TALZENNA

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TALZENNA
(talazoparib)

1. NAME OF THE MEDICINAL PRODUCT

TALZENNA 0.25 mg hard capsules
TALZENNA 1 mg hard capsules

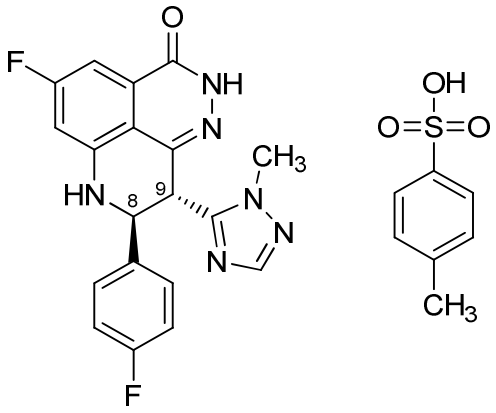
2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TALZENNA 0.25 mg hard capsules
Each capsule contains 0.363 mg talazoparib tosylate equivalent to 0.25 mg talazoparib free base.

TALZENNA 1 mg hard capsules
Each capsule contains 1.453 mg talazoparib tosylate equivalent to 1 mg talazoparib free base.

For the full list of excipients, see Section 6.1.

Structure:



3. PHARMACEUTICAL FORM

Hard capsule.

TALZENNA 0.25 mg hard capsules
Opaque, size #4 hard hypromellose (HPMC) capsule with an ivory cap (printed with "Pfizer" in black) and a white body (printed with "TLZ 0.25" in black).

TALZENNA 1 mg hard capsules
Opaque, size #4 hard hypromellose (HPMC) capsule with a light red cap (printed with "Pfizer" in black) and a white body (printed with "TLZ 1" in black).

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

TALZENNA is indicated for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA)-mutated human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments.

4.2. Posology and method of administration

Treatment with TALZENNA should be initiated and supervised by a physician experienced in the use of anticancer medicinal products.

Detection of mutations in hereditary breast cancer-related BRCA1 and BRCA2 genes should be determined by an experienced laboratory using a validated test method (see Section 5.1).

Posology
The recommended dose of TALZENNA is 1 mg capsule taken orally once daily. Patients should be treated until disease progression or unacceptable toxicity occurs.

Missing dose
If the patient vomits or misses a dose, an additional dose should not be taken. The next prescribed dose should be taken at the usual time.

Dose modifications
To manage adverse reactions, consider interruption of treatment or dose reduction based on severity and clinical presentation. Recommended dose reductions are indicated in Table 1.

Table 1. Dose Modification for Toxicities

	Dose Level
Recommended starting dose	1 mg (one 1 mg capsule) once daily
First dose reduction	0.75 mg (three 0.25 mg capsules) once daily
Second dose reduction	0.5 mg (two 0.25 mg capsules) once daily
Third dose reduction	0.25 mg (one 0.25 mg capsule) once daily

Complete blood count should be obtained prior to starting TALZENNA therapy and monitored monthly and as clinically indicated (see Table 2 and Section 4.4).

Table 2. Dose Modification and Management

	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-haematologic adverse reaction Grade 3 or Grade 4	≤Grade 1	Consider resuming TALZENNA at a reduced dose or discontinue

Concomitant treatment with inhibitors of P-glycoprotein (P-gp)
Strong inhibitors of P-gp may lead to increased talazoparib exposure. Concomitant use of strong P-gp inhibitors during treatment with talazoparib should be avoided. Coadministration should only be considered after careful evaluation of the potential benefits and risks. If coadministration with a strong P-gp inhibitor is unavoidable, the TALZENNA dose should be reduced to the next lower dose. When the strong P-gp inhibitor is discontinued, the TALZENNA dose should be increased (after 3 to 5 half-lives of the P-gp inhibitor) to the dose used prior to the initiation of the strong P-gp inhibitor (see Section 4.5).

Concomitant treatment with inhibitors of Breast Cancer Resistance Protein (BCRP)
The effect of coadministration of BCRP inhibitors with TALZENNA has not been studied. Therefore, concomitant use of strong BCRP inhibitors during treatment with talazoparib should be avoided (see Section 4.5).

