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NEWS RELEASE

U.S. FDA approves AKEEGA® as the first precision therapy for BRCA2-mutated metastatic castration-sensitive prostate cancer with 54% reduction in disease progression vs standard of care*

2025-12-12

Expanded indication for AKEEGA® (niraparib and abiraterone acetate dual-action tablet) plus prednisone marks the first FDA-approved precision medicine combination treatment for patients with BRCA2-mutated mCSPC

HORSHAM, Pa., Dec. 12, 2025 /PRNewswire/ -- Johnson & Johnson (NYSE:JNJ) announced today the U.S. Food and Drug Administration (FDA) approved the supplemental New Drug Application (sNDA) for AKEEGA® (niraparib and abiraterone acetate dual-action tablet) plus prednisone for the treatment of patients with BRCA2-mutated metastatic castration-sensitive prostate cancer (mCSPC).[1] Patients with BRCA mutations often have more aggressive forms of prostate cancer leading to poor prognosis, representing a significant unmet need not addressed by previously available therapies.[2]

"There remains an urgent need for novel therapies for patients with BRCA2-mutated mCSPC, who face significantly faster disease progression and often shorter survival compared to those without the mutation," said Bradley McGregor, M.D., Director of Clinical Research for the Lank Center of Genitourinary Oncology at Dana-Farber Cancer Institute. "AMPLITUDE is the first study to show that this precision medicine combination of a PARP inhibitor with an androgen receptor pathway inhibitor delays both radiographic and symptomatic disease progression."

The approval is based on positive results from AMPLITUDE (**NCT04497844**), a randomized, double-blind, placebo-controlled, international Phase 3 clinical study. In patients with BRCA2-mutated mCSPC, treatment with AKEEGA® plus prednisone and androgen deprivation therapy (ADT) significantly reduced the risk of radiographic progression or death by 54 percent (hazard ratio [HR] 0.46; 95 percent confidence interval [CI], 0.32–0.66)

compared to placebo/abiraterone acetate plus prednisone and ADT, which is the current standard of care.[1] AKEEGA® plus prednisone and ADT also significantly prolonged the time to symptomatic progression by 59 percent (HR 0.41; 95 percent CI, 0.29–0.65).[1]

The observed safety profile of the combination of AKEEGA® plus prednisone was consistent with the known safety profile of each FDA-approved monotherapy. In the AMPLITUDE clinical study, the most common adverse reactions (≥20%) including laboratory abnormalities, were decreased hemoglobin, decreased lymphocytes, musculoskeletal pain, fatigue, decreased platelets, increased alkaline phosphatase, constipation, hypertension, nausea, decreased neutrophils, increased creatinine, increased potassium, decreased potassium, decreased aspartate aminotransferase, fluid retention/edema, increased bilirubin, respiratory tract infection and arrhythmia.[1]

"This expanded indication for AKEEGA reflects our commitment to push the boundaries of science and deliver more personalized, effective treatment options across the prostate cancer continuum," said Mahadi Baig, M.D., M.H.C.M., Vice President, Head of Solid Tumors, U.S. Medical Affairs, Johnson & Johnson Innovative Medicine. "Supported by strong clinical data, AKEEGA is now the first and only PARP-based precision medicine combination treatment in BRCA2-mutated mCSPC, offering patients hope for more time with a new way to potentially delay their cancer from progressing."

Johnson & Johnson is committed to helping patients access our treatments. Once a patient and their doctor have decided that AKEEGA® is right for the patient, **J&J withMe** provides a simple, comprehensive patient support program offering cost support and educational resources, at no cost to the patient.

*The hazard ratio [HR] 0.46; 95 percent confidence interval [CI], 0.32–0.66) compared to standard of care, AKEEGA® plus prednisone and ADT also significantly prolonged the time to symptomatic progression by 59 percent (HR 0.41; 95 percent CI, 0.29–0.65).[1]

About AMPLITUDE

AMPLITUDE (**NCT04497844**) is an ongoing, Phase 3, randomized, double-blind, placebo-controlled, multicenter, global study evaluating the efficacy and safety of niraparib and abiraterone acetate in a dual-action tablet (DAT) formulation with prednisone plus androgen deprivation therapy (ADT) compared to matching oral placebo/abiraterone acetate with prednisone plus ADT in patients with deleterious germline or somatic homologous recombination repair (HRR) gene-altered metastatic castration-sensitive prostate cancer (mCSPC). The primary endpoint is radiographic progression-free survival (rPFS). The study enrolled 696 participants from 32 countries.

