HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TALZENNA safely and effectively. See full prescribing information for TALZENNA.

TALZENNA® (talazoparib) capsules, for oral use
Initial U.S. Approval: 2018

----------RECENT MAJOR CHANGES----------

Indications and Usage (1.2)	10/2026
Dosage and Administration (2.1, 2.3, 2.5, 2.6)	10/2026
Warnings and Precautions (5.1, 5.2)	10/2026

---------- INDICATIONS AND USAGE----------

TALZENNA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for:

Breast Cancer

- As a single agent, for the treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m) HER2-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-authorized companion diagnostic for TALZENNA. (1.1, 2.1)

Prostate Cancer

In combination with enzalutamide for the treatment of adult patients with:

- metastatic androgen pathway modulation-resistant (mAPMR) prostate cancer with homologous recombination repair (HRR) gene mutations, as detected by an FDA-authorized test. (1.2, 2.1)
- metastatic androgen pathway modulation-naïve or -sensitive (mAPMN/S) prostate cancer with HRR gene mutations, as detected by an FDA-authorized test. (1.2, 2.1)

---------- DOSAGE AND ADMINISTRATION- ----------

- Breast Cancer
  - The recommended dosage of TALZENNA is 1 mg orally once daily until disease progression or unacceptable toxicity. (2.2)
- Prostate Cancer
  - The recommended dosage of TALZENNA is 0.5 mg orally once daily with enzalutamide until disease progression or unacceptable toxicity. (2.3)
  - Patients should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had a bilateral orchiectomy. (2.3)
- Take TALZENNA with or without food. (2.4)
- Renal Impairment
  - Reduce the dose and monitor for increased adverse reactions for patients with moderate or severe renal impairment. (2.6, 8.7)

---------- DOSAGE FORMS AND STRENGTHS----------

Capsules: 0.1 mg, 0.25 mg, 0.35 mg, 0.5 mg, 0.75 mg, and 1 mg (3)

---------- CONTRAINDICATIONS ----------

None. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): MDS/AML occurred in patients exposed to TALZENNA, and some cases were fatal. Monitor patients for hematological toxicity and discontinue if MDS/AML is confirmed. (5.1)
- Myelosuppression: TALZENNA may affect hematopoiesis and can cause anemia, leukopenia/neutropenia, and/or thrombocytopenia. (5.2)
- Embryo-Fetal Toxicity: TALZENNA can cause fetal harm. Advise of the potential risk to the fetus and to use effective contraception. (5.3, 8.1, 8.3)

---------- ADVERSE REACTIONS ----------

Most common adverse reactions (≥20%) as a single agent, including laboratory abnormalities, are:

- Decreased hemoglobin, decreased neutrophils, decreased lymphocytes, decreased platelets, fatigue, increased glucose, increased aspartate aminotransferase, increased alkaline phosphatase, increased alanine aminotransferase, decreased calcium, nausea, headache, vomiting, alopecia, diarrhea, and decreased appetite. (6.1)

Most common adverse reactions (≥20%) in combination with enzalutamide, including laboratory abnormalities, are:

- Decreased hemoglobin, decreased neutrophils, decreased lymphocytes, decreased platelets, fatigue, decreased albumin, decreased calcium, back pain, decreased appetite, and nausea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- P-gp Inhibitors: Reduce the dose when coadministered with certain P-gp inhibitors. Monitor for increased adverse reactions. (2.7, 7.1)
- BCRP Inhibitors: Monitor for potential increased adverse reactions. (7.1)

---------- USE IN SPECIFIC POPULATIONS ----------

Lactation: Advise women not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 *BRCA*-mutated (g*BRCA*m) HER2-negative Locally Advanced or Metastatic Breast Cancer

TALZENNA is indicated as a single agent for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (*BRCA*)-mutated (g*BRCA*m) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-authorized companion diagnostic for TALZENNA *[see Dosage and Administration (2.1)]*.

1.2 HRR Gene-Mutated Metastatic Prostate Cancer

TALZENNA is indicated in combination with enzalutamide for the treatment of adult patients with:

- metastatic androgen pathway modulation-resistant (mAPMR) prostate cancer with homologous recombination repair (HRR) gene mutations, as detected by an FDA-authorized test *[see Dosage and Administration (2.1)]*.
- metastatic androgen pathway modulation-naïve or -sensitive (mAPMN/S) prostate cancer with HRR gene mutations, as detected by an FDA-authorized test *[see Dosage and Administration (2.1)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

g*BRCA*m HER2-negative Locally Advanced or Metastatic Breast Cancer
Select patients for the treatment of advanced breast cancer with TALZENNA based on the presence of germline *BRCA* mutations *[see Indications and Usage (1.1), Clinical Studies (14.1)]*.

HRR Gene-Mutated mAPMR and mAPMN/S Prostate Cancer
Select patients for the treatment of HRR gene-mutated mAPMR or mAPMN/S prostate cancer with TALZENNA based on the presence of alterations in genes directly or indirectly involved in HRR (*ATM*, *ATR*, *BRCA1*, *BRCA2*, *CDK12*, *CHEK2*, *FANCA*, *MLH1*, *MRE11A*, *NBN*, *PALB2*, or *RAD51C*) *[see Indications and Usage (1.2), Clinical Studies (14.2)]*.

Information on the FDA-authorized tests for the detection of genetic mutations is available at http://www.fda.gov/companiondiagnostics.

2.2 Recommended Dosage for g*BRCA*m HER2-negative Locally Advanced or Metastatic Breast Cancer

The recommended dosage of TALZENNA is 1 mg orally once daily, until disease progression or unacceptable toxicity.

2.3 Recommended Dosage for HRR Gene-Mutated mAPMR and mAPMN/S Prostate Cancer

The recommended dosage of TALZENNA is 0.5 mg orally once daily with enzalutamide until disease progression or unacceptable toxicity.

Refer to the enzalutamide prescribing information for recommended enzalutamide dosing information.

Patients receiving TALZENNA and enzalutamide should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had a bilateral orchiectomy.

2.4 Administration

Take TALZENNA with or without food *[see Clinical Pharmacology (12.3)]*.

Swallow TALZENNA capsules whole. Do not open or dissolve.

If a patient vomits or misses a dose of TALZENNA, instruct them to take the next prescribed dose at the usual time.

2.5 Dosage Modifications for Adverse Reactions

To manage adverse reactions, consider interruption of treatment with or without dose reduction based on severity and clinical presentation. Recommended dose reductions are indicated in Table 1 and Table 2. Treatment with TALZENNA should be permanently discontinued if more than 3 dose reductions are required.

g*BRCA*m HER2-negative Locally Advanced or Metastatic Breast Cancer

Table 1. Dose Reduction Levels for Adverse Reactions—Breast Cancer

Dose Reductions	**Dose Level**
Recommended starting dose	1 mg once daily
First dose reduction	0.75 mg once daily
Second dose reduction	0.5 mg once daily
Third dose reduction	0.25 mg once daily

HRR Gene-Mutated mAPMR and mAPMN/S Prostate Cancer

Table 2. Dose Reduction Levels for Adverse Reactions—mAPMR and mAPMN/S Prostate Cancer

Dose Reductions	**Dose Level**
Recommended starting dose	0.5 mg once daily
First dose reduction	0.35 mg once daily
Second dose reduction	0.25 mg once daily
Third dose reduction	0.1 mg once daily

Refer to the enzalutamide prescribing information for dose modifications for adverse reactions associated with enzalutamide.

g*BRCA*m HER2-negative Locally Advanced or Metastatic Breast Cancer; HRR Gene-Mutated mAPMR and mAPMN/S Prostate Cancer
Monitor complete blood counts monthly and as clinically indicated *[see Warnings and Precautions (5.2)]*.

Table 3. Dose Modification and Management for Adverse Reactions

Adverse Reactions	**Withhold TALZENNA Until Levels Resolve to**	**Resume TALZENNA**
Hemoglobin <8 g/dL	≥9 g/dL	Resume TALZENNA at a reduced dose
Platelet count <50,000/μL	≥75,000/μL	
Neutrophil count <1,000/μL	≥1,500/μL	
Non-hematologic Grade 3 or Grade 4	≤Grade 1	Consider resuming TALZENNA at a reduced dose or discontinue

2.6 Recommended Dosage in Patients with Renal Impairment

g*BRCA*m HER2-negative Locally Advanced or Metastatic Breast Cancer
The recommended dosage of TALZENNA for patients with moderate renal impairment (CLcr 30 - 59 mL/min) is 0.75 mg taken orally once daily *[see Use in Specific Populations (8.7)]*.

The recommended dosage of TALZENNA for patients with severe renal impairment (CLcr 15 - 29 mL/min) is 0.5 mg taken orally once daily *[see Use in Specific Populations (8.7)]*.

HRR Gene-Mutated mAPMR and mAPMN/S Prostate Cancer
The recommended dosage of TALZENNA for patients with moderate renal impairment (CLcr 30 - 59 mL/min) is 0.35 mg taken orally once daily with enzalutamide *[see Use in Specific Populations (8.7)]*.

The recommended dosage of TALZENNA for patients with severe renal impairment (CLcr 15 - 29 mL/min) is 0.25 mg taken orally once daily with enzalutamide *[see Use in Specific Populations (8.7)]*.

2.7 Dosage Modifications for P-glycoprotein Inhibitors

g*BRCA*m HER2-negative Locally Advanced or Metastatic Breast Cancer
Avoid coadministration of TALZENNA with the following P-glycoprotein (P-gp) inhibitors: itraconazole, amiodarone, carvedilol, clarithromycin, and verapamil. If coadministration of TALZENNA with these P-gp inhibitors cannot be avoided, reduce the dose of TALZENNA to 0.75 mg taken orally once daily. When the P-gp inhibitor is discontinued, increase the dose of TALZENNA (after 3 – 5 half-lives of the P-gp inhibitor) to the dose of TALZENNA that was used before starting the P-gp inhibitor *[see Drug Interactions (7.1)]*.

