RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	goserelin acetate
Policy Number:	RxA.576
Drug(s) Applied:	Zoladex®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Goserelin acetate (Zoladex®) is a gonadotropin-releasing hormone (GnRH) receptor agonist. Zoladex® is indicated for:

- Use in combination with flutamide for the management of locally confined Stage T2b-T4 (Stage B2-C) carcinoma of the prostate; treatment with Zoladex® and flutamide should start 8 weeks prior to initiating radiation therapy and continue during radiation therapy:
  - Zoladex® – 3.6 mg implant; 10.8 mg implant
- Palliative treatment of advanced carcinoma of the prostate:
  - Zoladex® – 3.6 mg implant; 10.8 mg implant
- Management of endometriosis, including pain relief and reduction of endometriotic lesions for the duration of therapy; experience with Zoladex® for the management of endometriosis has been limited to women 18 years of age and older treated for 6 months:
  - Zoladex® – 3.6 mg implant
- Use as an endometrial thinning agent prior to endometrial ablation for dysfunctional uterine bleeding
  - Zoladex® – 3.6 mg implant
- Use in the palliative treatment of advanced breast cancer in pre- and perimenopausal women
  - Zoladex® – 3.6 mg implant

Dosing Information

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 per 28 days
	Endometriosis	3.6 mg SC every 28 days	3.6 mg per 28 days
	Dysfunctional uterine bleeding	3.6 mg SC every 28 days	3.6 mg per 28 days (2 doses total per ablation procedure
	Breast cancer - palliative therapy	3.6 mg SC every 28 days	3.6 mg per 28 days

Dosage Forms

- Implant: 3.6 mg, 10.8 mg

Clinical Policy

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

I. Initial Approval Criteria

A. Prostate Cancer (must meet all):

1. Diagnosis of prostate cancer;
2. Request is for one of the following: (a or b);
   a. Locally confined Stage T2b-T4 (Stage B2-C) carcinoma of the prostate;
   b. Palliative treatment of advanced carcinoma of the prostate.
3. Prescribed by or in consultation with an oncologist or urologist;
4. Age 18 years of age or older;
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
Commercial: 12 months
Medicaid: 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 of age or older;
5. 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
Commercial: 12 months
Medicaid: 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 gynaecologist;
4. Age 18 years of age or older;
5. 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 anti-inflammatory drug;
ii. An oral or depot contraceptive;
iii. A progestin;

6. Dose does not exceed 3.6 mg per month.

Approval Duration
Commercial: 6 months
Medicaid: 6 months
Total duration of therapy should not exceed 12 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 gynaecologist;
4. Age 18 years of age or older;
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
Commercial: 2 implants per ablation procedure
Medicaid: 2 implants per ablation procedure

II. Continued Therapy Approval

A. Prostate Cancer (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications 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
Commercial: 12 months
Medicaid: 12 months

B. Breast Cancer (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications 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
Commercial: 12 months

Medicaid: 12 months

C. Endometriosis (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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. If request is for a dose increase, new dose does not exceed 3.6 mg per month.

Approval Duration
Commercial: 6 months
Medicaid: 6 months
Total duration of therapy should not exceed 12 months

D. Dysfunctional Uterine Bleeding (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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, 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
Commercial: 2 implants total per ablation procedure
Medicaid: 2 implants total per ablation procedure

III. Appendices

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

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

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,	Endometriosis 1 tablet PO once daily (may vary per specific prescribing information)	1 tablet per day (may vary per specific prescribing information)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
norelgestromin, norethindrone, norgestimate, or norgestrel); estradiol valerate + dienogest; mestranol + norethindrone		
Progestin-only oral contraceptives*: norethindrone	Endometriosis 0.35 mg PO once daily	0.35 mg PO once daily
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

APPENDIX D: General Information

- Transient worsening of tumor symptoms may occur during the first few weeks of treatment with ZOLADEX, which may include ureteral obstruction and spinal cord compression.

References

1. Zoladex® (3.6 mg) Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2019. Available at https://www.zoladexhcp.com . Accessed September 23, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. goserelin acetate. Available at nccn.org. Accessed September 23, 2020.
3. National Comprehensive Cancer Network. Prostate cancer (Version 2.2020). Available at https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf . Accessed September 23, 2020.
4. National Comprehensive Cancer Network. Breast cancer (Version 6.2020). Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf . Accessed September 23, 2020.
5. Committee on Practice Bulletins - Gynecology. Management of endometriosis. July 2010 (reaffirmed 2016); 116(1): 223-236.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020

Policy was reviewed: 1. Clinical policy title was updated. 2. Line of business policy applies to was updated to all lines of business. 3. Initial approval criteria I.A was updated: added request is for (Stage B2-C) carcinoma of the prostate or palliative treatment of advanced carcinoma of the prostate as per PI. 4. Continued therapy approval criteria II.A.1, II.B.2, II.C.1 & II.D.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…". 5. Appendix D added general information. 6. References were reviewed and updated.	9/23/2020	12/07/2020