Evidence and Value Summary: AKEEGA® (Niraparib and Abiraterone Acetate) Dual Action Tablet

Unmet Need in *BRCA*-mutated Metastatic Castration Resistant Prostate Cancer (mCRPC):

Metastasis at diagnosis reduces 5-year survival rates[1]

Patients with localized prostate cancer: ***>99%***

Patients with metastatic disease: ***30%***

Patients with ***BRCA*-mutations** are more likely to have[2,3]:

Aggressive disease | *Poor outcomes* | *Shorter survival time*

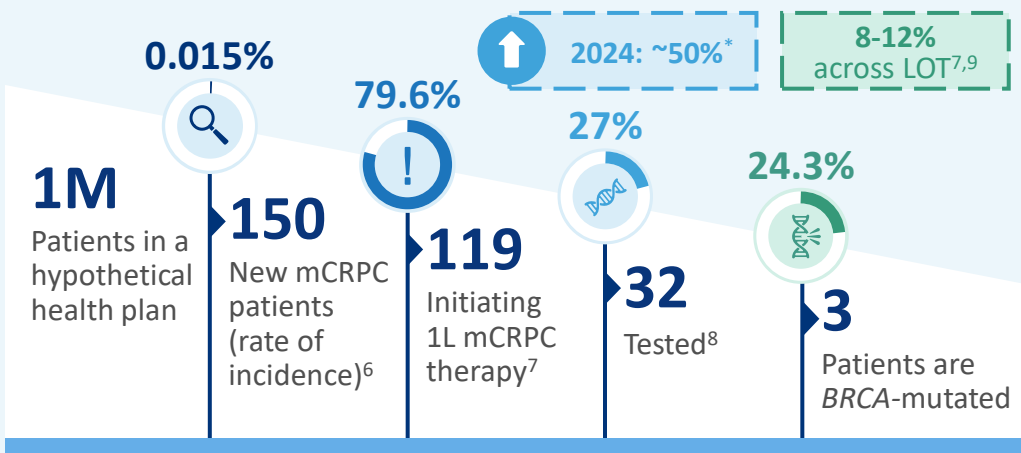
Patients with *BRCA*-mutations may progress faster to subsequent therapies[4]

Need for more effective targeted options in 1L mCRPC

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) For Prostate Cancer v.4.2023 Recommendation: niraparib/abiraterone:

Niraparib and abiraterone acetate (DAT) is recommended as a treatment option for patients with **mCRPC and a pathogenic *BRCA*-mutation** (germline and/or somatic) who have **not yet had treatment in the setting of mCRPC**, depending on prior treatment in other disease settings[5]

Treatment Eligible Populations



Precision medicine requires **genetic testing** to identify treatment eligible patients with mCRPC who may benefit from **targeted front-line PARPi combination therapy.**[5]

Anticipated Impact of AKEEGA® in *BRCA*-mutated 1L mCRPC in a hypothetical US million-member health plan **(<$0.01 PMPM)** is consistent across Commercial and Medicare payer channels.[4]

AKEEGA®: Indication

AKEEGA® is a combination of niraparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, and abiraterone acetate, a CYP17 inhibitor indicated with prednisone for the treatment of adult patients with deleterious or suspected deleterious *BRCA*-mutated metastatic castration-resistant prostate cancer (mCRPC). Select patients for therapy based on an FDA-approved test for AKEEGA®.[10]

Simplified treatment plan utilizing dual action tablet:

- One prescription
- One prior authorization
- One copay
- Two drugs in one tablet
- Reduced pill burden

AKEEGA®: Clinical Evidence

MAGNITUDE is a phase 3, randomized, double-blind study evaluating safety and efficacy of **AKEEGA® with prednisone in patients with or without HRR-associated gene alterations** compared to abiraterone acetate with prednisone.[10]

Key Attributes of the MAGNITUDE Study:[11]

- The **largest number of *BRCA*-mutated mCRPC patients** in PARPi combination trials to date
- Allowed **≤4 months prior AAP** in the first-line mCRPC setting
- **Prospective testing of both tissue and blood to determine HRR status** prior to enrollment
- **Statistical significance of rPFS** (primary endpoint) **was first analyzed in *BRCA*m patients**

Baseline Characteristics[12]