Monitor for increased adverse reactions and modify the dosage as recommended for adverse reactions when TALZENNA is coadministered with other P-gp inhibitors *[see Dosage and Administration (2.5)]*.

3 DOSAGE FORMS AND STRENGTHS

Table 4. Dosage Forms and Strengths

Capsule Strength	Description
0.1 mg	White cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.1” in black)
0.25 mg	Ivory cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.25” in black)
0.35 mg	Ivory cap (printed with “Pfizer” in black) and an ivory body (printed with “TLZ 0.35” in black)
0.5 mg	Light pink cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.5” in black)
0.75 mg	Light orange cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.75” in black)
1 mg	Light red cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 1” in black)

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Myelodysplastic Syndrome/Acute Myeloid Leukemia

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML), including cases with a fatal outcome, has been reported in patients who received TALZENNA.

In clinical studies, among 1,096 patients treated with TALZENNA as a single agent or as part of a combination regimen with enzalutamide, the cumulative incidence of MDS/AML was approximately 1% *[see Adverse Reactions (6.1)]* including 0.6% with fatal outcomes. The incidence of MDS/AML among patients treated with active control or with placebo in combination with enzalutamide was 0.2%. The median duration of therapy with TALZENNA in patients who developed MDS/AML was approximately 2.8 years (range: 1 to 5.8 years).

Do not start TALZENNA until patients have adequately recovered from hematological toxicity caused by previous chemotherapy. Monitor blood counts monthly during treatment with TALZENNA. For prolonged hematological toxicities, interrupt TALZENNA and monitor blood counts weekly until recovery. If counts do not recover within 4 weeks, refer the patient to a hematologist for further investigations including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue TALZENNA.

5.2 Myelosuppression

Myelosuppression consisting of anemia, leukopenia/neutropenia, and/or thrombocytopenia has been reported in patients treated with TALZENNA *[see Adverse Reactions (6.1)]*.

Grade ≥3 anemia, neutropenia, and thrombocytopenia were reported, respectively, in 39%, 21%, and 15% of patients receiving TALZENNA as a single agent. Discontinuation due to anemia, neutropenia, and thrombocytopenia occurred, respectively, in 0.7%, 0.3%, and 0.3% of patients.

Grade ≥3 anemia, neutropenia, and thrombocytopenia were reported, respectively, in 49%, 19%, and 9% of patients receiving TALZENNA in combination with enzalutamide. Forty-one percent of patients required a red blood cell transfusion, including 25% who required more than one transfusion. Discontinuation due to anemia, neutropenia, and thrombocytopenia occurred, respectively, in 7%, 4%, and 1% of patients.

Withhold TALZENNA until patients have adequately recovered from hematological toxicity caused by previous therapy. Monitor blood counts monthly during treatment with TALZENNA. If hematological toxicities do not resolve within 28 days, discontinue TALZENNA and refer the patient to a hematologist for further investigations including bone marrow analysis and blood sample for cytogenetics *[see Dosage and Administration (2.5)]*.

5.3 Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal data, TALZENNA can cause fetal harm when administered to a pregnant woman. In an animal reproduction study, administration of talazoparib to pregnant rats during the period of organogenesis caused fetal malformations and structural skeletal variations, and embryo-fetal death at exposures that were 0.24 times the area under the concentration-time curve (AUC) in patients receiving the recommended human dose of 1 mg daily. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 7 months following the last dose of TALZENNA *[see Use in Specific Populations (8.1, 8.3), Clinical Pharmacology (12.1)]*.

Based on findings from genetic toxicity and animal reproduction studies, advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 4 months following the last dose of TALZENNA *[see Use in Specific Populations (8.1, 8.3), Nonclinical Toxicology (13.1)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Myelodysplastic Syndrome/Acute Myeloid Leukemia *[see Warnings and Precautions (5.1)]*
- Myelosuppression *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in the WARNINGS AND PRECAUTIONS section reflect exposure to single agent TALZENNA among the 286 patients enrolled in the EMBRACA trial, TALZENNA 0.5 mg daily with enzalutamide in 511 patients enrolled in the TALAPRO-2 trial that included 197 patients with HRR gene-mutated mAPMR prostate cancer, and TALZENNA 0.5 mg daily with enzalutamide in 299 patients with HRR gene-mutated mAPMN/S prostate cancer enrolled in the TALAPRO-3 trial. Among the 810 patients with

prostate cancer, 68% were exposed for greater than 1 year, 52% were exposed for greater than 2 years, and 35% were exposed for greater than 3 years. In this safety population, the most common (≥20%) adverse reactions including laboratory abnormalities were decreased hemoglobin (86%), decreased neutrophils (68%), decreased lymphocytes (62%), decreased platelets (54%), fatigue (48%), decreased albumin (26%), decreased calcium (26%), back pain (24%), decreased appetite (22%), and nausea (21%).

g*BRCA*m HER2-negative Locally Advanced or Metastatic Breast Cancer

EMBRACA

The safety of TALZENNA as a single agent was evaluated in g*BRCA*m patients with HER2-negative locally advanced or metastatic breast cancer who had previously received no more than 3 lines of chemotherapy for the treatment of locally advanced/metastatic disease *[see Clinical Studies (14.1)]*. EMBRACA was a randomized, open-label, multi-center study in which 412 patients received either TALZENNA 1 mg once daily (N=286) or a chemotherapy agent (capecitabine, eribulin, gemcitabine, or vinorelbine) of the healthcare provider's choice (N=126) until disease progression or unacceptable toxicity. The median duration of study treatment was 6.1 months in patients who received TALZENNA and 3.9 months in patients who received chemotherapy.

Serious adverse reactions of TALZENNA occurred in 32% of patients. Serious adverse reactions reported in >2% of patients included anemia (6%) and pyrexia (2%). Fatal adverse reactions occurred in 1% of patients, including cerebral hemorrhage, liver disorder, veno-occlusive liver disease, and worsening neurological symptoms (1 patient each).

Permanent discontinuation due to adverse reactions occurred in 5% of TALZENNA patients. Dosing interruptions due to an adverse reaction of any grade occurred in 65% of patients receiving TALZENNA; dose reductions due to any cause occurred in 53% of TALZENNA patients.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased hemoglobin, decreased neutrophils, decreased lymphocytes, decreased platelets, fatigue, increased glucose, increased aspartate aminotransferase (AST), increased alkaline phosphatase (ALP), increased alanine aminotransferase (ALT), decreased calcium, nausea, headache, vomiting, alopecia, diarrhea, and decreased appetite.

Table 5 and Table 6 summarize the most common adverse reactions and laboratory abnormalities, respectively, in patients treated with TALZENNA or chemotherapy in the EMBRACA study.

Table 5. Adverse Reactions[a] (≥20%) in Patients Receiving TALZENNA in EMBRACA

	TALZENNA N=286 (%)			Chemotherapy N=126 (%)		
Adverse Reactions	**Grades 1-4**	**Grade 3**	**Grade 4**	**Grades 1-4**	**Grade 3**	**Grade 4**
General Disorders and Administration Site Conditions						
Fatigue[b]	62	3	0	50	5	0
Gastrointestinal Disorders						
Nausea	49	0.3	0	47	2	0
Vomiting	25	2	0	23	2	0
Diarrhea	22	1	0	26	6	0
Nervous System Disorders						
Headache	33	2	0	22	1	0
Skin and Subcutaneous Tissue Disorders						
Alopecia	25	0	0	28	0	0
Metabolism and Nutrition Disorders						
Decreased appetite	21	0.3	0	22	1	0

Abbreviation: N=number of patients.

a. Graded according to NCI CTCAE 4.03.

b. Includes fatigue and asthenia.

Clinically relevant adverse reactions in <20% of patients who received TALZENNA included abdominal pain (19%), dizziness (17%), dysgeusia (10%), dyspepsia (10%), stomatitis (8%), and febrile neutropenia (0.3%).

Table 6. Select Laboratory Abnormalities (≥25%) of Patients in EMBRACA

	TALZENNA Na=286 (%)			Chemotherapy Na=126 (%)		
Parameter	**Grades 1-4**	**Grade 3**	**Grade 4**	**Grades 1-4**	**Grade 3**	**Grade 4**
Hemoglobin decreased	90	39	0	77	6	0
Neutrophils decreased	68	17	3	70	21	17
Lymphocytes decreased	76	17	0.7	53	8	0.8
Platelets decreased	55	11	4	29	2	0
Glucose increased[b]	54	2	0	51	2	0
AST increased	37	2	0	48	3	0
ALP increased	36	2	0	34	2	0
ALT increased	33	1	0	37	2	0
Calcium decreased	28	1	0	16	0	0

Abbreviation: N=number of patients.

a. This number represents the safety population. The derived values in the table are based on the total number of evaluable patients for each laboratory parameter.

b. This number represents non-fasting glucose.

HRR Gene-Mutated Prostate Cancer

TALAPRO-2 for mAPMR Prostate Cancer
The safety of TALZENNA in combination with enzalutamide was evaluated in patients with HRR gene-mutated mAPMR prostate cancer enrolled in TALAPRO-2 *[see Clinical Studies (14.2)]*. Patients were randomized to receive either TALZENNA 0.5 mg with enzalutamide 160 mg once daily (n=197), or placebo with enzalutamide 160 mg once daily (n=199) until disease progression or unacceptable toxicity.

Serious adverse reactions of TALZENNA with enzalutamide occurred in 30% of patients. Serious adverse reactions reported in >2% of patients included anemia (9%) and fracture (3%). Fatal adverse reactions occurred in 1.5% of patients, including pneumonia, COVID infection, and sepsis (1 patient each).

Permanent discontinuation of TALZENNA due to adverse reactions occurred in 10% of patients treated in the TALZENNA with enzalutamide arm. The most common adverse reactions which resulted in permanent discontinuation of TALZENNA were anemia (4%), fatigue, bone fracture, ischemic heart disease, and spinal cord compression (1% each).

Dosage interruption of TALZENNA due to adverse reactions occurred in 58% of patients treated in the TALZENNA with enzalutamide arm. The most common adverse reactions that resulted in dose interruption of TALZENNA were anemia (42%), neutropenia (15%), thrombocytopenia (9%), and fatigue (5%).

