Reference number(s)
1918-A, 6056-A

SPECIALTY GUIDELINE MANAGEMENT

ZOLADEX (goserelin acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Prostate cancer
   a. 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.
   b. In the palliative treatment of advanced carcinoma of the prostate.
2. Endometriosis
   For the 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 strength only)
3. Endometrial thinning
   For use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding (Zoladex 3.6 mg strength only).
4. Advanced breast cancer
   For use in the palliative treatment of advanced breast cancer in pre-and perimenopausal women (Zoladex 3.6 mg strength only).

B. Compendial Uses
1. Breast cancer
2. Prostate cancer
3. Ovarian cancer
4. Gender dysphoria (also known as transgender and gender diverse [TGD] persons)
5. Preservation of ovarian function
6. Prevention of recurrent menstrual related attacks in acute porphyria
7. Treatment of chronic anovulatory uterine bleeding with severe anemia

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided for members with any of the following exclusions: Use of the 10.8 mg strength for diagnoses other than prostate cancer, breast cancer, and gender dysphoria.

III. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Hormone receptor status testing results (where applicable).

IV. PRESCRIBER SPECIALTIES

A. Gender dysphoria
The medication must be prescribed by or in consultation with a provider specialized in the care of transgender youth (e.g., pediatric endocrinologist, family or internal medicine physician, obstetrician-gynecologist) that has collaborated care with a mental health provider for members less than 18 years of age.

B. Prevention of recurrent menstrual related attacks in acute porphyria
The medication must be prescribed by or in consultation with a provider experienced in the management of porphyrias.

V. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of 12 months may be granted for the treatment of hormone receptor-positive breast cancer.

B. Prostate cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

C. Epithelial ovarian, fallopian tube, primary peritoneal cancer or malignant sex cord-stromal tumor
Authorization of 12 months may be granted for treatment of persistent or recurrent epithelial ovarian, fallopian tube, primary peritoneal cancer or malignant sex cord-stromal tumor when used as a single agent.

D. Endometriosis
Authorization of a total of 6 months may be granted to members for treatment of endometriosis.

E. Endometrial-thinning agent
1. Authorization of 2 doses may be granted for endometrial thinning prior to endometrial ablation or resection for dysfunctional uterine bleeding.
2. Authorization of a total of 6 months may be granted for treatment of chronic anovulatory uterine bleeding with severe anemia.

F. Gender dysphoria
1. Authorization of 12 months may be granted for pubertal hormonal suppression in an adolescent member when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in treatment.
   iii. The member has reached Tanner stage 2 of puberty or greater.
   iv. The member's comorbid conditions are reasonably controlled.
   v. The member has been educated on any contraindications and side effects to therapy.
   vi. The member has been informed of fertility preservation options.
2. Authorization of 12 months may be granted for gender transition when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in treatment.
   iii. The member will receive the requested medication concomitantly with gender-affirming hormones.
   iv. The member's comorbid conditions are reasonably controlled.
   v. The member has been educated on any contraindications and side effects to therapy.

vi. The member has been informed of fertility preservation options.

G. Preservation of ovarian function
Authorization of 3 months may be granted for preservation of ovarian function when the member is premenopausal and undergoing chemotherapy.

H. Prevention of recurrent menstrual related attacks in acute porphyria
Authorization of 12 months may be granted for prevention of recurrent menstrual related attacks in members with acute porphyria.

VI. CONTINUATION OF THERAPY

A. Breast cancer and ovarian cancer
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy and who have not experienced an unacceptable toxicity.

B. Prostate cancer
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization who are experiencing clinical benefit to therapy (e.g., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

C. Gender dysphoria
1. Authorization of 12 months may be granted for continued treatment for pubertal hormonal suppression in adolescent members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in treatment.
   iii. The member has previously reached Tanner stage 2 of puberty or greater.
   iv. The member's comorbid conditions are reasonably controlled.
   v. The member has been educated on any contraindications and side effects to therapy.
   vi. Before the start of therapy, the member has been informed of fertility preservation options.
2. Authorization of 12 months may be granted for continued treatment for gender transition in members requesting reauthorization when all of the following criteria are met:
   i. The member has a diagnosis of gender dysphoria.
   ii. The member is able to make an informed decision to engage in treatment.
   iii. The member will receive the requested medication concomitantly with gender-affirming hormones.
   iv. The member's comorbid conditions are reasonably controlled.
   v. The member has been educated on any contraindications and side effects to therapy.
   vi. Before the start of therapy, the member has been informed of fertility preservation options.

D. All members (including new members) requesting authorization for continuation of therapy for the specified indications below must meet all initial authorization criteria:
1. Endometriosis
2. Endometrial-thinning agent
3. Preservation of ovarian function
4. Prevention of recurrent menstrual related attacks in acute porphyria

VII. OTHER

Per state regulatory guidelines around gender dysphoria, age restrictions may apply.

VIII. REFERENCES

1. Zoladex 3.6 mg [package insert]. Deerfield, IL: TerSera Therapeutics LLC; March 2023.
2. Zoladex 10.8 mg [package insert]. Deerfield, IL: TerSera Therapeutics LLC; December 2020.
3. The NCCN Drugs & Biologics Compendium® © 2024 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 6, 2024.
4. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at http://www.micromedexsolutions.com. Accessed February 6, 2024.
5. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2017:102(11):3869–3903.
6. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
7. Coleman E, Radix AE, Brown GR, et al. Standards of care for the health of transgender and gender diverse people, version 8. 2022;23(Suppl 1):S1-S259. doi: 10.1080/26895269.2022.2100644
8. Noguchi S, Kim HJ, Jesena A, et al. Phase 3, open-label, randomized study comparing 3-monthly with monthly goserelin in pre-menopausal women with estrogen receptor-positive advanced breast cancer. *Breast Cancer (Tokyo, Japan)*. 2016;23(5):771-779. doi:10.1007/s12282-015-0637-4.
9. Moore HCF, Unger JM, Phillips K-A, et al. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. *N Engl J Med.* 2015;372:923-32. doi:10.1056/NEJMoa1413204.
10. Clowse MEB, Behera MA, Anders CK, et al. Ovarian preservation by GnRH agonists during chemotherapy: a meta-analysis. *J Womens Health (Larchmt)*. 2009 Mar; 18(3): 311–319. doi:10.1089/jwh.2008.0857.
11. Oktay K, Harvey BE, et al: Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. Journal of Clinical Oncology 36:1994-2003, 2018.
12. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 1.2024. https://www.nccg.org/professionals/ physician_gls/pdf/breast.pdf. Accessed February 6, 2024.
13. Stein P, Badminton M, Barth J, et al. British and Irish Porphyria Network. Best practice guidelines on clinical management of acute attacks of porphyria and their complications. Ann Clin Biochem. 2013 May;50(Pt 3):217-23.
14. Innala E, Bäckström T, Bixo M, et al. Evaluation of gonadotrophin-releasing hormone agonist treatment for prevention of menstrual-related attacks in acute porphyria. *Acta Obstet Gynecol Scand* 2010;89:95–100.
15. Mahfouda S, Moore JK, Siafarikas A, et al. Puberty suppression in transgender children and adolescents. *Lancet Diabetes Endocrinol*. 2017;5:816-26.
16. Health Care for Transgender and Gender Diverse Individuals. ©2021 The American College of Obstetricians and Gynecologists. Available at: https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2021/03/health-care-for-transgender-and-gender-diverse-individuals.