Special populations

Hepatic impairment
No dose adjustment is required for patients with mild hepatic impairment (total bilirubin ≤1 × upper limit of normal [ULN] and aspartate aminotransferase (AST) >ULN, or total bilirubin >1.0 to 1.5 × ULN and any AST), moderate hepatic impairment (total bilirubin >1.5 to 3.0 × ULN and any AST), or severe hepatic impairment (total bilirubin >3.0 × ULN and any AST) (see Section 5.2).

Renal impairment
No dose adjustment is required for patients with mild renal impairment (60 mL/min ≤ creatinine clearance [CrCL] < 90 mL/min). For patients with moderate renal impairment (30 mL/min ≤ CrCL < 60 mL/min), the recommended dose of TALZENNA is 0.75 mg once daily. For patients with severe renal impairment (15 mL/min ≤ CrCL < 30 mL/min), the recommended dose of TALZENNA is 0.5 mg once daily. TALZENNA has not been studied in patients requiring hemodialysis (see Section 5.2).

Elderly population
No dose adjustment is necessary in elderly (≥65 years of age) patients (see Section 5.2).

Pediatric population
The safety and efficacy of TALZENNA in children and adolescents <18 years of age have not been established.

4.3. Contraindications

None.

4.4. Special warnings and precautions for use

Myelosuppression
Myelosuppression consisting of anemia, leukopenia/neutropenia, and/or thrombocytopenia, have been reported in patients treated with talazoparib (see Section 4.8). Do not start talazoparib until patients have recovered from hematological toxicity caused by previous therapy (≤Grade 1).

Precautions should be taken to routinely monitor hematology parameters and signs and symptoms associated with anemia, leukopenia/neutropenia, and/or thrombocytopenia in patients receiving talazoparib. If such events occur, dose modifications (reduction or interruption) are recommended (see Section 4.2). Supportive care with or without blood and/or platelet transfusions and/or administration of colony stimulating factors may be used as appropriate.

Myelodysplastic syndrome/Acute Myeloid Leukemia
Myelodysplastic syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported in patients who received poly (adenosine diphosphate [ADP] ribose) polymerase (PARP) inhibitors. Overall, MDS/AML has been reported in <1% of solid tumor patients treated with talazoparib in clinical studies. Potential contributing factors for the development of MDS/AML include previous platinum-containing chemotherapy, other DNA damaging agents or radiotherapy. Complete blood counts should be obtained at baseline and monitored monthly for signs of hematologic toxicity during treatment. If MDS/AML is confirmed, talazoparib should be discontinued.

Embryo-fetal toxicity
Studies in animals have shown embryo-fetal toxicity and talazoparib was clastogenic in *in vitro* and in *in vivo* assays (see Section 5.3). Talazoparib should not be given to pregnant patients or those who plan to become pregnant during treatment. Women of childbearing potential should be advised to avoid becoming pregnant while receiving TALZENNA. TALZENNA may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus (see Section 4.6).

A highly effective method of contraception is required for female patients during treatment with TALZENNA, and for at least 7 months after completing therapy. Since the use of hormonal contraception is not recommended in patients with breast cancer, two non-hormonal and complementary contraception methods should be used. Advise male patients with female partners of reproductive potential and pregnant partners to use effective contraception (even after vasectomy), during treatment with TALZENNA and for at least 4 months after the final dose.

4.5. Interaction with other medicinal products and other forms of interaction

Talazoparib is a substrate for drug transporters P-gp and BCRP and mainly eliminated by renal clearance as unchanged compound.

Agents that may affect talazoparib plasma concentrations

Effect of P-gp inhibitors
Data from a drug-drug interaction study in patients with advanced solid tumors indicated that coadministration of multiple daily doses of a P-gp inhibitor, itraconazole 100 mg twice daily with a single 0.5 mg talazoparib dose increased talazoparib total exposure (AUC_{inf}) and peak concentration (C_{max}) by approximately 56% and 40%, respectively, relative to a single 0.5 mg talazoparib dose administered alone. Population pharmacokinetic (PK) analysis has shown that concomitant use of strong P-gp inhibitors with TALZENNA increased talazoparib exposure by 44.7%, relative to TALZENNA given alone. If patients must be coadministered a strong P-gp inhibitor, those that result in ≥2-fold increase in the exposure of an *in vivo* probe P-gp substrate, (including but not limited to amiodarone, carvedilol, clarithromycin, cobicistat, darunavir, dronedarone, erythromycin, indinavir, itraconazole, ketoconazole, lapatinib, lopinavir, propafenone, quinidine, ranolazine, ritonavir, saquinavir, telaprevir, tipranavir, valspodar, and verapamil), the TALZENNA dose should be reduced to the next lower dose (see Section 4.2).

