Clinical Policy: Goserelin Acetate (Zoladex)

Reference Number: ERX.SPA.145
Effective Date: 10.01.16
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Goserelin acetate (Zoladex®) is a gonadotropin-releasing hormone (GnRH) agonist.

FDA Approved Indication(s)
Zoladex 3.6 and 10.8 are indicated for the treatment of prostatic carcinoma:

- In combination with flutamide for the management of locally confined Stage T2b-T4 (Stage B2-C) carcinoma. Treatment should start 8 weeks prior to initiating radiation therapy and continue during radiation therapy
- As palliative treatment of advanced carcinoma

Zoladex 3.6 is indicated:

- For the management of endometriosis, including pain relief and reduction of endometriotic lesions for the duration of therapy
- As an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding
- For the palliative treatment of advanced breast cancer in pre- and perimenopausal women

Limitation(s) of use: Experience with Zoladex for the management of endometriosis has been limited to women 18 years of age and older treated for 6 months.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Zoladex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Prostate Cancer (must meet all)**:**

1. Diagnosis of prostate cancer;
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. Failure of one of the following, unless clinically significant adverse effects are experienced or all are contraindicated: leuprolide acetate injection (generic), Eligard®, Lupron® Depot (7.5 mg, 22.5 mg, 30 mg, or 45 mg);*
   **Prior authorization may be required for these agents*
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 3.6 mg per month and/or 10.8 mg per 3 months;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Breast Cancer (must meet all)**:**
1. Diagnosis of breast cancer;
2. Request is for Zoladex 3.6 mg;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Failure of Lupron Depot*, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required*
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 3.6 mg per month;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

C. Endometriosis (must meet all)**:**
1. Diagnosis of endometriosis
2. Request is for Zoladex 3.6 mg;
3. Prescribed by or in consultation with a gynecologist;
4. Age ≥ 18 years;
5. Failure of Lupron Depot*, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required*
6. Endometriosis as a cause of pain is one of the following (a or b):
   a. Surgically confirmed;
   b. Clinically suspected and member has failed a 3-month trial of one of the following agents within the last year or has a documented intolerance or contraindication to the agent (i, ii, or iii):
      i. A non-steroidal antiinflammatory drug;
      ii. An oral or depot contraceptive;
      iii. A progestin;
7. For members currently receiving treatment with goserelin, total duration of therapy has not exceeded 6 months;
8. Dose does not exceed 3.6 mg per month.

Approval duration: 6 months

D. Dysfunctional Uterine Bleeding (must meet all)**:**
1. Diagnosis of dysfunctional uterine bleeding;
2. Request is for Zoladex 3.6 mg;
3. Prescribed by or in consultation with a gynecologist;
4. Age ≥ 18 years;
5. Prescribed as an endometrial-thinning agent prior to endometrial ablation;
6. Member has not yet received two implants;
7. Dose does not exceed 3.6 mg per month.

Approval duration: 8 weeks (2 implants per ablation procedure)

E. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Prostate Cancer (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Zoladex for prostate cancer and has received this medication for at least 30 days;
2. Member is responding positively to therapy;

3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 3.6 mg per month and/or 10.8 mg per 3 months;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Breast Cancer (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Zoladex for breast cancer and has received this medication for at least 30 days;
2. Request is for Zoladex 3.6 mg;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 3.6 mg per month;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

C. Endometriosis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Request is for Zoladex 3.6 mg;
3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: improvement in dysmenorrhea, dyspareunia, pelvic pain/induration/tenderness, size of endometrial lesions;
4. Total duration of goserelin therapy has not exceeded 6 months;
5. If request is for a dose increase, new dose does not exceed 3.6 mg per month.

Approval duration: up to a total treatment duration of 6 months

D. Dysfunctional Uterine Bleeding (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Request is for Zoladex 3.6 mg;
3. Member has not yet received two implants;
4. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: improvement in dysmenorrhea, dyspareunia, pelvic pain/induration/tenderness, size of endometrial lesions;
5. If request is for a dose increase, new dose does not exceed 3.6 mg per month.