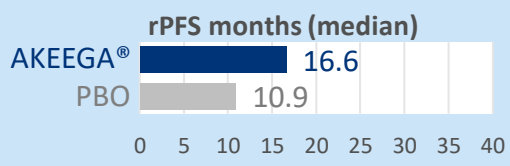
Three measures were imbalanced to the disadvantage of the AKEEGA® with prednisone arm:

- **23%** Visceral disease (vs. 20% in PBO+AAP)
- **39%** ECOG 1 status (vs. 29% in PBO+AAP)
- **88%** Bone metastases (vs. 83% in PBO+AAP)

Efficacy in *BRCA*-mutated patients[10]

A statistically significant **improvement in rPFS** for AKEEGA compared to abiraterone acetate was observed in ***BRCA*-mutated patients:**

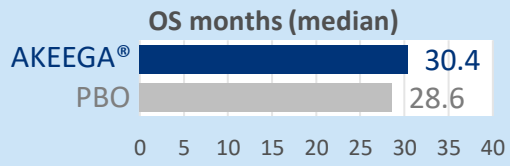
47% **Reduced risk of radiographic progression or death**



Hazard Ratio: 0.53 (95% CI: 0.36, 0.79) *P*=0.0014

In an exploratory analysis of OS in the subgroup of patients with *BRCA*-mutations:

21% **Reduced risk of death**



Hazard Ratio: 0.79 (95% CI: 0.55, 1.12)

In a **multivariate analysis of OS** to account for the **imbalance in prognostic factors** in the subgroup of patients with *BRCA*-mutations[12]:

34% **Reduced risk of death**

Hazard Ratio: 0.66 (95% CI: 0.46, 0.95)

Selected Safety Profile[10]

% of patients experiencing:

- **41%** Serious adverse reactions
- **50%** Dosage interruption of any component of AKEEGA® due to adverse reactions
- **15%** Permanent discontinuation of any component of AKEEGA® due to adverse reactions
- **9%** Fatal adverse reactions
- **28%** Dosage reduction of any component of AKEEGA® due to adverse reactions

Please refer to the full prescribing information for a complete listing of all adverse events, including other serious adverse events.

Provided in response to a medical information request; for informational purposes only; no further use is permitted. For additional information, please see AKEEGA® prescribing information using the following QR code:

BRCA-mutated includes *BRCA*1/2 positive mutations. *Please note that the following testing rates are calculated by fitting third degree polynomial trend line to 2013-2021 annual testing rates using Microsoft Excel[7]. 1L, first line; AAP, abiraterone acetate + prednisone/prednisolone; BRCA, Breast Cancer gene; CYP17, 17 α-hydroxylase/C17,20-lyase; DAT, Dual Action Tablet; ECOG, Eastern Cooperative Oncology Group; HRR, homologous recombination repair; LOT, line of therapy; mCRPC, metastatic castration resistant prostate cancer; NCCN, National Comprehensive Cancer Network® (NCCN®); OS, overall survival; PARPi, poly (adenosine diphosphate-ribose) polymerase inhibitor; PBO, placebo; PMPM, per member per month; rPFS, radiographic progression-free survival.

1. Siegel RL, et al. CA *Cancer J Clin*. 2019;69:7-34. 2. Castro E, et al., J Clin Oncol. 2013; 31:1748- 1757. 3. Kohli M, et al. *EBioMedicine*. 2020; 54: 102728. 4. Data on file. Janssen Scientific Affairs, LLC. 5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V4.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed February 21, 2024. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. 6. Scher H, et al. Poster presented at the Genitourinary Cancers Symposium, February 13-15, 2020, San Francisco, CA. 7. George DJ, Khilfeh I et al. Poster presented at Society of Urologic Oncology (SUO), November 30 - December 2, 2022. 8. George DJ, Khilfeh I, et al. Presentation at the International Prostate Cancer Update Conference, January 22-25, 2023. 9. Shore N, et al. *J Urol*. 2021 Apr;205(4):977-986 10. AKEEGA™ (niraparib and abiraterone acetate) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 11. Chi KN, Sandhu S, Smith MR, et al. Ann Oncol. doi:10.1016/j.annonc.2023.06.009. 12. Chi KN, et al. Presented at the 2023 ESMO Congress; October 20-24, 2023; Madrid, Spain.

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