



Drug Policy:

Luteinizing Hormone Releasing Hormone (LHRH) Agonists and Antagonists

POLICY NUMBER UM ONC_1041	SUBJECT Luteinizing Hormone Releasing Hormone (LHRH) Agonists and Antagonists [Eligard/Lupron/Lutrate Depot IM (leuprolide acetate), Camcevi SC Depot (leuprolide mesylate), Trelstar (triptorelin acetate), Zoladex (goserelin acetate), Firmagon (degarelix), Orgovyx (relugolix)]		DEPT/PROGRAM UM Dept	PAGE 1 OF 5
DATES COMMITTEE REVIEWED 01/12/11, 03/13/13, 02/12/14, 06/10/15, 10/12/15, 12/09/15, 08/25/16, 10/20/16, 11/08/16, 08/10/17, 08/08/18, 07/10/19, 08/14/19, 12/11/19, 08/12/20, 09/25/20, 10/14/20, 11/11/20, 12/09/20, 01/13/21, 02/10/21, 05/12/21, 09/08/21, 11/15/21, 02/09/22, 05/11/22, 07/13/22, 12/14/22, 02/08/23, 03/08/23, 05/10/23	APPROVAL DATE May 10, 2023	EFFECTIVE DATE May 26, 2023	COMMITTEE APPROVAL DATES 01/12/11, 03/13/13, 02/12/14, 06/10/15, 10/12/15, 12/09/15, 08/25/16, 10/20/16, 11/08/16, 08/10/17, 08/08/18, 07/10/19, 08/14/19, 12/11/19, 08/12/20, 09/25/20, 10/14/20, 11/11/20, 12/09/20, 01/13/21, 02/10/21, 05/12/21, 09/08/21, 11/15/21, 02/09/22, 05/11/22, 07/13/22, 12/14/22, 02/08/23, 03/08/23, 05/10/23	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM v8: UM 1-2; UM 2-1	NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Luteinizing Hormone Releasing Hormone (LHRH) Agonists or Antagonists [Eligard/Lupron IM/Lutrate Depot (leuprolide acetate), Camcevi SC Depot (leuprolide mesylate), Trelstar (triptorelin acetate), Zoladex (goserelin acetate), Firmagon (degarelix), Orgovyx (relugolix)] usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and, therefore, not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this NCH policy provided:

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Breast Cancer

1. Luteinizing Hormone Releasing Hormone (LHRH) Agonists (any of the following product) may be used in combination with endocrine therapy (e.g., tamoxifen, aromatase inhibitors) for ovarian suppression in premenopausal women and in men with ER/PR positive breast cancer as adjuvant therapy or as therapy for recurrent/metastatic disease.
 - a. Eligard SC/Lupron IM Depot (J9217 leuprolide acetate 7.5 mg monthly, 22.5 mg every 3 months, 30 mg every 4 months, 45 mg every 6 months)
 - b. Lutrate IM Depot (J1954 leuprolide acetate 22.5 mg every 3 months)
 - c. Camcevi SC Kit (J1952 leuprolide mesylate 46 mg every 6 months)
 - d. Trelstar IM Depot (J3315 triptorelin pamoate 3.75 mg monthly, 11.25 mg every 3 months, and 22.5 mg every 6 months)
 - e. Zoladex SC Implant (J9202 goserelin acetate 3.6 mg monthly and 10.8 every 3 months)

C. Fertility Preservation in Women Undergoing Cytotoxic Chemotherapy

1. For women undergoing cytotoxic chemotherapy, Luteinizing Hormone Releasing Hormone (LHRH) Agonists (any of the following product) may be used in conjunction with fertility preservation methods.
 - a. Eligard SC/Lupron IM Depot (J9217 leuprolide acetate 7.5 mg monthly, 22.5 mg every 3 months, 30 mg every 4 months, 45 mg every 6 months)
 - b. Lutrate IM Depot (J1954 leuprolide acetate 22.5 mg every 3 months)
 - c. Camcevi SC Kit (J1952 leuprolide mesylate 46 mg every 6 months)
 - d. Trelstar IM Depot (J3315 triptorelin pamoate 3.75 mg monthly, 11.25 mg every 3 months, and 22.5 mg every 6 months)
 - e. Zoladex SC Implant (J9202 goserelin acetate 3.6 mg monthly and 10.8 every 3 months).