Approval duration: 4 weeks (2 implants total per ablation procedure)

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GnRH: gonadotropin-releasing hormone
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
NSAIDs*: ibuprofen, naproxen, fenoprofen, ketoprofen, mefenamic acid, meclofenamate, indomethacin, tolmetin, diclofenac, etodolac, diflunisal, meloxicam, piroxicam	Endometriosis Varies – refer to specific prescribing information	Varies – refer to specific prescribing information
Combined oral estrogen-progesterone contraceptives*: ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, etonogestrel, levonorgestrel, norelgestromin, norethindrone, norgestimate, or norgestrel); estradiol valerate + dienogest; mestranol + norethindrone	Endometriosis 1 tablet PO QD (may vary per specific prescribing information)	1 tablet per day (may vary per specific prescribing information)
Progestin-only oral contraceptives*: norethindrone	Endometriosis 0.35 mg PO QD	0.35 mg PO QD
Depot progestin contraceptive*: medroxyprogesterone acetate	Endometriosis IM: 150 mg per 3 months (every 13 weeks) SC: 104 mg per 3 months (every 12-14 weeks)	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Examples provided may not be all-inclusive*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity
  - Pregnancy unless used for treatment of advanced breast cancer
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Goserelin acetate (Zoladex 3.6, 10.8)	Prostate cancer - stage B2-C	3.6 mg SC 8 weeks before radiotherapy, followed by 10.8 mg SC in 28 days (alternative: 4 injections of 3.6 mg at 28-day intervals, 2 preceding and 2 during radiotherapy)	See regimen
Goserelin acetate (Zoladex 3.6)	Prostate cancer - palliative therapy	3.6 mg SC every 28 days	3.6 mg/28 days

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Endometriosis	3.6 mg SC every 28 days	3.6 mg/28 days (6 months total treatment)
	Dysfunctional uterine bleeding	3.6 mg SC every 28 days	3.6 mg/28 days (2 doses total per ablation procedure)
	Breast cancer - palliative therapy	3.6 mg SC every 28 days	3.6 mg/28 days

VI. Product Availability
Implants: 3.6 mg, 10.8 mg

VII. References
1. Zoladex (3.6 mg) Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2020. Available at https://www.zoladexhcp.com. Accessed July 14, 2021.
2. Zoladex (10.8 mg) Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2020. Available at https://www.zoladexhcp.com. Accessed July 14, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Goserelin acetate. Available at nccn.org. Accessed July 14, 2021.
4. National Comprehensive Cancer Network. Prostate cancer (Version 2.2021). Available at https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed July 14, 2021.
5. National Comprehensive Cancer Network. Breast cancer (Version 5.2021). Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 14, 2021.
6. Committee on Practice Bulletins - Gynecology. Management of endometriosis. July 2010 (reaffirmed 2016); 116(1): 223-236.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: no significant changes; for oncology, summarized NCCN and FDA-approved uses for improved clarity (limited to diagnosis) and added specialist involvement in care; references reviewed and updated.	08.07.18	11.18
4Q 2019 annual review: for prostate cancer removed requirement for use of 3.6 mg or 10.8 mg strengths as those are the only available strengths, added urologist specialist option; references reviewed and updated.	07.29.19	11.19
4Q 2020 annual review: for prostate cancer, breast cancer, and endometriosis indications added leuprolide redirection; revised notation on endometriosis to state total duration of therapy should not exceed 6 months (previously stated 12 months) per the prescribing information; references reviewed and updated.	07.15.20	11.20
4Q 2021 annual review: added 8 week initial and 4 week continued approval duration for dysfunctional uterine bleeding indication; for endometriosis clarified total duration of therapy has not exceeded 6 months represented as a criteria requirement rather than a foot note in the criteria set; references reviewed and updated.	07.14.21	11.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of

physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.