Population PK analysis has shown that coadministration with relatively weak P-gp inhibitors (including azithromycin, atorvastatin, diltiazem, felodipine, fluvoxamine, and quercetin) in clinical studies had no significant effect on talazoparib exposure.

Effect of P-gp inducers
Data from a drug-drug interaction study in patients with advanced solid tumors indicated that coadministration of a P-gp inducer (rifampin 600 mg once daily) with a single 1 mg talazoparib dose increased talazoparib C_{max} by 37% with no effect on talazoparib exposure. This is probably the net effect of both P-gp induction and inhibition by rifampin under the tested conditions in the drug-drug interaction study. No talazoparib dose adjustments are required when co-administered with rifampin. However, the effect of other P-gp inducers on talazoparib exposure has not been studied. Other P-gp inducers (including but not limited to carbamazepine, phenytoin, and St. John's wort) may decrease talazoparib exposure.

Effect of BCRP inhibitors
The effect of BCRP inhibitors on PK of talazoparib has not been studied. Concomitant use of strong BCRP inhibitors (including but not limited to curcumin, cyclosporine, and elacridar [GF120918]) should be avoided (see Section 4.2).

Effect of acid-reducing agents
Population PK analysis indicates that coadministration of acid-reducing agents including proton pump inhibitors (PPI), histamine receptor 2 antagonists (H_2RA), or other acid-reducing agents had no significant impact on the absorption of talazoparib.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/contraception in males and females
Women of childbearing potential should not become pregnant while receiving TALZENNA and should not be pregnant at the beginning of treatment. A pregnancy test should be performed on all women of childbearing potential prior to treatment (see Section 4.4).

A highly effective method of contraception is required for female patients during treatment with TALZENNA, and for at least 7 months after completing therapy. Since the use of hormonal contraception is not recommended in patients with breast cancer, two non-hormonal and complementary contraception methods should be used. Advise male patients with female partners of reproductive potential and pregnant partners to use effective contraception (even after vasectomy) during treatment with TALZENNA and for at least 4 months after the final dose (see Section 4.4).

Pregnancy
There are no data from the use of TALZENNA in pregnant women. Studies in animals have shown embryo-fetal toxicity (see Section 5.3). TALZENNA may cause fetal harm when administered to a pregnant woman. TALZENNA is not recommended during pregnancy or for women of childbearing potential not using contraception (see Section 4.4).

Breastfeeding
It is unknown whether TALZENNA is excreted in human breast milk. A risk to newborns/infants cannot be excluded and therefore breastfeeding is not recommended during treatment with TALZENNA and for at least 1 month after the final dose.

Fertility
There is no information on fertility in patients. Based on non-clinical findings in testes and ovary, male and female fertility may be compromised by treatment with TALZENNA (see Section 5.3).

4.7 Effects on ability to drive and use machines

No studies have been conducted on the effects of talazoparib on the ability to drive or operate machinery. However, patients experiencing fatigue/asthenia or dizziness while taking talazoparib should exercise caution when driving or operating machinery.

4.8 Undesirable effects

The overall safety profile of TALZENNA is based on pooled data from 494 patients who received talazoparib at 1 mg daily in clinical studies for solid tumors, including 286 patients from a randomized Phase 3 study with germline BRCA-mutated, HER2-negative locally advanced or metastatic breast cancer and 83 patients from a nonrandomized Phase 2 study in patients with germline BRCA-mutated locally advanced or metastatic breast cancer.

The most common (≥25%) adverse reactions in patients receiving talazoparib in these clinical studies were fatigue (57.1%), anemia (49.6%), nausea (44.3%), neutropenia (30.2%), thrombocytopenia (29.6%), and headache (26.5%). The most common

(≥10%) Grade ≥3 adverse reactions of talazoparib were anemia (35.2%), neutropenia (17.4%), and thrombocytopenia (16.8%).