About Metastatic Castration-Sensitive Prostate Cancer

Metastatic castration-sensitive prostate cancer (mCSPC), also known as metastatic hormone-sensitive prostate

cancer (mHSPC), refers to prostate cancer that has spread to other parts of the body but still responds to hormone therapy (androgen deprivation therapy).[3] While the treatment landscape has advanced in recent years, almost all patients eventually develop resistance to therapy, and the disease progresses to metastatic castration-resistant prostate cancer (mCRPC) – an aggressive and currently incurable disease stage.[4] Approximately 25 percent of patients with mCSPC have HRR gene alterations, including BRCA, which have been shown to negatively impact outcomes.[2,5] Patients with BRCA mutations experience approximately 50 percent faster disease progression and shorter survival, representing a significant unmet medical need not addressed by previously available therapies.[2]

About AKEEGA® (niraparib and abiraterone acetate)

AKEEGA® is a dual-action tablet (DAT), combining niraparib, a highly selective poly (ADP-ribose) polymerase (PARP) inhibitor, and abiraterone acetate, a CYP17 inhibitor. AKEEGA® together with prednisone or prednisolone was approved in **April 2023** by the European Medicines Agency, and in **August 2023** by the U.S. FDA following Priority Review, for the treatment of patients with BRCA-mutated metastatic castration-resistant prostate cancer (mCRPC). AKEEGA® plus prednisone was approved by the U.S. FDA in December 2025 under Priority Review for the treatment of patients with BRCA2-mutated metastatic castration-sensitive prostate cancer (mCSPC). Patients are selected for therapy based on an FDA-approved test for genetic alterations. Additional marketing authorization applications are under review across a number of countries globally.

In April 2016, Janssen Biotech, Inc. entered a worldwide (except Japan) collaboration and license agreement with TESARO, Inc. (acquired by GlaxoSmithKline [GSK] in 2019) for exclusive rights to niraparib in prostate cancer.

For more information visit **www.akeegahcp.com**.

AKEEGA® INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

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 BRCA2-mutated (BRCA2m) metastatic castration-sensitive prostate cancer (mCSPC).
- deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC).
- Select patients for therapy based on an FDA approved test for AKEEGA®

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia

AKEEGA® may cause myelodysplastic syndrome/acute myeloid leukemia (MDS/AML).

In the individual AMPLITUDE and MAGNITUDE studies, MDS or AML, including cases with fatal outcomes, were reported in 0.6% (2/347) and 0.5% (1/212) of patients treated with AKEEGA® plus prednisone, respectively.

All patients in other tumor types treated with niraparib, a component of AKEEGA®, who developed secondary MDS/cancer-therapy-related AML had received previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

For suspected MDS/AML or prolonged hematological toxicities, refer the patient to a hematologist for further evaluation. Discontinue AKEEGA® if MDS/AML is confirmed.

Myelosuppression

AKEEGA® may cause myelosuppression (anemia, thrombocytopenia, or neutropenia).

In AMPLITUDE, Grade 3-4 anemia, neutropenia, and thrombocytopenia were reported, respectively in 29 %, 10 %, and 4.9% of patients receiving AKEEGA®. Overall, 25% of patients with anemia required a red blood cell transfusion, including 15% who required more than one transfusion. Discontinuation due to anemia occurred in 1.2% of patients.

In MAGNITUDE Cohort 1, Grade 3-4 anemia, thrombocytopenia, and neutropenia were reported, respectively in 28%, 8%, and 7% of patients receiving AKEEGA®. Overall, 27% of patients with anemia required a red blood cell transfusion, including 19.5% who required more than one transfusion. Discontinuation due to anemia occurred in 3% of patients.

