TALZENNA®
talazoparib 1 mg capsules

Talazoparib (TALZENNA) Received a Category 1 Recommendation From the National Comprehensive Cancer Network® (NCCN®)[1]

Category 1 definition: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

NCCN Category 1

Talazoparib (TALZENNA) is a preferred treatment option for recurrent or stage IV breast cancer patients with a germline *BRCA*1/2 mutation*

*Assess for germline *BRCA*1/2 mutations in all patients with recurrent or metastatic breast cancer to identify candidates for PARP inhibitor therapy.

The NCCN Guidelines above fall outside the talazoparib (TALZENNA) US Prescribing Information

TALZENNA INDICATION[2]

TALZENNA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (BRCA)-mutated (*gBRCAm*) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for TALZENNA.

The appropriate use of TALZENNA should be based on risk/benefit assessment by the practitioner for an individual patient.

A Once-Daily Oral Treatment Option[2]

1 DOSE | **1** TIME A DAY WITH OR WITHOUT FOOD

- The recommended dose of TALZENNA is 1 mg taken orally once daily, with or without food[2]
- The 0.25 mg capsule is available for dose reduction[2]

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IMPORTANT SAFETY INFORMATION

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported in patients who received TALZENNA. Overall, MDS/AML has been reported in 2 out of 584 (0.3%) solid tumor patients treated with TALZENNA in clinical studies. The duration of TALZENNA treatment in these two patients prior to developing MDS/AML was 4 months and 24 months, respectively. Both patients had received previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy.

Myelosuppression consisting of anemia, leukopenia/neutropenia, and/or thrombocytopenia have been reported in patients treated with TALZENNA. Grade ≥3 anemia, neutropenia, and thrombocytopenia were reported, respectively, in 39%, 21%, and 15% of patients receiving TALZENNA. Discontinuation due to anemia, neutropenia, and thrombocytopenia occurred, respectively, in 0.7%, 0.3%, and 0.3% of patients.

Monitor complete blood counts for cytopenia at baseline and monthly thereafter. Do not start TALZENNA until patients have adequately recovered from hematological toxicity caused by previous therapy. If hematological toxicity occurs, dose modifications (dosing interruption with or without dose reduction) are recommended. **With respect to MDS/AML**, for prolonged hematological toxicities, interrupt TALZENNA and monitor blood counts weekly until recovery. If the levels have not recovered after 4 weeks, refer the patient to a hematologist for further investigations. If MDS/AML is confirmed, discontinue TALZENNA.

TALZENNA can cause **fetal harm** when administered to pregnant women. Advise women of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose. A pregnancy test is recommended for females of reproductive potential prior to initiating TALZENNA treatment. Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment with TALZENNA and for at least 4 months after receiving the last dose. Based on animal studies, TALZENNA may impair fertility in males of reproductive potential. Advise women not to breastfeed while taking TALZENNA and for at least 1 month after receiving the last dose because of the potential for serious adverse reactions in nursing infants.

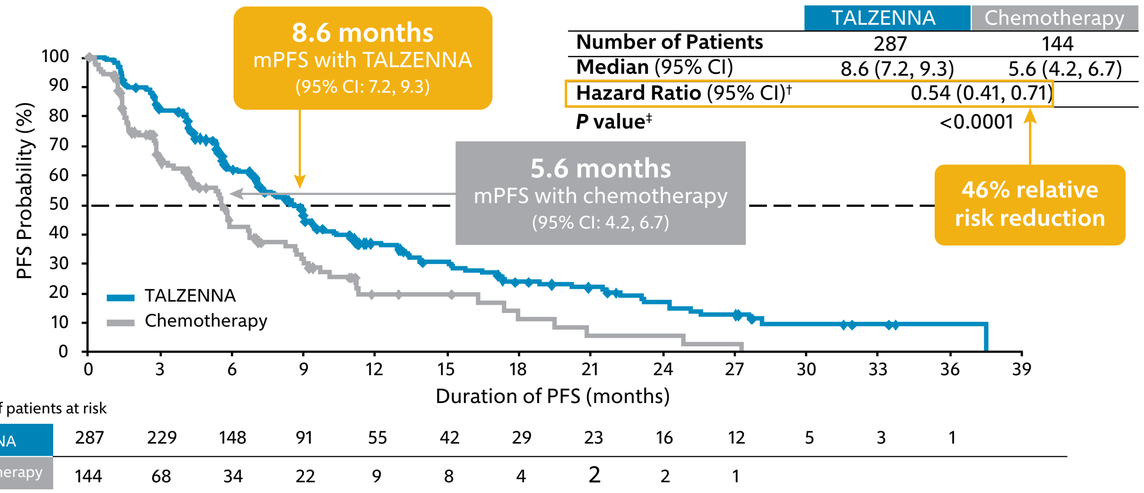
The **most common adverse reactions (≥20%)** of any grade for TALZENNA vs chemotherapy were fatigue (62% vs 50%), anemia (53% vs 18%), nausea (49% vs 47%), neutropenia (35% vs 43%), headache (33% vs 22%), thrombocytopenia (27% vs 7%), vomiting (25% vs 23%), alopecia (25% vs 28%), diarrhea (22% vs 26%), and decreased appetite (21% vs 22%).

Please see Important Safety Information continued on the next page. Click for the full Prescribing Information or visit TalzennaHCP.com.

