[redacted]

From: Lucy, Michael [redacted]
Sent: Tuesday, September 19, 2023 12:27 PM
To: DHA NCR J-6 Mailbox BAPREQUESTS
Subject: [Non-DoD Source] August 2023 DoD P&T Recommendations: Response Requested

Dear Sir or Madam,

Following the careful review of the DEPARTMENT OF DEFENSE PHARMACY AND THERAPEUTICS COMMITTEE RECOMMENDATIONS FROM THE AUGUST 2023 MEETING, INFORMATION FOR THE UNIFORM FORMULARY BENEFICIARY ADVISORY PANEL MEETING SEPTEMBER 27, 2023, we found medically incorrect information in the meeting minutes document regarding Inpefa. Given that fact, I'm respectfully requesting the statement be deleted from those meeting minutes as described below.

The medically incorrect information is referenced on page 30 of the final statement under Inpefa that starts on page 29 under, item number 9. The statement "Non-FDA-approved uses are not approved, including Type 1 Diabetes Mellitus, Heart Failure with preserved ejection fraction, or acute decompensated heart failure PA does not expire." Since this is inconsistent with the FDA approved label, we are requesting the entire statement be removed from the minutes prior to the Beneficiary Advisory Panel scheduled for September 27, 2023.

I can be reached at 908-303-1008 or at mlucy@lexpharma.com and would be happy to discuss this matter live at your convenience.

Sincerely,
Mike Lucy

Michael Lucy
Executive Director, Head of Market Access
Lexicon pharmaceuticals

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[redacted]

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[redacted]

From: Myovant Medical Information <medinfo@myovant.com>
Sent: Thursday, September 21, 2023 2:10 PM
To: DHA NCR J-6 Mailbox BAPREQUESTS
Cc: Pruett, Janis
Subject: [Non-DoD Source] Orgovyx: Written Comment to PA Criteria Recommendations
Attachments: DoD Orgovyx Prior Authorization Criteria Wrtten Comments.pdf; Orgovyx_Prescribing Information_March2023.pdf

Dear UF BAP Designated Federal Officer,

Please find attached the Orgovyx® (relugolix) Written Comments to the PA Criteria Recommendations and the most recent USPI. Thank you for the opportunity to submit this response for consideration during the General Meeting on Wednesday, September 27, 2023. Additionally, could the UF BAP Designated Federal Officer kindly acknowledge receipt of this email?

Thank you,

Medical Information
Sumitomo Pharma America, Inc.

DoD Orgovyx Prostate Cancer
Prior Authorization Criteria Written Comments

Sumitomo Pharma America, Inc. (SMPA) is providing this document in response to the initial recommendations for Orgovyx® (relugolix) Prior Authorization (PA) criteria. The information enclosed is a summary of the best available clinical data related to the initial PA criteria. Some of the data included in this response may be outside the FDA-approved prescribing information for the referenced product. SMPA does not intend to offer an opinion regarding the clinical relevance of these data or the advisability of administering any drug in a manner inconsistent with its approved labeling. Please refer to the enclosed Full Prescribing Information for complete information.

General Comments:

- Consider removing "Patient has tried and failed leuprolide acetate SC (Eligard) or degarelix SC (Firmagon)" from PA criteria.

Reasoning:

Orgovyx is the first and only orally active androgen deprivation therapy (ADT); it is a gonadotropin-releasing hormone (GnRH) antagonist that is given once daily.[1] The primary evidence of efficacy and safety comes from the pivotal phase 3 trial in men with advanced prostate cancer requiring at least 1 year of continuous ADT (HERO, NCT03085095)[2] with supportive data from the phase 2 study in men with localized intermediate-risk prostate cancer requiring 6 months of neoadjuvant/adjuvant ADT with external beam radiation therapy (EBRT) (C27003, NCT02135445).[3]

- **Route of administration**

Orgovyx is the first and only orally available ADT. Currently, all other FDA-approved ADTs for advanced prostate cancer are only available as injectable or implantable formulations, including a GnRH receptor antagonist (degarelix) and the luteinizing hormone releasing hormone (LHRH) agonists (i.e., leuprolide acetate [subcutaneous (SC), intramuscular (IM)], leuprolide mesylate [SC], goserelin acetate [SC], and triptorelin pamoate [IM]. While LHRH agonists are generally well tolerated, their use is often limited by their route of administration, initial testosterone surge, prolonged testosterone recovery after discontinuation, and increased risk of cardiovascular events. Degarelix dosing is also limited to injections in the office every 28 days.[4] Incidence of injection-site reactions for current LHRH agonists and GnRH antagonists vary from 3 to 44%.[4-6]

Injectable ADT is usually administered by a health care professional whereas Orgovyx is self-administered. Potential benefits of oral administration include decreased health care provider time (treatment administration, patient education on self-administration), avoidance of injection preparation, avoidance of injection site reactions, reduction in the number of office visits for ADT administration especially in the setting of the emergence of telehealth, and increased patient satisfaction with the convenience of the oral route of administration.

