Janssen Scientific Affairs, LLC

1125 Trenton-Harbourton Road
PO Box 200
Titusville, NJ 08560
800.526.7736 tel
609.730.3138 fax

February 26, 2021

Kristina Gregory
3025 Chemical Road
Plymouth Meeting, PA 19462
USA

Dear Ms. Gregory,

Please consider the following information.

Response(s):

- ERLEADA - NCCN Compendium Communication - ACIS Final Analysis - February 2021

I look forward to working with you as you consider the enclosed information. The information provided is not intended as an endorsement of any usage not contained in the Prescribing Information. For complete information, please refer to the full Prescribing Information, including the following sections: INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.

If you require further information, please feel free to contact me via the Janssen Medical Information Center at 1-800-JANSSEN (1-800-526-7736).

Sincerely,

Cynthia Toso

Cynthia Toso, PharmD

Associate Director
Medical Information

Inquiry #:01975714

Enclosure(s)/Electronic Link(s):

- ERLEADA ® (apalutamide) Prescribing Information at https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-50722e17-d630-456e-befb-8a37a3e3e99d
- Results from ACIS, a randomized, placebo-controlled double-blind phase 3 study of apalutamide and abiraterone acetate plus prednisone versus abiraterone in patients with chemo-naive metastatic castration-resistant prostate cancer
- ERLEADA Prescribing Information
- ZYTIGA Prescribing Information

Need Help? If you have any additional questions, please contact us via:

1-800-JANSSEN Monday - Friday, 9 am - 8 pm EST	**24x7 Access to Medical Information** www.janssenmd.com
Email Medical Information	**Locate Medical Science Liaison** www.janssenmsl.com

To report a possible adverse event or product quality complaint, please call the Medical Information Center immediately, at 1-800-JANSSEN (1-800-526-7736).

ERLEADA® (apalutamide)
NCCN Compendium Communication – ACIS Final Analysis - February 2021

February 25, 2021

Name: Cindy Toso, PharmD
Company/Organization: Janssen Biotech, Inc.
Address: 850 Ridgeview Drive Horsham, PA 19044
Phone: 215.605.7966
E-mail: ctoso@its.jnj.com
Date of request: February 25, 2021
NCCN Guidelines® Panel: Prostate Cancer

Dear NCCN,

On behalf of Janssen Biotech, Inc., I respectfully request the NCCN Guidelines® Prostate Cancer Panel review the enclosed efficacy and safety outcomes from the ACIS study, a phase 3, randomized, double-blind, placebo-controlled, multicenter study that compared apalutamide in combination with abiraterone acetate plus prednisone to placebo in combination with abiraterone acetate plus prednisone in patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC).[1]

Specific Change: We request that the compendium monograph and the Prostate Cancer Guidelines (V.1.2021) be updated to include ERLEADA® (apalutamide) in combination with ZYTIGA® (abiraterone acetate) plus prednisone with a Category 1 evidence level rating for M1 CRPC: adenocarcinoma in patients with no prior docetaxel/no prior novel hormone therapy (PROS-16, PROS-G, Discussion).

FDA Clearance: The FDA has approved ERLEADA® (apalutamide) for the treatment of patients with metastatic castration-sensitive prostate cancer and non-metastatic castration-resistant prostate cancer.[2] The FDA has approved ZYTIGA® (abiraterone acetate) in combination with prednisone for the treatment of patients with mCRPC and metastatic high-risk castration-sensitive prostate cancer.[3]

The data in this submission are considered off-label.

Rationale: ACIS was a phase 3, randomized, double-blind, placebo-controlled, multicenter study that evaluated the use apalutamide and abiraterone acetate plus prednisone compared to placebo and abiraterone acetate plus prednisone in 982 patients with chemotherapy-naïve mCRPC. Patients included in the study also did not receive prior therapy with androgen signaling inhibitors for castration-resistant disease. Patients were randomized 1:1 to receive apalutamide 240 mg orally once daily and abiraterone acetate 1,000 mg orally once daily plus prednisone 5 mg orally twice daily (n=492) or placebo and abiraterone acetate 1,000 mg orally once daily plus prednisone 5 mg orally twice daily (n=490). All patients received ongoing androgen deprivation therapy (ADT) throughout the study. Patients were stratified by presence or absence of visceral metastases, Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 or 1, and geographical region. The primary endpoint was radiographic progression-free survival (rPFS; by investigator).[1]