Dose reduction of TALZENNA due to adverse reactions occurred in 52% of patients treated in the TALZENNA with enzalutamide arm. The most common adverse reactions which resulted in dose reduction of TALZENNA were anemia (43%), neutropenia (15%), thrombocytopenia (6%), and fatigue (4%).

Table 7 and Table 8 summarize the most common adverse reactions and laboratory abnormalities, respectively, in the TALAPRO-2 study.

Table 7. Adverse Reactions[a] (≥10%) in Patients Receiving TALZENNA (with a Difference Between Arms of ≥2%) in TALAPRO-2

	TALZENNA with Enzalutamide N=197			Placebo with Enzalutamide N=199		
	Grades 1-4 %	Grade 3 %	Grade 4 %	Grades 1-4 %	Grade 3 %	Grade 4 %
General Disorders and Administration Site Conditions						
Fatigue[b]	49	4	0	40	1	0
Gastrointestinal Disorders						
Nausea	21	2	0	17	1	0.5
Metabolism and Nutrition Disorders						
Decreased appetite	20	1	0	14	1	1
Injury, Poisoning and Procedural Complications						
Fractures[c]	14	3	0	10	1.5	0
Nervous System Disorder						
Dizziness[d]	13	1.5	0	9	1.5	0
Dysgeusia[e]	10	0	0	4.5	0	0

Abbreviation: N=number of patients.

a. Graded according to NCI CTCAE 4.03.

b. Includes fatigue and asthenia.

c. Fractures include multiple similar terms.

d. Includes dizziness, dizziness postural, vertigo.

e. Includes ageusia, anosmia, dysgeusia.

Clinically relevant adverse reactions in <10% of patients who received TALZENNA with enzalutamide included abdominal pain (9%), vomiting (9%), alopecia (7%), dyspepsia (4%), venous thromboembolism (3%), and stomatitis (2%).

Table 8. Select Laboratory Abnormalities (≥10%) That Worsened from Baseline in Patients Who Received TALZENNA (with a Difference Between Arms of ≥2%) in TALAPRO-2

	TALZENNA with Enzalutamide N=197[a]			Placebo with Enzalutamide N=199[a]		
Laboratory Abnormality	**Grades 1-4 %**	**Grade 3 %**	**Grade 4 %**	**Grades 1-4 %**	**Grade 3 %**	**Grade 4 %**
Hemoglobin decreased	79	41	0	34	6	0
Neutrophils decreased	60	18	1	18	0	1
Lymphocytes decreased	58	13	0	36	7	0
Platelets decreased	45	6	3	8	0.5	0
Calcium decreased	25	0	1	11	0	1
Sodium decreased	22	3	0	20	1.5	0
Phosphate decreased	17	3	1	13	2	0
Magnesium decreased	14	0	1	12	0	0.5
Bilirubin increased	11	0.5	0	7	0	0
Potassium decreased	11	0	1	7	1	0.5

Abbreviation: N=number of patients.

[a] The denominator used to calculate the rate varied from 198 to 199 in the placebo with enzalutamide arm based on the number of patients with a baseline value and at least one post-treatment value.

TALAPRO-3 for mAPMN/S Prostate Cancer

The safety of TALZENNA in combination with enzalutamide was evaluated in patients with HRR gene-mutated mAPMN/S prostate cancer enrolled in TALAPRO-3 *[see Clinical Studies (14.2)]*. Patients were randomized to receive either TALZENNA 0.5 mg with enzalutamide 160 mg once daily (n=299), or placebo with enzalutamide 160 mg once daily (n=295) until disease progression or unacceptable toxicity.

Serious adverse reactions of TALZENNA in combination with enzalutamide occurred in 42% of patients. Serious adverse reactions reported in >2% of patients included anemia (14%), thrombocytopenia (3%), and urinary tract infection (2%). Fatal adverse reactions occurred in 3% of patients, including cardiac arrest, death, general physical health deterioration, idiopathic pulmonary fibrosis, pancytopenia, and second primary malignancy (1 patient each).

Permanent discontinuation of TALZENNA due to adverse reactions occurred in 19% of patients. The most common adverse reactions that resulted in permanent discontinuation of TALZENNA were neutropenia (6%), anemia (5%), thrombocytopenia and fatigue (2% each), MDS/AML, dizziness, leukopenia, dyspnea, nausea, second primary malignancy, and spinal cord compression (1% each).

Dosage interruption of TALZENNA due to adverse reactions occurred in 69% of patients. The most common adverse reactions that resulted in dosage interruption of TALZENNA were anemia (42%), neutropenia (17%), thrombocytopenia (12%), fatigue (11%), and COVID-19 (5%).

Dose reduction of TALZENNA due to adverse reactions occurred in 60% of patients. The most common adverse reactions that resulted in dose reduction of TALZENNA were anemia (45%), neutropenia (15%), thrombocytopenia and fatigue (6% each).

Table 9 and Table 10 summarize the most common adverse reactions and laboratory abnormalities, respectively, in the TALAPRO-3 study.

Table 9. Adverse Reactions[a] (≥10%) in Patients Receiving TALZENNA (with a Difference Between Arms of ≥2%) in TALAPRO-3

	TALZENNA with Enzalutamide N=299			Placebo with Enzalutamide N=295		
	Grades 1-4 %	Grade 3 %	Grade 4 %	Grades 1-4 %	Grade 3 %	Grade 4 %
General Disorders and Administration Site Conditions						
Fatigue[b]	46	9	0	28	1	0
Metabolism and Nutrition Disorders						
Decreased appetite	20	2	0	10	1	0
Gastrointestinal Disorders						
Constipation	18	0	0	12	0	0
Nausea	17	0	0	8	0	0
Diarrhea[b]	14	2	0	11	1	0
Abdominal pain[b]	11	1	0	6	0	0
Nervous System Disorders						
Dizziness[b]	13	0	0	11	1	0
Dysgeusia[b]	11	0	0	8	0	0
Infections and Infestations						
Urinary tract infection[b]	12	2	0	7	1	0
Psychiatric Disorders						
Insomnia	11	1	0	7	0	0
Investigations						
Weight decreased	10	1	0	5	0	0

a. Graded according to NCI CTCAE 4.03.

b. Includes multiple terms.

Clinically relevant adverse reactions in <10% of patients who received TALZENNA in combination with enzalutamide included headache (6%), vomiting (5%), alopecia (4%), dyspepsia (4%), second primary malignancies (3%), venous thromboembolism (2%), and stomatitis (2%).

Table 10. Select Laboratory Abnormalities (≥10%) That Worsened from Baseline in Patients Who Received TALZENNA (with a Difference Between Arms of ≥2%) in TALAPRO-3

	TALZENNA with Enzalutamide[a]			Placebo with Enzalutamide[a]		
Laboratory Abnormality	**Grades 1-4 %**	**Grade 3 %**	**Grade 4 %**	**Grades 1-4 %**	**Grade 3 %**	**Grade 4 %**
Hematology						
Hemoglobin decreased	88	49	0	46	3.4	0
Neutrophils decreased	71	18	4	24	2.4	0.3
Lymphocytes decreased	60	11	3.3	39	6	0
Platelets decreased	57	7	3	20	0.3	0.3
Chemistry						
Calcium decreased	22	0.3	0.3	17	1	0.7
Blood bilirubin increased	18	1.3	0	14	0.3	0
Phosphate decreased	13	1.7	0	9	0.7	0

a. The denominator used to calculate the rate varied from 289 to 299 for TALZENNA with enzalutamide and 282 to 294 for placebo with enzalutamide based on the number of patients with a baseline value and at least one post-treatment value.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on TALZENNA

Effect of P-gp Inhibitors

Breast Cancer

Avoid coadministration of TALZENNA with the following P-gp inhibitors: itraconazole, amiodarone, carvedilol, clarithromycin, and verapamil. If coadministration of TALZENNA with these P-gp inhibitors cannot be avoided, reduce the dose of TALZENNA *[see Dosage and Administration (2.7)]*. When the P-gp inhibitor is discontinued, increase the dose of TALZENNA *[see Dosage and Administration (2.7)]*.

Coadministration of TALZENNA with these P-gp inhibitors increased talazoparib concentrations *[see Clinical Pharmacology (12.3)]*, which may increase the risk of adverse reactions.

Monitor for increased adverse reactions and modify the dosage as recommended for adverse reactions when TALZENNA is coadministered with other P-gp inhibitors *[see Dosage and Administration (2.5)]*.

HRR Gene-Mutated mAPMR and mAPMN/S Prostate Cancer

The effect of coadministration of P-gp inhibitors on talazoparib exposure when TALZENNA is taken with enzalutamide has not been studied. Monitor patients for increased adverse reactions and modify the dosage as recommended for adverse reactions when TALZENNA is coadministered with a P-gp inhibitor *[see Dosage and Administration (2.5)]*.

Effect of Breast Cancer Resistance Protein (BCRP) Inhibitors
Monitor patients for increased adverse reactions and modify the dosage as recommended for adverse reactions when TALZENNA is coadministered with a BCRP inhibitor *[see Dosage and Administration (2.5)]*.

Coadministration of TALZENNA with BCRP inhibitors may increase talazoparib exposure *[see Clinical Pharmacology (12.3)]*, which may increase the risk of adverse reactions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
Based on findings from animal studies and its mechanism of action *[see Clinical Pharmacology (12.1)]*, TALZENNA can cause embryo-fetal harm when administered to a pregnant woman. There are no available data on TALZENNA use in pregnant women to inform a drug-associated risk. In an animal reproduction study, the administration of talazoparib to pregnant rats during the period of organogenesis caused fetal malformations and structural skeletal variations and embryo-fetal death at maternal exposures that were 0.24 times the AUC in patients receiving the recommended dose of 1 mg daily *(see Data)*. Apprise pregnant women and females of reproductive potential of the potential risk to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the general U.S. population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies are 2% to 4% and 15% to 20%, respectively.