D. Prostate Cancer

1. Luteinizing Hormone Releasing Hormone (LHRH) Agonists and Antagonists (any of the following product) may be used as a single agent or in combination with an antiandrogen with or without chemotherapy for the treatment of castrate sensitive or castrate resistant M0 or M1 prostate cancer.

- a. Eligard SC/Lupron IM Depot (J9217 leuprolide acetate 7.5 mg monthly, 22.5 mg every 3 months, 30 mg every 4 months, 45 mg every 6 months)
- b. Lutrate IM Depot (J1954 leuprolide acetate 22.5 mg every 3 months)
- c. Camcevi SC Kit (J1952 leuprolide mesylate 46 mg every 6 months)
- d. Trelstar IM Depot (J3315 triptorelin pamoate 3.75 mg monthly, 11.25 mg every 3 months, and 22.5 mg every 6 months)
- e. Zoladex SC Implant (J9202 goserelin acetate 3.6 mg monthly and 10.8 every 3 months)
- f. Orgovyx (J8999 relugolix 360 mg on day 1 followed by 120 mg oral daily)
- g. Firmagon SC Kit (J9155 degarelix 240 mg followed by 80 mg every 4 weeks).

III. EXCLUSION CRITERIA

- A. Dosing exceeds single dose limit of Lupron Depot/Eligard (leuprolide acetate) IM Depot 45 mg every 6 months, Lutrate Depot (leuprolide acetate) 22.5 mg every 3 months, Camcevi SC Depot (leuprolide mesylate) 42 mg every 6 months, Zoladex (goserelin) 10.8 mg every 3 months, Trelstar (triptorelin) 22.5 mg every 6 months, Firmagon (degarelix) 240 mg (for loading dose) or 80 mg every month (continuation dose), and Orgovyx (relugolix) 360 mg (for loading dose) or 120 mg (continuation dose).
- B. Treatment exceeds the maximum limit of Orgovyx (relugolix) 30 (120 mg) tablets per month.
- C. Investigational use of [Lupron IM/Lutrate Depot/Camcevi SC Depot (leuprolide), Trelstar (triptorelin), Zoladex (goserelin), Firmagon (degarelix), Orgovyx (relugolix)] with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
 1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
 4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
 5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
 6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
 7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

- A. Loren AW, et al. American Society of Clinical Oncology. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2013 Jul 1;31(19):2500-10.
- B. Moore HC, et al. POEMS/S0230 Clinical Trial. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. *N Engl J Med*. 2015 Mar 5;372(10):923-32.
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- D. Clowse ME, et al. Ovarian preservation by GnRH agonists during chemotherapy: a meta-analysis. *J Womens Health (Larchmt)*. 2009;18(3):311-319. doi:10.1089/jwh.2008.0857.
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- N. Trelstar prescribing information. Verity Pharmaceuticals, Inc. Wayne, PA 2020.
- O. Zoladex prescribing information. TerSera Therapeutics LLC Lake Forest, IL 2021.
- P. Firmagon prescribing information. Ferring Pharmaceuticals Inc. Parsippany, NJ. 2021.
- Q. Clinical Pharmacology Elsevier Gold Standard 2023.

- R. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.
- S. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.
- T. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.
- U. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.
- V. NCQA UM 2023 Standards and Elements.

VIII. ADDENDUM

- A. For Fidelis Care 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 the use of LHRH analogs for fertility preservation in woman undergoing cytotoxic chemotherapy.