Clinical Policy: Goserelin Acetate (Zoladex)
Reference Number: ERX.SPA.145
Effective Date: 10.01.16
Last Review Date: 11.17

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/perimenopausal;
   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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flutamide</td>
<td>Prostate Cancer - Stage B2-C 250 mg PO TID</td>
<td>750 mg/day</td>
</tr>
<tr>
<td>Lupron Depot® 7.5, 22.5, 30, 45 (leuprolide acetate)</td>
<td>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</td>
<td>See regimen</td>
</tr>
<tr>
<td>NSAIDs*: ibuprofen, naproxen, fenoprofen, ketoprofen, mefenamic acid, meclofenamate, indomethacin, tolmetin, diclofenac, etodolac, diflunisal, meloxicam, piroxicam</td>
<td>Endometriosis Varies – refer to specific prescribing information</td>
<td>Varies – refer to specific prescribing information</td>
</tr>
<tr>
<td>Combined oral estrogen-progesterone contraceptives*: ethinyl estradiol + (desogestrel, ethynodiol diacetate, drospirenone, estradiol valerate + dienogest; mestranol + norethindrone)</td>
<td>Endometriosis 1 tablet PO QD (may vary per specific prescribing information)</td>
<td>1 tablet/day (may vary per specific prescribing information)</td>
</tr>
<tr>
<td>Progestin-only oral contraceptives*: norethindrone</td>
<td>Endometriosis 0.35 mg PO QD</td>
<td>0.35 mg PO QD</td>
</tr>
<tr>
<td>Depot progestin contraceptive*: medroxyprogesterone acetate</td>
<td>Endometriosis IM: 150 mg/3 months (every 13 weeks) SC: 104 mg/3 months (every 12-14 weeks)</td>
<td>See regimen</td>
</tr>
</tbody>
</table>

*Examples provided may not be all-inclusive
V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goserelin acetate (Zoladex 3.6, 10.8)</td>
<td>Prostate cancer - stage B2-C</td>
<td>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)</td>
<td>See regimen</td>
</tr>
<tr>
<td>Goserelin acetate (Zoladex 3.6)</td>
<td>Prostate cancer - palliative therapy</td>
<td>3.6 mg SC every 28 days</td>
<td>3.6 mg/28 days</td>
</tr>
<tr>
<td></td>
<td>Endometriosis</td>
<td>3.6 mg SC every 28 days</td>
<td>3.6 mg/28 days</td>
</tr>
<tr>
<td></td>
<td>Dysfunctional uterine bleeding</td>
<td>3.6 mg SC every 28 days</td>
<td>3.6 mg/28 days</td>
</tr>
<tr>
<td></td>
<td>Breast cancer - palliative therapy</td>
<td>3.6 mg SC every 28 days</td>
<td>3.6 mg/28 days</td>
</tr>
</tbody>
</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goserelin acetate (Zoladex 3.6)</td>
<td>Implant: 3.6 mg (every 28 days)</td>
</tr>
<tr>
<td>Goserelin acetate (Zoladex 10.8)</td>
<td>Implant: 10.8 mg (every 12 weeks)</td>
</tr>
</tbody>
</table>

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Converted to new template.</td>
<td>05.16</td>
<td>09.16</td>
</tr>
<tr>
<td>Changed 3 month trial of analgesics and/or hormonal contraceptives to NSAIDS and/or hormonal contraceptives.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Added pregnancy contraindication.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate and breast cancer: Off-label NCCN recommended uses added. Max doses removed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continued: Added requirement for positive response to therapy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4Q17 Annual Review</td>
<td>09.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Dosing added to oncology criteria.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive therapeutic response examples added for oncology and endometriosis criteria.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncology FDA/NCCN (categories 1 and 2A) indications listed separately.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2016 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.