Data
Animal Data
In an embryo-fetal development toxicity study, pregnant rats received oral doses of 0.015, 0.05, and 0.15 mg/kg/day talazoparib during the period of organogenesis. Talazoparib caused embryo-fetal death at doses ≥0.015 mg/kg/day (approximately 0.24 times the AUC in patients at the recommended dose of 1 mg daily). A dose of 0.015 mg/kg/day caused decreased fetal body weights and an increased incidence of fetal malformations (depressed eye bulge, small eye, split sternebra, and fused cervical vertebral arch) and structural variations including misshapen or incomplete ossification of the sternebra, skull, rib, and vertebra.

8.2 Lactation

Risk Summary
There are no data on the presence of talazoparib in human milk, the effects of the drug on milk production, or the effects of the drug on the breastfed child. Because of the potential for serious adverse reactions in a breastfed child from talazoparib, advise lactating women not to breastfeed during treatment with TALZENNA and for 1 month after the last dose.

8.3 Females and Males of Reproductive Potential

TALZENNA can cause fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing
Verify pregnancy status in females of reproductive potential prior to initiating TALZENNA treatment.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment and for 7 months following the last dose of TALZENNA.

Males

Based on genotoxicity and animal reproduction studies, advise male patients with female partners of reproductive potential and pregnant partners to use effective contraception during treatment with TALZENNA and for 4 months following the last dose *[see Use in Specific Populations (8.1), Nonclinical Toxicology (13.1)]*.

Infertility

Males

Based on animal studies, TALZENNA may impair fertility in males of reproductive potential *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of TALZENNA have not been established in pediatric patients.

8.5 Geriatric Use

In clinical trials of TALZENNA enrolling 494 patients with advanced solid tumors who received TALZENNA 1 mg daily as a single agent, 85 (17%) patients were ≥65 years of age, and this included 19 (4%) patients who were ≥75 years old. There were 5 patients ≥85 years old. No overall differences in safety or effectiveness of TALZENNA were observed between patients ≥65 years of age and younger patients.

In clinical trials of TALZENNA enrolling 810 patients who received TALZENNA in combination with enzalutamide, 624 (77%) patients were ≥65 years of age, including 262 (32%) patients who were ≥75 years old. Grade 3 to 5 adverse reactions (91% vs 75%), permanent discontinuations (31% vs 14%), dosage interruptions (75% vs 63%), and dose reductions (65% vs 53%) occurred more frequently in patients ≥75 years of age than in patients <75 years of age. The differences in Grade 3 to 5 adverse reactions between patients ≥75 years of age and patients <75 years of age were primarily driven by an increased incidence of myelosuppression. No overall differences in effectiveness of TALZENNA were observed between patients ≥75 years of age and patients <75 years of age.

8.6 Hepatic Impairment

No dosage modification is recommended for patients with hepatic impairment *[see Clinical Pharmacology (12.3)]*.

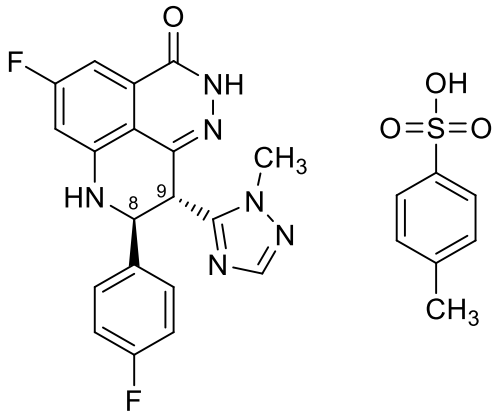
8.7 Renal Impairment

Reduce the recommended dosage of TALZENNA in patients with moderate (CLcr 30 – 59 mL/min) and severe (CLcr 15 – 29 mL/min) renal impairment *[see Dosage and Administration (2.6)]*. Monitor patients with severe renal impairment for increased adverse reactions and modify the dosage as recommended for adverse reactions *[see Dosage and Administration (2.5)]*.

No dose adjustment is recommended for patients with mild renal impairment (CLcr 60 – 89 mL/min). TALZENNA has not been studied in patients requiring hemodialysis.

11 DESCRIPTION

Talazoparib is an inhibitor of mammalian polyadenosine 5'-diphosphoribose (ADP-ribose) polymerase (PARP) enzymes. The chemical name of talazoparib tosylate is (8*S*,9*R*)-5-Fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-2,7,8,9-tetrahydro-3*H*-pyrido[4,3,2-*de*]phthalazin-3-one 4-methylbenzenesulfonate (1:1). The chemical formula of talazoparib tosylate is $C_{26}H_{22}F_2N_6O_4S$, and the relative molecular mass is 552.56 Daltons. The chemical structure of talazoparib tosylate is shown below:



Talazoparib tosylate is a white to yellow solid. TALZENNA capsules for oral use are available as:

- 0.1 mg hard hypromellose (HPMC) capsule that contains 0.145 mg talazoparib tosylate equivalent to 0.1 mg talazoparib free base, or
- 0.25 mg HPMC capsule that contains 0.363 mg talazoparib tosylate equivalent to 0.25 mg talazoparib free base, or
- 0.35 mg HPMC capsule that contains 0.509 mg talazoparib tosylate equivalent to 0.35 mg talazoparib free base, or
- 0.5 mg HPMC capsule that contains 0.727 mg talazoparib tosylate equivalent to 0.5 mg talazoparib free base, or
- 0.75 mg HPMC capsule that contains 1.09 mg talazoparib tosylate equivalent to 0.75 mg talazoparib free base, or
- 1 mg HPMC capsule that contains 1.453 mg talazoparib tosylate equivalent to 1 mg talazoparib free base.

Inactive ingredients: silicified microcrystalline cellulose (sMCC). The capsule shells contain hypromellose (HPMC), yellow iron oxide, red iron oxide and titanium dioxide; and the printing ink contains shellac, black iron oxide, potassium hydroxide, ammonium hydroxide, and propylene glycol.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Talazoparib is an inhibitor of PARP enzymes, including PARP1 and PARP2, which play a role in DNA repair. *In vitro* studies with cancer cell lines that harbored defects in DNA repair genes, including *BRCA1* and *BRCA2*, have shown that talazoparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, decreased cell proliferation, and

apoptosis. Talazoparib anti-tumor activity was observed in patient-derived xenograft breast cancer models bearing mutated *BRCA1* or mutated *BRCA2* or wild type *BRCA1* and *BRCA2*.

12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of TALZENNA have not been fully characterized.

Cardiac Electrophysiology
At a dose of 1 mg (the recommended dosage for treatment of breast cancer), TALZENNA had no large QTc prolongation (i.e., >20 ms).

12.3 Pharmacokinetics

After administration of TALZENNA 1 mg orally once daily as a single agent (the recommended dosage for breast cancer), the mean [% coefficient of variation (CV%)] AUC and maximum observed plasma concentration (C_{max}) of talazoparib at steady-state was 208 (37%) ng.hr/mL and 16.4 (32%) ng/mL, respectively. The mean (CV%) steady-state C_{trough} was 3.53 (61%) ng/mL.

After administration of TALZENNA 0.5 mg orally once daily (the recommended dosage for prostate cancer) with enzalutamide, the mean (CV%) steady-state C_{trough} ranged from 3.29 to 3.99 ng/mL (43% to 49%).

The pharmacokinetics (PK) of talazoparib is linear from 0.025 mg to 2 mg (2 times the recommended dose for breast cancer). The median accumulation ratio of talazoparib following 1 mg orally once daily is 2.3 to 5.2. Talazoparib plasma concentrations reached steady-state within 2 to 3 weeks when administered as a single agent and within 9 weeks when coadministered with enzalutamide.

Absorption
The median time to C_{max} (T_{max}) was generally between 1 to 2 hours after dosing.

Food Effect
Following a single TALZENNA 0.5 mg dose with high-fat, high-calorie food (approximately 800 to 1,000 calories with 150, 250, and 500 to 600 calories from protein, carbohydrate, and fat, respectively), the mean C_{max} was decreased by 46%, the median T_{max} was delayed from 1 to 4 hours, and AUC was not affected.

Distribution
The mean apparent volume of distribution of talazoparib is 420 L. *In vitro*, protein binding of talazoparib is 74% and is independent of talazoparib concentration.

Elimination
The mean terminal plasma half-life (±standard deviation) is 90 (±58) hours and the mean apparent oral clearance (inter-subject variability) is 6.45 L/h (31%).

Metabolism
Talazoparib undergoes minimal hepatic metabolism. The identified metabolic pathways include mono-oxidation, dehydrogenation, cysteine conjugation of mono-desfluoro-talazoparib, and glucuronide conjugation.

Excretion
Excretion of talazoparib in urine was the major route of elimination. Approximately 68.7% (54.6% unchanged) of the total administered radiolabeled dose of talazoparib was recovered in urine, and 19.7% (13.6% unchanged) was recovered in feces.

Specific Populations
Age (18 to 88 years), sex, race (361 White, 41 Asian, 16 Black, 9 Others, and 63 Not Reported), body weight (36 to 162 kg), and mild to severe hepatic impairment had no clinically significant effect on the PK of talazoparib.

Patients with Renal Impairment
Mild (eGFR 60 – 89 mL/min/1.73 m^2) renal impairment had no clinically significant effect on talazoparib pharmacokinetics. Talazoparib steady-state total exposure (AUC) increased by 43% in subjects with moderate (eGFR 30 – 59 mL/min/1.73 m^2) renal impairment and 163% in patients with severe (eGFR 15 – 29 mL/min/1.73 m^2) renal impairment relative to subjects with normal renal function (eGFR ≥90 mL/min/1.73 m^2). Talazoparib steady-state peak concentration (C_{max}) increased by 32% in subjects with moderate renal impairment and 89% in subjects with severe renal impairment, relative to subjects with normal renal function. Similar increases in AUC were observed with talazoparib when given with enzalutamide for patients with moderate and severe renal impairment. The PK of talazoparib has not been studied in patients requiring hemodialysis. There was no evidence of a relationship between the protein binding of talazoparib and renal function.