Monitor complete blood counts weekly during the first month of AKEEGA® treatment, every two weeks for the next two months, monthly for the remainder of the first year and then every other month, and as clinically indicated. Do not start AKEEGA® until patients have adequately recovered from hematologic toxicity caused by previous therapy. If hematologic toxicities do not resolve within 28 days following interruption, discontinue AKEEGA® and refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics.

Hypokalemia, Fluid Retention, and Cardiovascular Adverse Reactions

AKEEGA® may cause hypokalemia and fluid retention as a consequence of increased mineralocorticoid levels

resulting from CYP17 inhibition. In post-marketing experience, QT prolongation and Torsades de Pointes have been observed in patients who develop hypokalemia while taking abiraterone acetate, a component of AKEEGA®. Hypertension and hypertensive crisis have also been reported in patients treated with niraparib, a component of AKEEGA®.

In AMPLITUDE, which used prednisone 5 mg daily in combination with AKEEGA®, Grades 3-4 hypokalemia was detected in 9% of patients on the AKEEGA® arm, and Grades 3-4 hypertension was observed in 30% of patients on the AKEEGA® arm.

In MAGNITUDE Cohort 1, which used prednisone 10 mg daily in combination with AKEEGA®, Grades 3-4 hypokalemia was detected in 2.7% of patients on the AKEEGA® arm and Grades 3-4 hypertension was observed in 14% of patients on the AKEEGA® arm.

Monitor patients for hypertension, hypokalemia, and fluid retention at least weekly for the first two months, then once a month. Closely monitor patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia, or fluid retention, such as those with heart failure, recent myocardial infarction, cardiovascular disease, or ventricular arrhythmia. Control hypertension and correct hypokalemia before and during treatment with AKEEGA®. Discontinue AKEEGA® in patients who develop hypertensive crisis or other severe cardiovascular adverse reactions.

The safety of AKEEGA® in patients with New York Heart Association (NYHA) Class II to IV heart failure has not been established because these patients were excluded from AMPLITUDE and MAGNITUDE.

Hepatotoxicity

AKEEGA® may cause hepatotoxicity.

Hepatotoxicity in patients receiving abiraterone acetate, a component of AKEEGA®, has been reported in clinical trials. In post-marketing experience, there have been abiraterone acetate-associated severe hepatic toxicity, including fulminant hepatitis, acute liver failure, and deaths.

In AMPLITUDE, Grade 3-4 ALT or AST increases (at least 5x ULN) were reported in 1.9% and 1.3% of patients, respectively.

In MAGNITUDE Cohort 1, Grade 3-4 ALT or AST increases (at least 5x ULN) were reported in 1.8% and 0.9% of patients respectively.

The safety of AKEEGA in patients with moderate or severe hepatic impairment has not been established as these

patients were excluded from AMPLITUDE and MAGNITUDE.

Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with AKEEGA®, every two weeks for the first three months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring and may require dosage modifications.

Permanently discontinue AKEEGA® for patients who develop a concurrent elevation of ALT greater than 3 x ULN and total bilirubin greater than 2 x ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation, or in patients who develop ALT or AST ≥20 x ULN at any time after receiving AKEEGA®.

Adrenocortical Insufficiency

AKEEGA® may cause adrenal insufficiency.

Adrenocortical insufficiency has been reported in clinical trials in patients receiving abiraterone acetate, a component of AKEEGA®, in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Monitor patients for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress. Symptoms and signs of adrenocortical insufficiency may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with abiraterone acetate. If clinically indicated, perform appropriate tests to confirm the diagnosis of adrenocortical insufficiency. Increased doses of corticosteroids may be indicated before, during, and after stressful situations.

Hypoglycemia

AKEEGA® may cause hypoglycemia in patients being treated with other medications for diabetes.

Severe hypoglycemia has been reported when abiraterone acetate, a component of AKEEGA®, was administered to patients receiving medications containing thiazolidinediones (including pioglitazone) or repaglinide.

