Clinical Policy: Goserelin Acetate (Zoladex)

Reference Number: ERX.SPA.145
Effective Date: 10.01.16
Last Review Date: 11.17 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 (which may include office chart notes and lab results) supporting that member has met all approval criteria.

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. Request is for Zoladex (3.6 and/or 10.8);
2. Diagnosis of prostate cancer;
3. Age ≥ 18 years;
4. Meets (a or b):
   a. FDA approved use:
      i. In combination with flutamide for the management of locally confined stage T2b-T4 (stage B2-C) disease;
      ii. Palliative treatment of advanced disease:
   b. NCCN recommended use - categories 1 and 2A (any of the following):
      i. Adjuvant androgen deprivation therapy (ADT) as a single agent or in combination with an antiandrogen if positive lymph nodes found during pelvic lymph node dissection;
      ii. Initial ADT as a single agent or in combination with an antiandrogen (a, b, or c):
         1. With radiation therapy for (1, 2, or 3):
            1) Intermediate risk disease;
            2) High or very high risk disease +/- docetaxel;
            3) Regional disease (any T, N1, M0);
         2. For very high risk disease if not a candidate for definitive therapy;
         3. For regional disease (any T, N1, M0) or metastatic disease (M1);
      iii. ADT as a single agent or in combination with an antiandrogen (a or b):

a) For biochemical failure following radical prostatectomy (1 or 2):
1) With radiation therapy if no distant metastases;
2) +/- radiation therapy if distant metastases;
b) For positive digital rectal examination following radiation therapy (1 or 2):
1) If biopsy is negative and there are no distant metastases;
2) If not a candidate for local therapy;

iv. For progressive castration-naive disease (a, b, or c):
a) As a single agent;
b) With an antiandrogen;
c) With docetaxel +/- prednisone +/- an antiandrogen for metastatic (M1) disease;

v. For castration-recurrent disease to maintain castrate levels of serum testosterone as a single agent or with an antiandrogen;

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

Approval duration: 12 months

B. Breast Cancer (must meet all)**:**

1. Request is for Zoladex (3.6);
2. Diagnosis of breast cancer;
3. Age ≥ 18 years;
4. Member is pre/peri-menopausal;
5. Member meets (a or b):
   a. FDA approved use:
      i. Palliative therapy for advanced disease;
   b. NCCN recommended use - categories 1 and 2A:
      i. In combination with (a or b):
         a) Adjuvant endocrine therapy (e.g., tamoxifen or an aromatase inhibitor) for hormone receptor-positive disease;
         b) Endocrine therapy for recurrent or stage IV disease;
6. At the time of request, member is not pregnant;
7. Request meets one of the following:
   a. Dose does not exceed 3.6 mg/month;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

C. Endometriosis (must meet all)**:**

1. Request is for Zoladex (3.6);
2. Diagnosis of endometriosis;
3. Prescribed by or in consultation with a gynecologist;
4. Age ≥ 18 years;
5. Endometriosis as a cause of pain is (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 nonsteroidal antiinflammatory drug;
      ii. An oral or depot contraceptive;
      iii. A progestin;
6. At the time of request, member is not pregnant;
7. Dose does not exceed 3.6 mg/month.

Approval duration: 6 months

D. Dysfunctional Uterine Bleeding (must meet all)**:**
1. Request is for Zoladex (3.6);
2. Diagnosis of dysfunctional uterine bleeding;
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. At the time of request, member is not pregnant;
7. Dose does not exceed 3.6 mg/month.

Approval duration: 6 months (up to 2 implants for one procedure)

C. 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. Request is for Zoladex (3.6 and/or 10.8);
3. Member is responding positively to therapy (e.g., improved quality of life, no unacceptable toxicity);
4. If request is for a dose increase, request meets one of the following:
   a. New dose does not exceed 3.6 mg/month and/or 10.8 mg/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*).

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);
3. Member is responding positively to therapy (e.g., improved quality of life, no unacceptable toxicity);
4. If request is for a dose increase, request meets one of the following:
   a. New dose does not exceed 3.6 mg/month;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

C. Endometriosis (must meet all)**:**
1. Previously received 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);
3. Member is responding positively to therapy (e.g., improvement in dysmenorrhea, dyspareunia, pelvic pain/induration/tenderness, size of endometrial lesions);
4. If request is for a dose increase, new dose does not exceed 3.6 mg/month.

Approval duration: 6 months (*up to 12 months total*)

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);
3. Member has not yet received two implants;

4. Member is responding positively to therapy (e.g., 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/month.

Approval duration: 6 months (up to 2 implants for one 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
ADT: androgen deprivation therapy
GnRH: gonadotropin-releasing hormone

Appendix B: General Information
Biochemical failure is defined as either: 1) failure of prostate specific antigen (PSA) to fall to undetectable levels (PSA persistence) or 2) undetectable PSA after radical prostatectomy with a subsequent detectable PSA that increases on 2 more determinations (PSA recurrence).

Appendix C: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Flutamide	Prostate Cancer - Stage B2-C 250 mg PO TID	750 mg/day
Lupron Depot® 7.5, 22.5, 30, 45 (leuprolide acetate)	Prostate Cancer - Palliative Therapy IM: 7.5 mg/4 weeks, 22.5 mg/12 weeks, 30 mg/16 weeks, or IM 45 mg/24 weeks	See regimen
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/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/3 months (every 13 weeks) SC: 104 mg/3 months (every 12-14 weeks)	See regimen

**Examples provided may not be all-inclusive*

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.

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
	Endometriosis	3.6 mg SC every 28 days	3.6 mg/28 days
	Dysfunctional uterine bleeding	3.6 mg SC every 28 days	3.6 mg/28 days
	Breast cancer - palliative therapy	3.6 mg SC every 28 days	3.6 mg/28 days

VI. Product Availability

Drug Name	Availability
Goserelin acetate (Zoladex 3.6)	Implant: 3.6 mg (every 28 days)
Goserelin acetate (Zoladex 10.8)	Implant: 10.8 mg (every 12 weeks)

VII. References

1. Zoladex (3.6 mg) Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2016. Available at https://www.zoladexhcp.com. Accessed July 26, 2017.
2. Zoladex (10.8 mg) Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2016. Available at https://www.zoladexhcp.com. Accessed July 26, 2017.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Goserelin acetate. Available at nccn.org. Accessed July 26, 2017.
4. National Comprehensive Cancer Network. Prostate cancer (Version 2.2017). Available at nccn.org. Accessed July 26, 2017.
5. National Comprehensive Cancer Network. Breast cancer (Version 2.2017). Available at nccn.org. Accessed July 26, 2017.
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
Policy created	05.16	09.16
Converted to new template. Changed 3 month trial of analgesics and/or hormonal contraceptives to NSAIDS and/or hormonal contraceptives. Added pregnancy contraindication. Prostate and breast cancer: Off-label NCCN recommended uses added. Max doses removed. Continued: Added requirement for positive response to therapy.	07.17	08.17
4Q17 Annual Review Dosing added to oncology criteria. Positive therapeutic response examples added for oncology and endometriosis criteria. Oncology FDA/NCCN (categories 1 and 2A) indications listed separately.	09.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Endometriosis step therapy edited from estrogen/progestin OC to OC or depot contraceptive or progestin. Total approval duration increased from 6 to 12 months. Specialist requirement added for endometriosis, DUB. Pregnancy added for breast cancer per expert recommendation.		

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.

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