Drug Interaction Studies
Clinical Studies
Effect of P-gp Inhibitors: Coadministration of a P-gp inhibitor (itraconazole) with a single 0.5 mg dose of TALZENNA increased talazoparib AUC and C_{max} by approximately 56% and 40%, respectively. Coadministration with the following other P-gp inhibitors: amiodarone, carvedilol, clarithromycin, itraconazole, and verapamil increased talazoparib exposure by 45%.

Coadministration with other P-gp inhibitors (including azithromycin, atorvastatin, diltiazem, felodipine, fluvoxamine, and quercetin) had no clinically significant effect on talazoparib pharmacokinetics.

Effect of P-gp Inducers: Coadministration of a P-gp inducer (rifampin) with a single 1 mg dose of TALZENNA increased talazoparib C_{max} by 37% with no effect on talazoparib AUC.

Effect of Acid-Reducing Agents: Coadministration of acid-reducing agents including proton pump inhibitors (PPI), histamine receptor 2 antagonists (H_2RA), or other acid-reducing agents has no effect on the absorption of talazoparib.

Enzalutamide: Coadministration of enzalutamide with TALZENNA increased talazoparib exposure approximately 2-fold.

In Vitro Studies
Transporters: Talazoparib is a substrate of P-gp and BCRP transporters, but not a substrate of OATP1B1, OATP1B3, OCT1, OCT2, OAT1, OAT3, BSEP, MATE1, or MATE2-K.

Talazoparib is not an inhibitor of P-gp, BCRP, OATP1B1, OATP1B3, OCT1, OCT2, OAT1, OAT3, BSEP, MATE1, or MATE2-K.

CYP Enzymes: Talazoparib is not an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4/5.

Talazoparib is not an inducer of CYP1A2, CYP2B6, or CYP3A4.

UGT: Talazoparib is not an inhibitor of UGT isoforms (1A1, 1A4, 1A6, 1A9, 2B7, and 2B15).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with talazoparib.

Talazoparib was clastogenic in an in vitro chromosomal aberration assay in human peripheral blood lymphocytes and in an in vivo bone marrow micronucleus assay in rats. This clastogenicity is consistent with genomic instability resulting from the primary pharmacology of talazoparib, indicating the potential for genotoxicity in humans. Talazoparib was not mutagenic in a bacterial reverse mutation (Ames) test.

Fertility studies in animals have not been conducted with talazoparib. In repeat-dose toxicity studies up to 3-months duration, talazoparib-related findings in the testis and epididymis at doses ≥0.04 mg/kg/day in rats and ≥0.01 mg/kg/day in dogs included decreased organ weights, luminal cellular debris, reduced sperm, and degeneration/atrophy. These doses in rats and dogs resulted in approximately 1.0 times and 0.2 times, respectively, the exposure (AUC) in humans at the recommended dose of 1 mg daily. Follicular atresia of the ovary was observed in rats at doses ≥1 mg/kg/day talazoparib, approximately 9.5 times the AUC in patients at the recommended dose of 1 mg daily.

14 CLINICAL STUDIES

14.1 Deleterious or Suspected Deleterious Germline *BRCA*-mutated HER2-negative Locally Advanced or Metastatic Breast Cancer

EMBRACA (NCT01945775) was an open-label study in which patients (N=431) with g*BRCA*m HER2-negative locally advanced or metastatic breast cancer were randomized 2:1 to receive TALZENNA 1 mg or healthcare provider's choice of chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine) until disease progression or unacceptable toxicity. Randomization was stratified by prior lines of chemotherapy for metastatic disease (0 vs 1, 2, or 3), by triple-negative disease status [triple-negative breast cancer (TNBC) vs non-TNBC], and history of central nervous system (CNS) metastasis (yes vs no).

Patients received no more than 3 prior cytotoxic chemotherapy regimens for their metastatic or locally advanced disease. Patients were required to have received treatment with an anthracycline and/or a taxane (unless contraindicated) in the neoadjuvant, adjuvant, and/or metastatic treatment setting. First-line treatment for advanced or metastatic disease with no prior adjuvant chemotherapy was allowed if the investigator determined that 1 of the 4 chemotherapy choices in the control arm would be an appropriate treatment option for the patient. Patients with prior platinum therapy for advanced disease were required to have no evidence of disease progression during platinum therapy. No prior treatment with a PARP inhibitor was permitted. Of the 431 patients randomized in the EMBRACA study, 408 (95%) were centrally confirmed to have a deleterious or suspected deleterious g*BRCA*m using a clinical trial assay; out of which 354 (82%) were confirmed using the BRACAnalysis CDx®. *BRCA* mutation status [breast cancer susceptibility gene 1 (*BRCA1*)-positive or breast cancer susceptibility gene 2 (*BRCA2*)-positive] was similar across both treatment arms.

The median age of patients treated with TALZENNA was 46 years (range: 28 to 84) and 51 years (range: 24 to 89) among patients treated with chemotherapy. Among all randomized patients, 1% vs 2% were males, 67% vs 75% were White; 11% vs 11% were Asian, and 4% vs 1% were Black or African American in the TALZENNA and chemotherapy arms, respectively. Almost all patients (98%) in both arms had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Approximately 56% of patients had estrogen receptor-positive and/or progesterone receptor-positive disease; 44% of patients had triple-negative disease, and the proportions were balanced across both treatment arms. Fifteen percent (15%) of patients in the TALZENNA arm and 14% of patients in the chemotherapy arm had a history of CNS metastases. Ninety-one percent (91%) of patients in the TALZENNA arm had received prior taxane therapy, and 85% had received prior anthracycline therapy in any setting. Sixteen percent (16%) of patients in the TALZENNA arm and 21% of patients in the chemotherapy arm had received prior platinum treatment in any setting. The median number of prior cytotoxic regimens for patients with advanced breast cancer was one; 38% received no prior cytotoxic regimens for advanced or metastatic disease, 37% received one, 20% received two, and 5% received three or more prior cytotoxic regimens.

The major efficacy outcome measure was progression-free survival (PFS) evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, as assessed by blinded independent central review (BICR). A statistically significant improvement in PFS was demonstrated for TALZENNA compared to chemotherapy. A sensitivity analysis of investigator-assessed PFS was consistent with the BICR-assessed PFS results. Consistent PFS results were observed across patient subgroups defined by study stratification factors (prior lines of chemotherapy, TNBC status, and history of CNS metastases). Efficacy data from the EMBRACA study are summarized in Table 11, and the Kaplan-Meier curves for PFS are shown in Figure 1 and final overall survival (OS) in Figure 2.

Table 11. Efficacy Results – EMBRACA Study

	TALZENNA	Chemotherapy
PFS by BICR	N=287	N=144
Disease progression or deaths, n (%)	186 (65)	83 (58)
Median months (95% CI)	8.6 (7.2, 9.3)	5.6 (4.2, 6.7)
Hazard ratio (95% CI)[a]	0.54 (0.41, 0.71)	
p-value[b]	p<0.0001	
Patients with Measurable Disease by Investigator[c]	N=219	N=114
ORR, % (95% CI)[d]	50.2 (43.4, 57.0)	18.4 (11.8, 26.8)
Median[e] DOR months (95% CI)	6.4 (5.4, 9.5)	3.9 (3.0, 7.6)
OS	N=287	N=144
Deaths, n (%)	216 (75)	108 (75)
Median months (95% CI)	19.3 (16.6, 22.5)	19.5 (17.4, 22.4)
Hazard ratio (95% CI)[a]	0.85 (0.67, 1.07)	
p-value[b]	p=0.1693	

Abbreviations: BICR=blinded independent central review; CI=confidence interval; DOR=duration of response; ITT=intent-to-treat; N=number of patients; ORR=objective response rate; OS=overall survival; PFS=progression-free survival.

a. Hazard ratio is estimated from a Cox proportional hazards model stratified by prior use of chemotherapy for metastatic disease (0 vs 1, 2, or 3), by triple-negative disease status [triple-negative breast cancer (TNBC) vs non-TNBC], and by history of central nervous system metastasis (yes vs no) and is relative to overall chemotherapy with <1 favoring talazoparib.

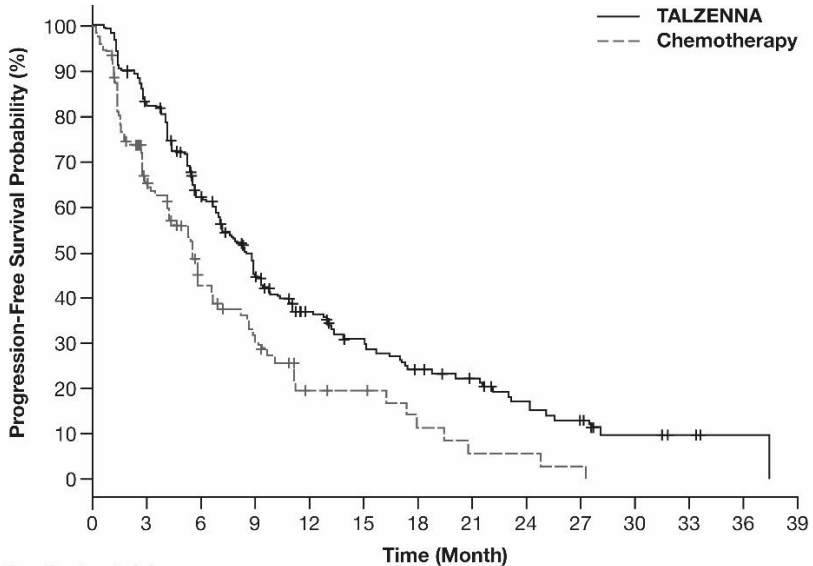
b. p-values (2-sided) from the log-rank test stratified by number of prior cytotoxic chemotherapy regimens, triple-negative status and history of central nervous system metastasis.

c. Conducted in ITT population with measurable disease at baseline.

d. Response rate based on confirmed responses.

