

Clinical Policy: Goserelin Acetate (Zoladex)

Reference Number: CP.PHAR.171

Effective Date: 10.01.16

Last Review Date: 11.22

Line of Business: HIM, Medicaid

[Coding Implications](#)[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) receptor 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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 \geq 18 years;
4. 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 \geq 18 years;
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: 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 \geq 18 years;
5. Endometriosis as a cause of pain is one of the following (a or b):
 - a. Surgically confirmed;
 - b. Both of the following (i and ii):
 - i. Clinically suspected;
 - ii. Failure of a 3-month trial of one of the following within the last year, unless clinically adverse effects are experienced or all are contraindicated (1, 2, or 3):
 1. A nonsteroidal anti-inflammatory drug (*see Appendix B for examples*);
 2. An oral or injectable depot contraceptive (*see Appendix B for examples*);
 3. A progestin (*see Appendix B for examples*);
6. For members currently receiving treatment with goserelin, total duration of therapy has not exceeded 6 months;
7. 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 \geq 18 years;
5. Prescribed as an endometrial-thinning agent prior to endometrial ablation;
6. For members currently receiving treatment with goserelin, 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. Gender Dysphoria, Gender Transition (off-label) (must meet all):

1. Diagnosis of gender dysphoria or request is for gender transition;
2. Prescribed by or in consultation with an endocrinologist and a provider with expertise in gender dysphoria and transgender medicine based on a certified training program or affiliation with local transgender health services (e.g., mental health professional such as psychologist, psychiatrist, see *Appendix D*);
3. Age and pubertal development - meets (a or b):
 - a. Member has reached or passed through Tanner Stage 2* and is < 18 years of age;

**Age ranges approximating Tanner Stage 2 pubertal development extend from 8 to 13 years of age in girls and 9 to 14 years of age in boys.*

- b. Member is ≥ 18 years of age and has failed to achieve physiologic hormone levels with gender-affirming hormonal therapy (e.g., estrogen, testosterone) unless contraindicated or clinically significant adverse effects are experienced;
4. Member demonstrates understanding of expected GnRH analogue treatment outcomes and has given consent for such treatment;
5. If member has a psychiatric comorbidity, member is followed by mental health provider;
6. Psychosocial support will be provided during treatment;
7. Dose is within FDA maximum limit for any FDA-approved indication (see Section V) or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

F. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Prostate Cancer (must meet all):

1. Currently receiving medication via Centene benefit, 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 Centene benefit, 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. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
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. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
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. Member has not yet received two implants;
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. Gender Dysphoria, Gender Transition (off-label) (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication (see Section V) or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

F. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, 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

WPATH: World Professional Association
for Transgender Health

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 for all relevant lines of business 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

Appendix D: General Information

- World Professional Association for Transgender Health (WPATH) offers their Global Education Institute (GEI) Certified Training Courses: Best Practices in Transgender Medical and Mental Health Care. Additionally, the following link provides a search tool to locate WPATH member providers: <https://www.wpath.org/provider/search>
- Transgender Care Therapy Certification Training is also offered by the International Transgender Certification Association (ITCA). Professionals with expertise in

transgender care can be located using the following search tool:
<https://transgendercertification.com/locate-a-professional/>

- The draft of WPATH Standards of Care Version 8 are available and open for public comment. These standards of care recommend that adolescents are managed by a multidisciplinary care team that involves both medical and mental health professionals. The list of key disciplines includes but is not limited to: adolescent medicine/primary care, endocrinology, psychology, psychiatry, speech/language pathology, fertility, social work, support staff, and the surgical team. The need to include a healthcare professional with some expertise in mental health does not dictate the inclusion of a psychologist, psychiatrist or social work in every assessment. Instead, a general practitioner, nurse or other qualified clinician could fulfill this requirement as long as they have sufficient expertise to diagnose gender incongruence, recognize mental health concerns, distinguish between these concerns and gender dysphoria, incongruence or diversity, assist a transgender person in care planning and preparing for gender affirmative medical and surgical treatments, and refer to a mental health professional if needed.

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 per 28 days |
| | Endometriosis | 3.6 mg SC every 28 days | 3.6 mg per 28 days (6 months total treatment) |
| | 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 |

VI. Product Availability

Implant: 3.6 mg, 10.8 mg

VII. References

1. Zoladex (3.6 mg) Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; December 2020. Available at <https://www.zoladexhcp.com>. Accessed July 26, 2022.
2. Zoladex (10.8 mg) Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; December 2020. Available at <https://www.zoladexhcp.com>. Accessed July 26, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Goserelin acetate. Available at nccn.org. Accessed July 26, 2022.
4. National Comprehensive Cancer Network. Prostate cancer (Version 4.2022). Available at https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed July 26, 2022.
5. National Comprehensive Cancer Network. Breast cancer (Version 4.2022). Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 26, 2022.
6. Committee on Practice Bulletins - Gynecology. Management of endometriosis. July 2010 (reaffirmed 2016); 116(1): 223-236.
7. Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender nonconforming people. WPATH: World Professional Association for Transgender Health. 7th version; 2012. Available at https://www.wpath.org/media/cms/Documents/SOC%20v7/SOC%20V7_English2012.pdf?t=1613669341. Accessed July 26, 2022.
8. WPATH: World Professional Association for Transgender Health Standards of Care Version 8 Draft. Available at: <https://www.wpath.org/soc8>. Accessed July 26, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPSC Codes | Description |
|-------------|---------------------------------------|
| J9202 | Goserelin acetate implant, per 3.6 mg |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|--|----------|-------------------|
| 4Q 2018 annual review: no significant changes; added HIM; for oncology, summarized NCCN and FDA-approved uses for improved clarity (limited to diagnosis); specialist involvement in care and continuation of care added; references reviewed and updated. | 08.07.18 | 11.18 |
| 4Q 2019 annual review: removed pregnancy safety requirement for breast cancer and endometriosis indications; added oncologist prescriber requirement for breast cancer; 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; for dysfunctional uterine bleeding added requirement to Section I and II to validate member has not yet received two implants; references reviewed and updated. | 07.29.19 | 11.19 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|--|----------|-------------------|
| 4Q 2020 annual review: no significant changes; 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 to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated. | 07.14.21 | 11.21 |
| Added criteria set for off-label use in gender dysphoria, gender transition; references reviewed and updated. | 12.14.21 | 02.22 |
| 4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section. | 07.26.22 | 11.22 |

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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