Monitor blood glucose in patients with diabetes during and after discontinuation of treatment with AKEEGA®. Assess if antidiabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

Increased Fractures and Mortality in Combination with Radium 223 Dichloride

AKEEGA® with prednisone is not recommended for use in combination with Ra-223 dichloride outside of clinical trials.

The clinical efficacy and safety of concurrent initiation of abiraterone acetate plus prednisone/prednisolone and

radium Ra 223 dichloride was assessed in a randomized, placebo-controlled multicenter study (ERA-223 trial) in 806 patients with asymptomatic or mildly symptomatic castration-resistant prostate cancer with bone metastases. The study was unblinded early based on an Independent Data Monitoring Committee recommendation.

At the primary analysis, increased incidences of fractures (29% vs 11%) and deaths (39% vs 36%) have been observed in patients who received abiraterone acetate plus prednisone/prednisolone in combination with radium Ra 223 dichloride compared to patients who received placebo in combination with abiraterone acetate plus prednisone.

It is recommended that subsequent treatment with Ra-223 not be initiated for at least five days after the last administration of AKEEGA®, in combination with prednisone.

Posterior Reversible Encephalopathy Syndrome

AKEEGA® may cause Posterior Reversible Encephalopathy Syndrome (PRES).
PRES has been observed in patients treated with niraparib as a single agent at higher than the recommended dose of niraparib included in AKEEGA®.

Monitor all patients treated with AKEEGA® for signs and symptoms of PRES. If PRES is suspected, promptly discontinue AKEEGA® and administer appropriate treatment. The safety of reinitiating AKEEGA® in patients previously experiencing PRES is not known.

Embryo-Fetal Toxicity

The safety and efficacy of AKEEGA® have not been established in females. Based on animal reproductive studies and mechanism of action, AKEEGA® can cause fetal harm and loss of pregnancy when administered to a pregnant female.

Niraparib has the potential to cause teratogenicity and/or embryo-fetal death since niraparib is genotoxic and targets actively dividing cells in animals and patients (e.g., bone marrow).

In animal reproduction studies, oral administration of abiraterone acetate to pregnant rats during organogenesis caused adverse developmental effects at maternal exposures approximately ≥ 0.03 times the human exposure (AUC) at the recommended dose.

Advise males with female partners of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of AKEEGA®. Females who are or may become pregnant should handle AKEEGA® with protection, e.g., gloves.

ADVERSE REACTIONS

BRCA2-mutated Metastatic Castration-Sensitive Prostate Cancer (mCSPC)

Serious adverse reactions occurred in 36% of patients who received AKEEGA®. Serious adverse reactions reported in >2% of patients included anemia (4.9%), and pneumonia (3.7%). Fatal adverse reactions occurred in 4.9% of patients who received AKEEGA®, including sudden death (1. 9%), COVID-19 pneumonia (1.2%), pneumocystis jirovecii pneumonia (0.6%), pneumonia (0.6%), and cardio-respiratory arrest (0.6%).

The most common adverse reactions (>20%), including laboratory abnormalities, in patients who received AKEEGA® were decreased hemoglobin, decreased lymphocyte count, hypertension, decreased neutrophil count, musculoskeletal pain, decreased platelet count, constipation, fatigue, decreased potassium, increase creatinine, nausea, increased alkaline phosphate, increased aspartate aminotransferase, respiratory tract infection, arrhythmia, increased blood bilirubin, and fluid retention/edema.

BRCA-mutated Metastatic Castration-Resistant Prostate Cancer (mCRPC)

Serious adverse reactions occurred in 41% of patients who received AKEEGA®. Serious adverse reactions reported in >2% of patients included COVID-19 (7%), anemia (4.4%), pneumonia (3.5%), and hemorrhage (3.5%). Fatal adverse reactions occurred in 9% of patients who received AKEEGA®, including COVID-19 (5%), cardiopulmonary arrest (1%), dyspnea (1%), pneumonia (1%), and septic shock (1%).