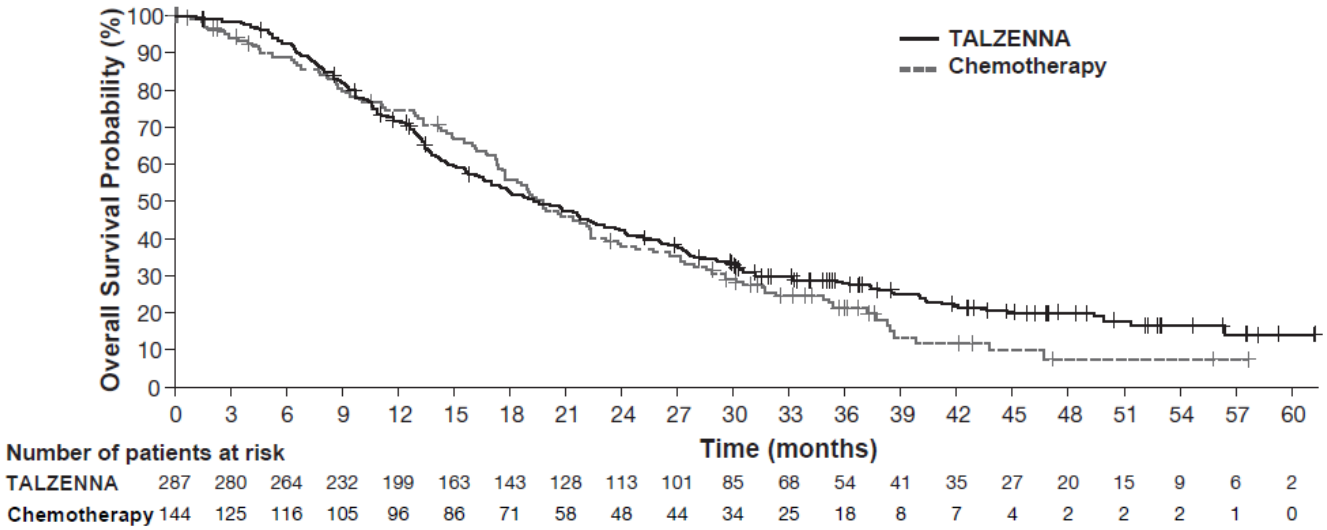
e. Median estimated from Kaplan-Meier probabilities.

Figure 1. Kaplan-Meier Curves of PFS – EMBRACA Study



Abbreviation: PFS=progression-free survival.

Figure 2. Kaplan-Meier Curves of OS – EMBRACA Study (ITT Population)



Abbreviations: ITT=intent-to-treat; OS=overall survival.

14.2 HRR Gene-Mutated Prostate Cancer

mAPMR Prostate Cancer

TALAPRO-2

The efficacy of TALZENNA with enzalutamide was evaluated in TALAPRO-2 (NCT03395197), a randomized, double-blind, placebo-controlled, multi-cohort trial in which 399 patients with HRR gene-mutated (HRRm) mAPMR prostate cancer were randomized 1:1 to receive enzalutamide 160 mg daily plus either TALZENNA 0.5 mg or placebo daily until unacceptable toxicity or disease progression. Mutation status of HRR genes was determined prospectively using solid tumor tissue or circulating tumor DNA (ctDNA)-based next generation sequencing tests. Patients were required to have a mutation in at least one of 12 genes involved directly or indirectly in the HRR pathway (*ATM*, *ATR*, *BRCA1*, *BRCA2*, *CDK12*, *CHEK2*, *FANCA*, *MLH1*, *MRE11A*, *NBN*, *PALB2*, or *RAD51C*). All patients received a GnRH analog or had had a prior bilateral orchiectomy and needed to have progressed on prior androgen deprivation therapy. Prior treatment with a CYP17 inhibitor or docetaxel for mAPMN/S prostate cancer was permitted. Randomization was stratified by previous treatment with a CYP17 inhibitor or docetaxel (yes/no).

The median age was 70 years (range: 41 to 90); 100% were male; 68% were White, 21% Asian, 2.8% Black, 0.8% Other, 7% unknown/not reported; 12% were Hispanic/Latino; and baseline ECOG performance status was 0 (62%) or 1 (38%). Thirty-nine percent of patients had bone-only disease; 15% had visceral disease. In the mAPMN/S prostate cancer setting, 29% of patients had received docetaxel and 9% had received a prior CYP17 inhibitor. The most commonly mutated HRR genes (>5%), including co-occurring mutations, were: *BRCA2* (34%), *ATM* (22%), *CDK12* (19%), *CHEK2* (18%), and *BRCA1* (6%).

The major efficacy outcome measure was radiographic progression-free survival (rPFS) evaluated according to RECIST, version 1.1 and Prostate Cancer Working Group (PCWG3) (bone) criteria, assessed by blinded independent central review (BICR). An additional efficacy outcome measure was overall survival (OS).

Statistically significant improvements in rPFS and OS were demonstrated in patients randomized to TALZENNA with enzalutamide compared with placebo with enzalutamide. Efficacy results are presented in Table 12, and Figures 3 and 4.

Table 12. Efficacy Results – TALAPRO-2 (HRRm mAPMR Prostate Cancer)

	TALZENNA with Enzalutamide N=200	Placebo with Enzalutamide N=199
Radiographic Progression-Free Survival by BICR		
Number of events, n (%)	66 (33)	104 (52)
Median months (95% CI)	NR (21.9, NR)	13.8 (11.0, 16.7)
Hazard ratio (95% CI)[a]	0.45 (0.33, 0.61)	
p-value[b]	p<0.0001	
Overall Survival		
Deaths, n (%)	93 (47)	126 (63)
Median months (95% CI)	45.1 (35.4, NR)	31.1 (27.3, 35.4)
Hazard ratio (95% CI)[a]	0.62 (0.48, 0.81)	
p-value[b]	p=0.0005	

Abbreviations: CI=confidence interval; NR=not reached.

a. Hazard ratio and CI are based on Cox PH model stratified by previous treatment for APMN/S prostate cancer.

b. p-value (2-sided) is based on log-rank test stratified by previous treatment for APMN/S prostate cancer.

Figure 3. Kaplan-Meier Curves of rPFS - TALAPRO-2 (HRRm mAPMR Prostate Cancer)

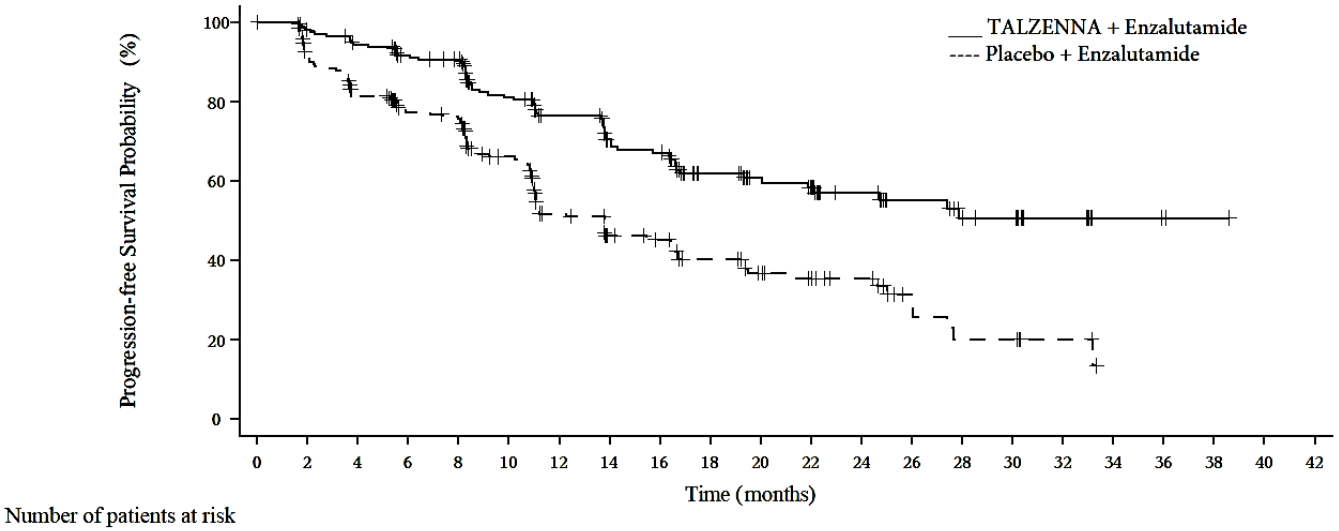
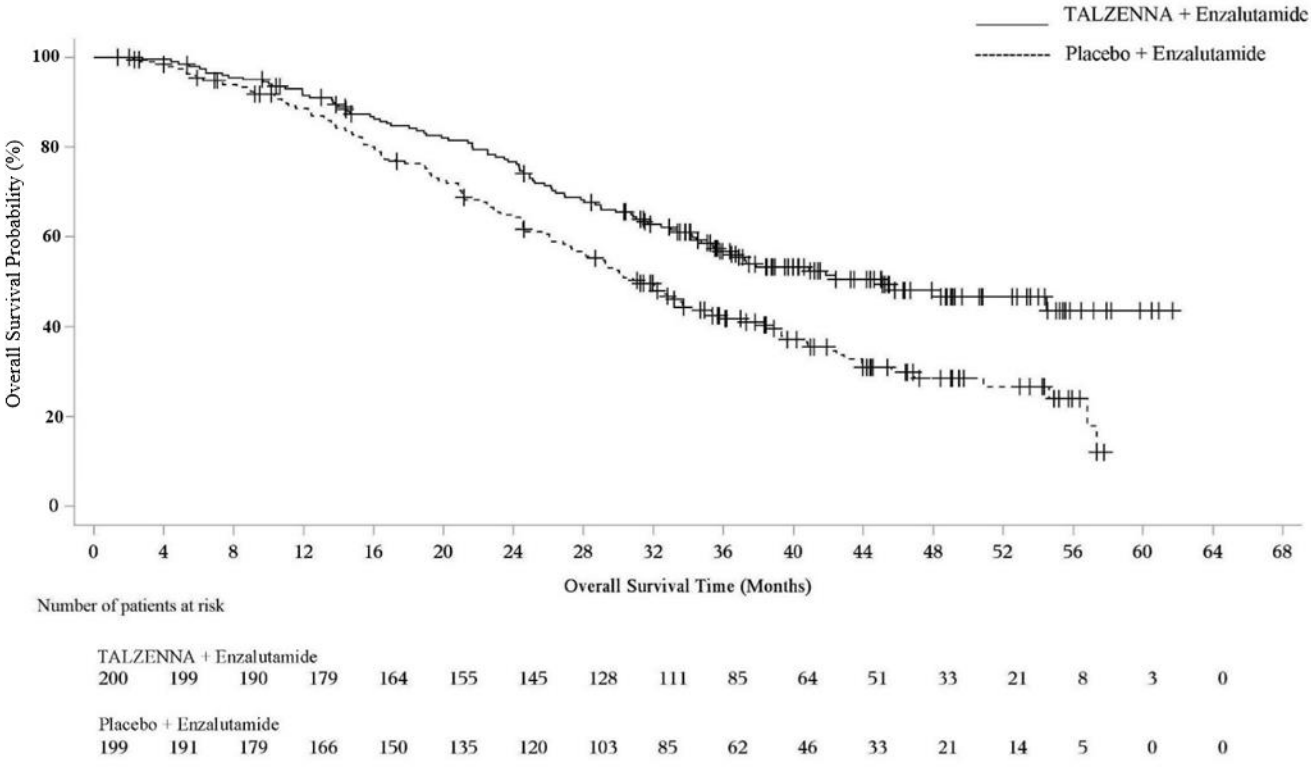