At the primary analysis for rPFS, after a median follow-up of 25.7 months, a statistically significant improvement in median rPFS was observed: 22.6 months in the apalutamide and abiraterone acetate plus prednisone group vs 16.6 months in the placebo and abiraterone acetate plus prednisone group (HR, 0.69; 95% CI, 0.58-0.83, $P<0.0001$), demonstrating a 31% reduction in risk of radiographic progression or death in the apalutamide and abiraterone acetate plus prednisone group.[1]

At the final analysis for rPFS, after a median follow-up of 54.8 months, further improvement in median rPFS was observed with apalutamide and abiraterone acetate plus prednisone compared with placebo and abiraterone acetate plus prednisone (24.0 months vs 16.6 months, respectively; HR: 0.70; 95% CI: 0.60-0.83). Results for median overall survival (OS), a prespecified secondary endpoint, were similar in both treatment groups: 36.2 months in the apalutamide and abiraterone acetate plus prednisone group and 33.7 months in the placebo and abiraterone acetate plus prednisone group (HR, 0.95; 95% CI, 0.81-1.11, *P*=0.498). The treatment effect of apalutamide and abiraterone acetate plus prednisone on rPFS and OS was favorable in prespecified subgroups of patients with visceral metastases and patients ≥75 years.[1]

Any treatment-emergent adverse events (TEAEs) were observed in 98.8% (484/490) of patients in the apalutamide and abiraterone acetate plus prednisone group and 96.7% (473/489) of patients in the placebo and abiraterone acetate plus prednisone group. The combination of apalutamide with abiraterone acetate plus prednisone showed consistent safety outcomes with the previously reported safety profiles of each drug and no new safety signals were observed in this study. TEAEs of special interest (all grades) that were reported in ≥10% of patients in the apalutamide and abiraterone acetate plus prednisone group and placebo and abiraterone acetate plus prednisone group included: fatigue (43.5% vs 37.4%), hypertension (32.2% vs 26.6%), fall (21.8% vs 3.3%), skin rash (20.6% vs 10.0%), cardiac disorders (19.0% vs 19.2%), hypokalemia (16.1% vs 15.1%), peripheral edema (18.8% vs 19.0%), and fracture and osteoporosis (15.1% vs 12.1%). Health-related quality of life was comparable between treatment groups based on Functional Assessment of Cancer Therapy-Prostate (FACT-P) total score.[1]

Please refer to the enclosed oral presentation for additional secondary and exploratory endpoint and safety results.[1]

The following oral presentation is submitted with the ERLEADA® (apalutamide) and ZYTIGA® (abiraterone acetate) Full Prescribing Information:

- Rathkopf DE, Efstathiou E, Attard G, et al. Results from ACIS, a randomized, placebo-controlled double-blind phase 3 study of apalutamide and abiraterone acetate plus prednisone versus abiraterone in patients with chemo-naïve metastatic castration-resistant prostate cancer. Oral presentation presented at: American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium; February 11-13, 2021; Virtual.

Sincerely,

Cindy Toso, PharmD
Associate Director, Payer & Health Systems, Medical Information & Knowledge Integration
Janssen Scientific Affairs, LLC

REFERENCES

1. Rathkopf DE, Efstathiou E, Attard G, et al. Results from ACIS, a randomized, placebo-controlled double-blind phase 3 study of apalutamide and abiraterone acetate plus prednisone versus abiraterone in patients with chemo-naïve metastatic castration-resistant prostate cancer. Oral presentation presented at: American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium; February 11-13, 2021; Virtual.
2. ERLEADA (apalutamide) [Prescribing Information]. Horsham, PA: Janssen Products, LP; https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-50722e17-d630-456e-befb-8a37a3e3e99d.
3. ZYTIGA (abiraterone acetate) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.; https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-ecaf8e16-61b7-48c6-a6ad-2594b810a4af.