The most common adverse reactions (>20%), including laboratory abnormalities, in patients who received AKEEGA® were hemoglobin decreased, lymphocyte decreased, musculoskeletal pain, fatigue, platelets decreased, constipation, alkaline phosphatase increased, hypertension, nausea, neutrophils decreased, creatinine increased, potassium increased, potassium decreased, and aspartate aminotransferase increased.

DRUG INTERACTIONS

Effect of Other Drugs on AKEEGA®

Avoid coadministration with strong CYP3A4 inducers.

Abiraterone is a substrate of CYP3A4. Strong CYP3A4 inducers may decrease abiraterone concentrations, which may reduce the effectiveness of abiraterone.

Effects of AKEEGA® on Other Drugs

CYP2D6 Substrates

Avoid coadministration unless otherwise recommended in the Prescribing Information for CYP2D6 substrates for which minimal changes in concentration may lead to serious toxicities. If alternative treatments cannot be used, consider a dose reduction of the concomitant CYP2D6 substrate drug.

Abiraterone is a CYP2D6 moderate inhibitor. AKEEGA® increases the concentration of CYP2D6 substrates, which may increase the risk of adverse reactions related to these substrates.

CYP2C8 Substrates
Monitor patients for signs of toxicity related to a CYP2C8 substrate for which a minimal change in plasma concentration may lead to serious or life-threatening adverse reactions.

Abiraterone is a CYP2C8 inhibitor. AKEEGA® increases the concentration of CYP2C8 substrates, which may increase the risk of adverse reactions related to these substrates.

USE IN SPECIFIC POPULATIONS

Geriatric Use

Of the 162 patients with BRCA2 gene alteration(s) who received AKEEGA® in AMPLITUDE, 40% of patients were less than 65 years, 36% of patients were 65 years to 74 years, and 23% were 75 years and over.

Of the 113 patients with BRCA gene alteration(s) who received AKEEGA® in MAGNITUDE, 34.5% of patients were less than 65 years, 38.9% of patients were 65 years to 74 years, and 26.5% were 75 years and over.

No overall differences in effectiveness were observed between patients 65 years of age or older and younger patients in AMPLITUDE or MAGNITUDE. Patients 75 years of age or older who received AKEEGA® experienced a higher incidence of fatal adverse reactions than younger patients. The incidence of fatal adverse reactions was 4.3% in patients younger than 75 and 13% in patients 75 or older.

Hepatic Impairment

Avoid use in patients with moderate or severe hepatic impairment. No dosage modification is necessary for patients with mild hepatic impairment.

Renal Impairment

Monitor patients with severe renal impairment for increased adverse reactions and modify dosage as recommended for adverse reactions. No dosage modification is recommended for patients with mild to moderate renal impairment.

Please see the full **Prescribing Information** for AKEEGA®.

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at **https://www.jnj.com/** or at **www.innovativemedicine.jnj.com**. Janssen Research & Development, LLC and Janssen Biotech, Inc. are Johnson & Johnson companies.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of AKEEGA®. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's most recent Annual Report on Form 10-K, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at **www.sec.gov**, **www.jnj.com** or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

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[1] AKEEGA® U.S. Prescribing Information.
[2] Olmos D, Lorente D, Jambrina A, et al. BRCA1/2 and homologous recombination repair alterations in high- and low-volume metastatic hormone-sensitive prostate cancer: prevalence and impact on outcomes. Ann Oncol. 2025;36(10):1190-1202. doi:10.1016/j.annonc.2025.05.534
[3] National Cancer Institute. Hormone-sensitive prostate cancer. Accessed December 2025. **https://www.cancer.gov/publications/dictionaries/cancer-terms/def/hormone-sensitive-prostate-cancer**
[4] Narayan V, et al. Treatment patterns and survival outcomes among androgen receptor pathway inhibitor-experienced patients with metastatic castration-resistant prostate cancer. Clin Genitourin Cancer. 2024;22(6):1-14. doi:10.1016/j.clgc.2024.102188
[5] Gonzalez D, Mateo J, Stenzinger A, et al. Practical considerations for optimising homologous recombination repair mutation testing in patients with metastatic prostate cancer. J Pathol Clin Res. 2021;7(4):311-325. doi:10.1002/cjp2.203

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