Figure 4. Kaplan-Meier Curves of OS – TALAPRO-2 (HRRm mAPMR Prostate Cancer)



Exploratory subgroup analyses of rPFS and OS for patients with *BRCA*-mutated (*BRCA*m) and non-*BRCA*m HRRm are presented in Table 13.

Table 13. Exploratory rPFS and OS Subgroup Analyses by *BRCA*m Status for TALAPRO-2 (HRRm mAPMR Prostate Cancer)

	***BRCA*m**		**Non-*BRCA*m HRRm***	
	TALZENNA with Enzalutamide N=71	**Placebo with Enzalutamide N=84**	**TALZENNA with Enzalutamide N=129**	**Placebo with Enzalutamide N=115**
Radiographic Progression-Free Survival				
Number of events, n (%)	15 (21)	54 (64)	51 (40)	50 (43)
Median months (95% CI)	NR (NR, NR)	11.0 (8.3, 11.1)	24.7 (16.4, NR)	16.7 (13.8, 27.7)
Hazard ratio (95% CI)	0.20 (0.11, 0.36)		0.74 (0.50, 1.09)	
Overall Survival				
Deaths, n (%)	30 (42)	56 (67)	63 (49)	70 (61)
Median months (95% CI)	NR (35.4, NR)	28.5 (24.5, 34.4)	42.4 (34.2, NR)	32.6 (28.0, 42.2)
Hazard ratio (95% CI)[a]	0.48 (0.31, 0.75)		0.71 (0.51, 1.00)	

Abbreviations: CI=confidence interval; NR=not reached.

* Includes 4 patients who were incorrectly randomized in the HRRm stratum who did not have HRR gene mutations.

[a.] Hazard ratio and CI are based on Cox PH model unstratified by previous treatment for APMN/S prostate cancer.

mAPMN/S Prostate Cancer

TALAPRO-3

The efficacy of TALZENNA in combination with enzalutamide was evaluated in TALAPRO-3 (NCT04821622), a randomized, double-blind, placebo-controlled, trial in which 599 patients with HRRm mAPMN/S prostate cancer were randomized 1:1 to receive enzalutamide 160 mg daily plus either TALZENNA 0.5 mg or placebo daily until unacceptable toxicity or disease progression. Mutation status of HRR genes was determined prospectively using solid tumor tissue or ctDNA-based next generation sequencing tests. Patients were required to have a mutation in at least one of 12 genes involved directly or indirectly in the HRR pathway (*ATM*, *ATR*, *BRCA1*, *BRCA2*, *CDK12*, *CHEK2*, *FANCA*, *MLH1*, *MRE11A*, *NBN*, *PALB2*, or *RAD51C*). All patients received a GnRH analog, or had a prior bilateral orchiectomy. Patients must have initiated androgen deprivation therapy or undergone a bilateral orchiectomy in the mAPMN/S prostate cancer setting up to 3 months prior to randomization with or without an androgen receptor pathway inhibitor (ARPI) but were not allowed to have received prior docetaxel. Randomization was stratified by de novo mAPMN/S vs relapsed mAPMN/S prostate cancer, high vs low volume disease, and *BRCA* vs non-*BRCA* mutational status.

The median age was 70 years (range: 44 to 89); 100% were male; 57% were White, 39% Asian, 2% Black, 1% Other, 2% unknown/not reported; 10% were Hispanic/Latino, 87% were Not Hispanic or Latino, 3% unknown/not reported; and baseline ECOG performance status was 0 (68%) or 1 (32%). Thirteen percent of patients had received a prior ARPI in the mAPMN/S setting. There were 398 (66%) and 438 (73%) patients with high volume disease and de novo mAPMN/S prostate cancer, respectively, and 307 (51%) with both de novo and high-volume disease. The most commonly mutated HRR genes (>5%), including co-occurring mutations, were: *BRCA2* (30%), *ATM* (28%), *CDK12* (19%), *CHEK2* (15%) and *ATR* (7%).

The major efficacy outcome measure was rPFS evaluated according to RECIST, version 1.1 and PCWG3 (bone) criteria, assessed by investigator. An additional efficacy outcome measure was OS.

A statistically significant improvement in rPFS was demonstrated in patients randomized to TALZENNA with enzalutamide compared with those randomized to placebo with enzalutamide. At the time of the rPFS analysis, OS data were immature with 28% deaths in the overall population. Efficacy results are presented in Table 14 and Figure 5.

Table 14. Efficacy Results – TALAPRO-3 (HRRm mAPMN/S Prostate Cancer)

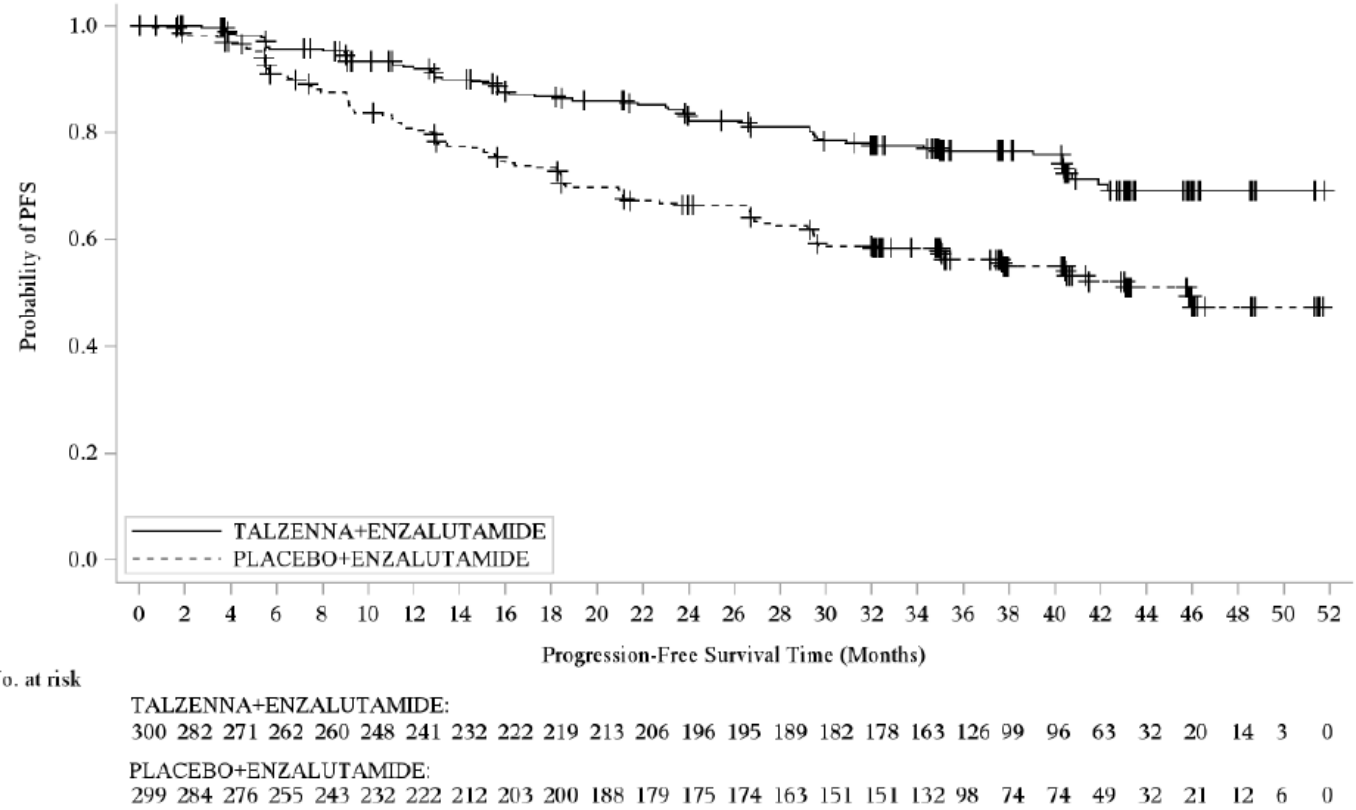
	TALZENNA with Enzalutamide N=300	**Placebo with Enzalutamide N=299**
Radiographic Progression-Free Survival by Investigator		
Number of events, n (%)	67 (22)	126 (42)
Median months (95% CI)	NR (NR, NR)	45.8 (37.7, NR)
Hazard ratio (95% CI)[a]	0.48 (0.36, 0.65)	
p-value[b]	p<0.0001	

Abbreviations: CI=confidence interval; NR=not reached.

a. Hazard ratio is based on a Cox PH model, stratified by de novo vs relapsed mAPMN/S prostate cancer, high vs low volume disease, and *BRCA* vs non-*BRCA* mutational status, with HR < 1 favoring talazoparib + enzalutamide.

b. p-value (2-sided) is based on a log-rank test stratified by de novo vs relapsed mAPMN/S prostate cancer, high vs low volume disease, and *BRCA* vs non-*BRCA* mutational status.

