Drug Policy:

LHRH (agonists and antagonist)

POLICY NUMBER UM ONC_1041	SUBJECT Luteinizing Hormone Releasing Hormone (LHRH) Agonists and Antagonist [Lupron/Lutrate Depot IM/Camcevi SC Depot (leuprolide), Trelstar (triptorelin), Zoladex (goserelin), Firmagon (degarelix), Orgovyx (relugolix)]	DEPT/PROGRAM UM Dept	PAGE 1 OF 5

DATES COMMITTEE REVIEWED	APPROVAL DATE	EFFECTIVE DATE	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	March 8, 2023	March 31, 2023	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

PRIMARY BUSINESS OWNER: UM	COMMITTEE/BOARD APPROVAL Utilization Management Committee

URAC STANDARDS	NCQA STANDARDS	ADDITIONAL AREAS OF IMPACT
HUM v8: UM 1-2; UM 2-1	UM 2	

CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS	APPLICABLE LINES OF BUSINESS
		Commercial, Exchange, Medicaid

I. PURPOSE

To define and describe the accepted indications for LHRH agonists or antagonist [Lupron IM/Lutrate Depot /Camcevi SC Depot (leuprolide), Trelstar (triptorelin), Zoladex (goserelin), 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. Per NCH Policy, LHRH analogs are Approvable for ovarian suppression in breast cancer with the exceptions listed in the NOTE below.
2. NOTE 1: Per NCH Policy, the following LHRH analog products are not approvable for use in breast cancer:
   a. Lupron Depot (J1950 leuprolide acetate 3.75 mg or 11.25 mg)
   b. Lutrate Depot (J1954 leuprorelin acetate 22.5 mg)
   c. Zoladex (J9202 goserelin acetate).
   d. Camcevi SC Depot (J1952 leuprolide mesylate)
   e. Firmagon (J9155 degarelix)
   f. Orgovyx (J8999 relugolix).
3. NOTE 2: The above Policy Positions for Not Approvable drugs are based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) showing superior outcomes with one LHRH analog or one dosage form over another in the treatment of breast cancer. Please refer to NCH alternative agents/regimens recommended by NCH, including but not limited to regimens available at http://pathways.newcenturyhealth.com.

C. Fertility Preservation in Women Undergoing Cytotoxic Chemotherapy

1. Per NCH Policy, LHRH analogs are Approvable for members receiving fertility-impairing anti-cancer therapy who desire fertility preservation, with the exceptions listed in the NOTE below.
2. NOTE 1: Per NCH Policy, the following LHRH analog products are Not Approvable for fertility preservation:
   g. Lupron Depot (J1950 leuprolide acetate 3.75 mg or 11.25 mg)
   h. Lutrate Depot (J1954 leuprorelin acetate 22.5 mg)
   i. Zoladex (J9202 goserelin acetate)
   j. Camcevi SC Depot (J1952 leuprolide mesylate)
   k. Firmagon (J9155 degarelix)
   l. Orgovyx (J8999 relugolix).
3. An exception would be made to the above policy if the fertility preservation physician/specialist requests a specific agent and/or a specific dosage form.
4. NOTE 2: The above Policy Positions for the Not Approvable drugs are based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) showing superior outcomes with one LHRH analog over another for fertility preservation. Please refer to NCH alternative agents/regimens recommended by NCH, including but not limited to regimens available at http://pathways.newcenturyhealth.com.

D. Prostate Cancer

1. Per NCH Policy, LHRH analogs are supported for use in prostate cancer with the exceptions listed in the NOTE below.
2. NOTE 1: Per NCH Policy, the following LHRH analogs are Not Approvable for prostate cancer:
    a. Lupron Depot Depot (J1950 leuprolide acetate 3.75 mg or 11.25 mg)
    b. Lutrate Depot (J1954 leuprorelin acetate 22.5 mg)
    c. Camcevi SC Depot (J1952 leuprolide mesylate)
    d. Zoladex (J9202 goserelin acetate)
    e. Orgovyx (J8999 relugolix).
3. NOTE 2: The above Policy Positions for Not Approvable products are based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) showing superior outcomes and/or better toxicity profiles with one LHRH analog over another in the treatment of prostate cancer. Please refer to NCH alternative agents/regimens recommended by NCH, including but not limited to regimens available at http://pathways.newcenturyhealth.com.

III. EXCLUSION CRITERIA

A. Zoladex (goserelin), Trelstar (triptorelin), or Lupron Depot/Lutrate Depot (leuprolide acetate) is being used in postmenopausal female member.

B. Zoladex (goserelin), Trelstar (triptorelin), or Lupron/Lutrate (Leuprolide) is being used in member with hormone receptor negative (ER and/or PR negative) breast cancer, except when being used for fertility preservation or for other non-cancer indications.

C. Camcevi SC Depot (J1952 leuprolide mesylate), Firmagon (J9155 degarelix), or Orgovyx (J8999 relugolix) is being used in members with breast cancer or for fertility preservation in women undergoing cytotoxic chemotherapy.

D. 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 meseylate) 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).

E. Treatment exceeds the maximum limit of Orgovyx (relugolix) 30 (120 mg) tablets per month.

F. 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. Shore et al, HERO trial, N Engl J Med 2020; 382:2187-2196. DOI: 10.1056/NEJMoa200432.

B. 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.

C. Dowsett M, Mehta A, Mansi J, Smith IE. A dose-comparative endocrine-clinical study of leuprorelin in premenopausal breast cancer patients. Br J Cancer. 1990;62(5):834-837.

D. Kendzierski DC, et al. Efficacy of Different Leuprolide Administration Schedules in Premenopausal Breast Cancer: A Retrospective Review. Clin Breast Cancer. 2018;18(5):e939-e942.

E. Frampton JE. Triptorelin: A Review of its Use as an Adjuvant Anticancer Therapy in Early Breast Cancer. Drugs. 2017;77(18):2037-2048.

F. Rossi E, Morabito A, De Maio E, et al. Endocrine effects of adjuvant letrozole + triptorelin compared with tamoxifen + triptorelin in premenopausal patients with early breast cancer. J Clin Oncol. 2008;26(2):264-270.

G. Lambertini M, et al. Ovarian Suppression With Triptorelin During Adjuvant Breast Cancer Chemotherapy and Long-term Ovarian Function, Pregnancies, and Disease-Free Survival: A Randomized Clinical Trial. JAMA. 2015;314(24):2632-2640.

H. Lutrate prescribing information. GP-PHARM, S.A, Spain 2018.

I. Orgovyx prescribing information. Myovant Sciences, Inc., Brisbane, CA 2021.

J. Lupron prescribing information. AbbVie Inc. North Chicago, IL 2020.

K. Eligard prescribing information. Tolmar Pharmaceuticals, Inc. Fort Collins, CO 2019.

L. Trelstar prescribing information. Verity Pharmaceuticals, Inc. Wayne, PA 2020.

M. Zoladex prescribing information. TerSera Therapeutics LLC Lake Forest, IL 2021.

N. Firmagon prescribing information. Ferring Pharmaceuticals Inc. Parsippany, NJ. 2021.

O. Clinical Pharmacology Elsevier Gold Standard 2023.

P. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.

Q. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

R. 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.

S. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.

T. 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.