The BAP background document highlights that Orgovyx provides convenience to the patient but that data are limited on long-term compliance. Efficacy, safety, and pharmacokinetic information from two phase I studies, two phase II studies, and the phase III safety and efficacy study (HERO) were used to develop a population pharmacokinetic (PopPK) model and a semi-mechanistic population pharmacokinetic/pharmacodynamic (PopPK/PD) model that characterizes relugolix exposure and its relationship to testosterone concentrations. Simulations using the PopPK/PD model predicts that 97.3% and 85.5% of the patients remain at castration levels (<50 ng/dL) upon temporary interruption of treatment for 7 days and 14 days, respectively.[7]

Background

HERO is a multinational, randomized, open-label, phase 3 study to evaluate the efficacy and safety of Orgovyx in men with androgen-sensitive advanced prostate cancer who required at least one year of continuous ADT. Patients enrolled in the study were randomized 2:1 to receive either Orgovyx (120 mg once daily after a single oral loading dose of 360 mg) or leuprolide acetate (22.5 mg [or 11.25 mg in

Japan and Taiwan per local guidelines, and is not recommended for this indication in the United States] by injection every 3 months) for 48 weeks.[2]

Study C27003 was a phase 2, randomized, open-label, parallel group study evaluating the safety and efficacy of Orgovyx in men with intermediate-risk prostate cancer who required 6 months of neoadjuvant/adjuvant ADT in conjunction with EBRT. Patients enrolled in the study were randomized 3:2 to receive 24 weeks of either Orgovyx (loading dose of 320 mg on Day 1 followed by 120 mg daily thereafter) or degarelix subcutaneous depot injection (loading dose of 240 mg on Day 1 followed by 80 mg every 4 weeks).[3] The overall AE profile was similar between Orgovyx and degarelix except for findings of increased alanine aminotransferase (13%) and injection site erythema (11%) in the degarelix group compared to 0% for both alanine aminotransferase and injection site erythema in the Orgovyx group.[3]

References

1. Myovant Sciences. Orgovyx® (relugolix) Prescribing Information. Available at: https://www.myovant.com/orgovyx-prescribing-information.pdf
2. Shore ND, Saad F, Cookson MS, et al. Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer. *N Engl J Med.* Jun 4 2020;382(23):2187-2196. https://www.ncbi.nlm.nih.gov/pubmed/32469183
3. Dearnaley DP, Saltzstein DR, Sylvester JE, et al. The Oral Gonadotropin-releasing Hormone Receptor Antagonist Relugolix as Neoadjuvant/Adjuvant Androgen Deprivation Therapy to External Beam Radiotherapy in Patients with Localised Intermediate-risk Prostate Cancer: A Randomised, Open-label, Parallel-group Phase 2 Trial. *Eur Urol.* Aug 2020;78(2):184-192. https://www.ncbi.nlm.nih.gov/pubmed/32273183
4. Ferring Pharmaceuticals Inc. Firmagon® (degarelix for injection) Prescribing Information. February 2020. Available at: https://firmagon.com/hcp
5. TerSera Therapeutics LLC. Zoladex® (goserelin implant) Prescribing Information. March 2023. Available at: https://documents.tersera.com/zoladex-us/3.6mg_MagnumPI.pdf
6. Tolmar I. Eligard® (leuprolide acetate) Prescribing Information. April 2019. Available at: https://www.tolmar.com/sites/default/files/resources/ELI_Full_PI.pdf
7. Lee TY, Pierrillas PB, Lin YW, et al. Population PK and Semi-Mechanistic PK/PD Modeling and Simulation of Relugolix Effects on Testosterone Suppression in Men with Prostate Cancer. *Clin Pharmacol Ther.* Sep 8 2022 https://www.ncbi.nlm.nih.gov/pubmed/36073238