EMBRACA: a Phase 3, open-label, 2:1 randomized study of TALZENNA vs chemotherapy in patients with gBRCAm HER2-negative (HR+ or triple negative) locally advanced or metastatic breast cancer (N=431; 56% HR+/HER2-, 44% TNBC)[2]*

Primary Endpoint: Statistically significant improvement in progression-free survival (PFS) for TALZENNA compared with chemotherapy[2]

Kaplan-Meier Curves of PFS[2]



	TALZENNA	Chemotherapy
Number of Patients	287	144
Median (95% CI)	8.6 (7.2, 9.3)	5.6 (4.2, 6.7)
Hazard Ratio (95% CI)†	0.54 (0.41, 0.71)	
***P* value**‡	<0.0001	

Number of patients at risk

TALZENNA	287	229	148	91	55	42	29	23	16	12	5	3	1
Chemotherapy	144	68	34	22	9	8	4	2	2	1			

CI=confidence interval; CNS=central nervous system; HR=hormone receptor; mPFS=median PFS; TNBC=triple-negative breast cancer.
*Capecitabine, eribulin, gemcitabine, or vinorelbine.
†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 TNBC status (TNBC vs non-TNBC), and by history of CNS metastasis (yes vs no).
‡*P* values from stratified log-rank test (2-sided).

Adverse Reactions

The most common adverse reactions (≥20%) of any grade for TALZENNA vs chemotherapy were fatigue (62% vs 50%), anemia (53% vs 18%), nausea (49% vs 47%), neutropenia (35% vs 43%), headache (33% vs 22%), thrombocytopenia (27% vs 7%), vomiting (25% vs 23%), alopecia (25% vs 28%), diarrhea (22% vs 26%), and decreased appetite (21% vs 22%).[2]

Secondary Endpoint: Confirmed ORR[2§‖]

50.2% of patients — **TALZENNA** n=219 (95% CI: 43.4, 57.0)

18.4% of patients — **Chemotherapy** n=114 (95% CI: 11.8, 26.8)

Secondary Endpoint: OS[3]

- Final OS analysis did not reach statistical significance
- Median OS: 19.3 months (95% CI: 16.6, 22.5) with TALZENNA vs 19.5 months (95% CI: 17.4, 22.4) with chemotherapy (HR=0.85 [95% CI: 0.67, 1.07]; *P*=0.17)

Exploratory Endpoint: DOR[2‖¶]

- Median DOR was 6.4 months (95% CI: 5.4, 9.5) with TALZENNA vs 3.9 months (95% CI: 3.0, 7.6) with chemotherapy

DOR=duration of response; ORR=objective response rate; OS=overall survival.
§Conducted in the intent-to-treat (ITT) population, with measurable disease at baseline.
‖Response rate based on confirmed responses. Confirmed response: best overall response of partial response or complete response, confirmed by a subsequent tumor assessment (at least 4 weeks later) by investigator assessment.
¶Analyzed in the ITT patients who experienced an objective response as assessed by the investigator.

IMPORTANT SAFETY INFORMATION (Continued from the first page)

The **most frequently reported Grade ≥3 adverse reactions (≥10%)** for TALZENNA vs chemotherapy were anemia (39% vs 5%), neutropenia (21% vs 35%), and thrombocytopenia (15% vs 2%).

The **most common lab abnormalities (≥25%)** for TALZENNA vs chemotherapy were decreases in hemoglobin (90% vs 77%), leukocytes (84% vs 73%), lymphocytes (76% vs 53%), neutrophils (68% vs 70%), platelets (55% vs 29%), and calcium (28% vs 16%) and increases in glucose (54% vs 51%), aspartate aminotransferase (37% vs 48%), alkaline phosphatase (36% vs 34%), and alanine aminotransferase (33% vs 37%).

Coadministration with P-gp inhibitors or **BCRP inhibitors** may increase TALZENNA exposure. If coadministering with the P-gp inhibitors amiodarone, carvedilol, clarithromycin, itraconazole, or verapamil is unavoidable, reduce the TALZENNA dose to 0.75 mg once daily. When the P-gp inhibitor is discontinued, increase the TALZENNA dose (after 3–5 half-lives of the P-gp inhibitor) to the dose used prior to the initiation of the P-gp inhibitor. When coadministering TALZENNA with other known P-gp inhibitors or BCRP inhibitors, monitor patients for potential increased adverse reactions.

For patients with moderate **renal impairment**, the recommended dose of TALZENNA is 0.75 mg once daily. For patients with severe renal impairment, the recommended dose of TALZENNA is 0.5 mg once daily. No dose adjustment is required for patients with mild renal impairment. TALZENNA has not been studied in patients requiring hemodialysis.

TALZENNA has not been studied in patients with moderate or severe **hepatic impairment**. No dose adjustment is required for patients with mild hepatic impairment.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.6.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed September 10, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** TALZENNA [prescribing information]. New York, NY: Pfizer Inc.; 2020. **3.** Litton JK, Hurvitz SA, Mina LA, et al. Talazoparib versus chemotherapy in patients with germline BRCA1/2-mutated HER2-negative advanced breast cancer: final overall survival results from the EMBRACA trial, *Ann Oncol* (2020). doi: 10.1016/j.annonc.2020.08.2098.

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Pfizer Oncology

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