Figure 5. Kaplan-Meier Curves of rPFS - TALAPRO-3 (HRRm mAPMN/S Prostate Cancer)



Exploratory subgroup analyses of rPFS for patients with *BRCA*m and non-*BRCA*m HRRm are presented in Table 15.

Table 15. rPFS Subgroup Analyses by *BRCA*m[a] Status for TALAPRO-3 (HRRm mAPMN/S Prostate Cancer)

	***BRCA*m**		**Non-*BRCA*m HRRm**	
	TALZENNA with Enzalutamide N=104	**Placebo with Enzalutamide N=103**	**TALZENNA with Enzalutamide N=196**	**Placebo with Enzalutamide N=196**
Radiographic Progression-Free Survival by Investigator				
Number of events, n (%)	22 (21)	49 (48)	45 (23)	77 (39)
Median months (95% CI)	NR (NR, NR)	35.1 (18.6, NR)	NR (NR, NR)	NR (40.5, NR)
Hazard ratio (95% CI)[b]	0.37 (0.22, 0.61)		0.57 (0.39, 0.82)	

Abbreviations: CI=confidence interval; IRT=interactive response technology; NR=not reached.

a. *BRCA*m per IRT.

b. Hazard ratio is based on a Cox proportional hazards model with <1 favoring talazoparib + enzalutamide.

16 HOW SUPPLIED/STORAGE AND HANDLING

TALZENNA is supplied in strengths and package configurations as described in Table 16:

Table 16. TALZENNA Capsules

Package Configuration	**Capsule Strength (mg)**	**NDC**	**Print**
Bottles of 30 capsules	0.1	NDC 0069-1031-30	White cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.1” in black).
Bottles of 30 capsules	0.25	NDC 0069-0296-30	Ivory cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.25” in black).
Bottles of 30 capsules	0.35	NDC 0069-1235-30	Ivory cap (printed with “Pfizer” in black) and an ivory body (printed with “TLZ 0.35” in black).
Bottles of 30 capsules	0.5	NDC 0069-1501-30	Light pink cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.5” in black).
Bottles of 30 capsules	0.75	NDC 0069-1751-30	Light orange cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.75” in black).
Bottles of 30 capsules	1	NDC 0069-1195-30	Light red cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 1” in black).

Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

- MDS/AML: Advise patients to contact their healthcare provider if they experience weakness, feeling tired, fever, weight loss, frequent infections, bruising, bleeding easily, breathlessness, blood in urine or stool, and/or laboratory findings of low blood cell counts, or a need for blood transfusions. This may be a sign of hematological toxicity or a more serious uncommon bone marrow problem called MDS or AML, which have been reported in patients who received PARP inhibitors *[see Warnings and Precautions (5.1)]*.

- Myelosuppression: Advise patients that TALZENNA may affect hematopoiesis and can cause anemia, leukopenia/neutropenia, and/or thrombocytopenia *[see Warnings and Precautions (5.2)]*.

- Administration Instructions: Advise patients that TALZENNA can be taken once daily with or without food. Instruct patients that if they miss a dose of TALZENNA, they should take their next normal dose at the usual time. Also advise patients to swallow each capsule whole, and that capsules must not be opened or dissolved *[see Dosage and Administration (2.4)]*.

- Embryo-Fetal Toxicity: Advise females to inform their healthcare provider if they are pregnant or become pregnant. Inform female patients of the risk to a fetus and potential loss of the pregnancy *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment with TALZENNA and for 7 months after the last dose. Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 4 months after receiving the last dose of TALZENNA *[see Warnings and Precautions (5.3), Use in Specific Populations (8.1, 8.3)]*.

- Lactation: Advise patients not to breastfeed while taking TALZENNA and for 1 month after receiving the last dose *[see Use in Specific Populations (8.2)]*.

This product's labeling may have been updated. For the most recent prescribing information, please visit http://www.pfizer.com.

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New York, NY 10001

LAB-1271-10.0

PATIENT INFORMATION
TALZENNA® (Tal-ZEN-ah)
(talazoparib)
capsules

What is the most important information I should know about TALZENNA?

TALZENNA may cause serious side effects, including:

- **Bone marrow problems called Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML).** Some people who have cancer and who have received previous treatment with chemotherapy or certain other medicines for their cancer have developed MDS or AML during or after treatment with TALZENNA. MDS or AML may lead to death. If you develop MDS or AML, your healthcare provider will stop treatment with TALZENNA.
- TALZENNA may affect how your body makes bloods cells. This may lead to low red blood cell counts (anemia), low white blood cell counts, and low platelet counts. Symptoms of low blood cell counts are common during treatment with TALZENNA, but can be a sign of serious problems, including MDS or AML.
  Tell your healthcare provider if you develop any of the following symptoms during treatment with TALZENNA:
  - weakness
  - weight loss
  - fever
  - frequent infections
  - blood in urine or stool
  - shortness of breath
  - feeling very tired
  - bruising or bleeding more easily

  Your healthcare provider will do blood tests to check your blood cell counts:
  - every month during treatment with TALZENNA.
  - weekly if you have low blood cell counts that last a long time.

Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with TALZENNA if you get certain side effects.

See "What are the possible side effects of TALZENNA?" below for other side effects of TALZENNA.

What is TALZENNA?

TALZENNA is a prescription medicine used:

- alone to treat adults with human epidermal growth factor receptor 2 (HER2)-negative breast cancer:
  - who have a certain type of an abnormal inherited *BRCA* gene, **and**
  - whose cancer has spread to other parts of the body (locally advanced or metastatic).
- in combination with a medicine called enzalutamide, to treat adults with prostate cancer who have certain abnormal inherited or acquired genes called homologous recombination repair (HRR) genes, and whose cancer has spread to other parts of the body (metastatic) and:
  - no longer responds to hormone therapy or surgical treatment to lower testosterone, **or**
  - has not yet been treated with, or still responds to, hormone therapy or surgical treatment to lower testosterone.

Your healthcare provider will perform a test to make sure that TALZENNA is right for you.

It is not known if TALZENNA is safe and effective in children.

Before taking TALZENNA, tell your healthcare provider about all of your medical conditions, including if you:

- have kidney problems.
- are pregnant or plan to become pregnant. TALZENNA can harm your unborn baby and may cause loss of pregnancy (miscarriage). You should not become pregnant during treatment with TALZENNA.

  Females who are able to become pregnant:
  - Your healthcare provider may do a pregnancy test before you start treatment with TALZENNA.
  - Use effective birth control (contraception) during treatment with TALZENNA and for 7 months after the last dose of TALZENNA. Talk to your healthcare provider about forms of birth control that may be right for you.
  - Tell your healthcare provider right away if you are pregnant or think you are pregnant during treatment with TALZENNA.

  Males with female partners who are pregnant or are able to become pregnant:
  - Use effective birth control during treatment with TALZENNA and for 4 months after the last dose of TALZENNA.
- are breastfeeding or plan to breastfeed. It is not known if TALZENNA passes into your breast milk. **Do not** breastfeed during treatment with TALZENNA and for 1 month after the last dose of TALZENNA. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking TALZENNA with certain other medicines can affect how TALZENNA works and may cause side effects.

Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take TALZENNA?

- Take TALZENNA exactly as your healthcare provider tells you.
- **Do not** change your dose or stop taking TALZENNA without first talking with your healthcare provider.
- If you are prescribed TALZENNA for breast cancer, take TALZENNA 1 time a day.
- If you are prescribed TALZENNA for prostate cancer:
  - Take TALZENNA with enzalutamide 1 time a day.
  - You should start or continue a gonadotropin-releasing hormone (GnRH) analog therapy during your treatment with TALZENNA and enzalutamide unless you have had a surgery to lower the amount of testosterone in your body (surgical castration).
- Take TALZENNA with or without food.
- Swallow TALZENNA capsules whole. **Do not** open or dissolve TALZENNA capsules.
- If you vomit or miss a dose of TALZENNA, take your next dose at your regular time. **Do not** take an extra dose to make up for a missed dose.

What are the possible side effects of TALZENNA?

TALZENNA may cause serious side effects, including:

- **See "What is the most important information I should know about TALZENNA?"**

The most common side effects of TALZENNA when taken alone include:

- decreased red blood cell counts
- decreased white blood cell counts
- decreased platelet counts
- tiredness or weakness
- increased blood sugar levels
- increased liver function tests
- decreased blood calcium levels
- nausea
- headache
- vomiting
- hair loss
- diarrhea
- decreased appetite

The most common side effects of TALZENNA when taken in combination with enzalutamide include:

- decreased red blood cell counts
- decreased white blood cell counts
- decreased platelet counts
- tiredness or weakness
- decreased protein (albumin) levels in the blood
- decreased blood calcium levels
- back pain
- decreased appetite
- nausea

TALZENNA may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of TALZENNA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store TALZENNA?

- Store TALZENNA at 68°F to 77°F (20°C to 25°C).

Keep TALZENNA and all medicines out of the reach of children.

General information about the safe and effective use of TALZENNA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. **Do not** use TALZENNA for a condition for which it is not prescribed. **Do not** give TALZENNA to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about TALZENNA that is written for health professionals.

What are the ingredients in TALZENNA?

Active ingredient: talazoparib tosylate

Inactive ingredients: silicified microcrystalline cellulose (sMCC). The capsule shells contain hypromellose (HPMC), yellow iron oxide, red iron oxide and titanium dioxide. The printing ink contains shellac, black iron oxide, potassium hydroxide, ammonium hydroxide, and propylene glycol.



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LAB-1272-7.0

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 10/2026