPY:**

A. ALL INDICATIONS:
1. Reauthorization will not be allowed for greater than 2 doses for endometrial thinning or greater than 6 months of therapy for endometriosis
AND
2. 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
3. Documentation of improvement and/or stabilization of disease due to therapy

**DURATION OF APPROVAL:**

Initial authorization:
Prostate cancer: 12 months
Breast cancer: 12 months
Endometriosis: 6 months (lifetime maximum)
Dysfunctional uterine bleeding/uterine leiomyomas: 6 months

Prevention of chemotherapy–induced premature ovarian insufficiency: 6 months

Continuation of Therapy:
Prostate cancer: 12 months Breast cancer: 12 months
Endometriosis: 6 months (lifetime maximum)
Dysfunctional uterine bleeding/uterine leiomyomas: 6 months
Prevention of chemotherapy–induced premature ovarian insufficiency: 6 months

**PRESCRIBER REQUIREMENTS:**
Prostate cancer or breast cancer: Prescribed by or in consultation with an oncologist.
Endometriosis or dysfunctional uterine bleeding/uterine leiomyomas: Prescribed by or in consultation with a gynecologist
Prevention of chemotherapy–induced premature ovarian insufficiency: Prescribed by or in consultation with a gynecologist or oncologist.
[If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

**AGE RESTRICTIONS:**
PREVENTION OF CHEMOTHERAPY–INDUCED PREMATURE OVARIAN INSUFFICIENCY- patient must be post-puberty
All other indications: 18 years of age and older

**QUANTITY:**
Prostate cancer: Zoladex one 3.6 mg implant per 4 weeks OR one 10.8 mg implant per 12 weeks
Breast cancer: Zoladex 3.6 mg implant administered every 28 days
Endometriosis: Zoladex 3.6 mg dose every 28 days for up to 6 months
Endometrial Thinning: Zoladex 3.6 mg every 28 days for up to 2 doses.
Dysfunctional uterine bleeding/uterine leiomyomas: Zoladex 3.6 mg implant administered every 28 days
Prevention of chemotherapy–induced premature ovarian insufficiency: Zoladex 3.6 mg dose every 28 days

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

## DRUG INFORMATION

**ROUTE OF ADMINISTRATION:**
Subcutaneous

**DRUG CLASS:**
Antineoplastic – Hormonal and related agents

**FDA-APPROVED USES:**
*Zoladex 3-month implant 10.8mg* indicated for: Use in combination with flutamide for the management of locally confined carcinoma of the prostate, Use as palliative treatment of advanced carcinoma of the prostate

*Zoladex 1 month implant 3.6mg* indicated for: Use in combination with flutamide for the management of locally confined carcinoma of the prostate, Palliative treatment of advanced carcinoma of the prostate, management of endometriosis, Use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding, Use in the palliative treatment of advanced breast cancer in pre- and perimenopausal women

**COMPENDIAL APPROVED OFF-LABELED USES:**

Prevention of Chemotherapy-induced premature ovarian insufficiency

## APPENDIX

**APPENDIX:**

None

## BACKGROUND AND OTHER CONSIDERATIONS

**BACKGROUND:**

Zoladex (goserelin acetate) Implant 3.6 mg is a man-made form of a hormone used in men to treat symptoms of prostate cancer, and in women to treat breast cancer or endometriosis. Zoladex is also used in women to prepare the lining of the uterus for endometrial ablation (a surgery to correct abnormal uterine bleeding).

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**

All other uses of Zoladex (goserelin acetate) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Zoladex (goserelin acetate) is contraindicated in members that are pregnant unless being used for advanced breast cancer.

**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 harvestingfor 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 pelvicirradiation 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,2cm and invasion, 10 mm. In the treatment of other gynecologic malignancies, interventions to spare fertilityhave 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 (e.g., 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 |
|---|---|
| J9202 | goserelin acetate implant, per 3.6mg |

**AVAILABLE DOSAGE FORMS**:
Zoladex 1-month implant 3.6mg
Zoladex 3-month implant 10.8mg

## REFERENCES


1. Zoladex 10.8mg [package insert]. Deerfield, IL; TerSera TherapeuticsLLC; December 2020
2. Zoladex 3.6mg [package insert]. Deerfield, IL; TerSera Therapeutics LLC; December 2020
3. National Comprehensive Cancer Network. 2022. Breast Cancer (Version 4.2022). [online] Available at: < breast.pdf (nccn.org) > [Accessed 30 June 2022]
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5. Peccatori FA, Azim HA Jr, Orecchia R, et al: Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 24:vi160-vi170, 2013 (suppl 6)
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8. Blumenfeld Z, von Wolff M: GnRH-analogues and oral contraceptives for fertility preservation in women during chemotherapy. Hum Reprod Update 14: 543-552, 2008
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10. Blumenfeld, Z. (2018). Fertility Preservation by Endocrine Suppression of Ovarian Function Using Gonadotropin-Releasing Hormone Agonists: The End of the Controversy? Journal of Clinical Oncology, 36(19), 1895-1897. doi: 10.1200/jco.2018.78.9347
11. Oktay K, Harvey BE, Partridge AH, et al. Fertility Preservation in Patients with Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol 2018; 36:1994.
12. Ethics Committee of the American Society for Reproductive Medicine. Electronic address: ASRM@asrm.org. Fertility preservation and reproduction in patients facing gonadotoxic therapies: an Ethics Committee opinion. Fertil Steril 2018; 110:380.

| SUMMARY OF REVIEW/REVISIONS | DATE |
|---|---|
| REVISION- Notable revisions:<br>Duration of Approval<br>Compendial Approved Off Labeled uses<br>References | Q3 2022 |
| Q2 2022 Established tracking in new format | Historical changes on file |
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