Dose modifications (dose reductions or dose interruptions) due to any adverse reaction occurred in 62.3% of patients receiving TALZENNA. The most common adverse reactions leading to dose modifications were anemia (33.0%), neutropenia (15.8%), and thrombocytopenia (13.4%).

Permanent discontinuation due to an adverse reaction occurred in 3.6% of patients receiving TALZENNA. The median duration of exposure was 5.4 months (range 0.03-61.1).

Table 3 summarizes adverse reactions based on pooled dataset listed by system organ class, and frequency category. Frequency categories defined as: very common (≥1/10) and common (≥1/100 to <1/10). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 3. Adverse Reactions Based on Pooled Dataset from 5 Studies (N=494)

System Organ Class **Frequency** **Preferred Term**	**All Grades*** **n (%)**	**Grade 3** **n (%)**	**Grade 4** **n (%)**
Blood and lymphatic system disorders			
Very common			
Thrombocytopenia[a]	146 (29.6)	63 (12.8)	20 (4.0)
Anemia[b]	245 (49.6)	172 (34.8)	2 (0.4)
Neutropenia[c]	149 (30.2)	77 (15.6)	9 (1.8)
Leukopenia[d]	77 (15.6)	24 (4.9)	1 (0.2)
Common			
Lymphopenia[e]	30 (6.1)	13 (2.6)	0 (0.0)
Metabolism and nutrition disorders			
Very common			
Decreased appetite	100 (20.2)	2 (0.4)	0 (0.0)
Nervous system disorders			
Very common			
Dizziness	69 (14.0)	1 (0.2)	N/A
Headache	131 (26.5)	5 (1.0)	N/A
Common			
Dysgeusia	42 (8.5)	N/A	N/A
Gastrointestinal disorders			
Very common			
Vomiting	110 (22.3)	7 (1.4)	0 (0.0)
Diarrhoea	112 (22.7)	3 (0.6)	0 (0.0)
Nausea	219 (44.3)	4 (0.8)	N/A
Abdominal pain[f]	105 (21.3)	8 (1.6)	N/A
Common			
Stomatitis	32 (6.5)	0 (0.0)	0 (0.0)
Dyspepsia	41 (8.3)	0 (0.0)	N/A

Skin and subcutaneous tissue disorders *Very common* Alopecia[g]	110 (22.3)	N/A	N/A
General disorders and administration site conditions *Very common* Fatigue[h]	282 (57.1)	17 (3.4)	1 (0.2)

Abbreviations: n=number of patients; N/A=not applicable.
* There were no Grade 5 adverse drug reactions.
a. Includes preferred terms of thrombocytopenia and platelet count decreased.
b. Includes preferred terms of anemia, hematocrit decreased and hemoglobin decreased.
c. Includes preferred terms of neutropenia, and neutrophil count decreased.
d. Includes preferred terms of leukopenia and white blood cell count decreased.
e. Includes preferred terms of lymphocyte count decreased and lymphopenia.
f. Includes preferred terms of abdominal pain, abdominal pain upper, abdominal discomfort and abdominal pain lower.
g. For talazoparib Grade 1 is 21% and Grade 2 is 2%.
h. Includes preferred terms of fatigue and asthenia.

Description of selected adverse reactions

Myelosuppression
Myelosuppression-related adverse reactions of anemia, neutropenia, and thrombocytopenia were very commonly reported in patients treated with talazoparib 1 mg/day. Grade 3 and Grade 4 myelosuppression-related events were reported for anemia 34.8% and 0.4%, neutropenia 15.6% and 1.8%, and thrombocytopenia 12.8% and 4.0%. No deaths were reported due to myelosuppression-related adverse reactions. Myelosuppression-related adverse events associated with dose modifications were reported for up to approximately 30% of patients in the talazoparib 1 mg/day population and those associated with permanent study drug discontinuation were reported for less than 1% of patients.

4.9 Overdose

There is no specific treatment in the event of talazoparib overdose, and symptoms of overdose are not established. In the event of overdose, treatment with talazoparib should be stopped, and physicians should consider gastric decontamination, follow general supportive measures and treat symptomatically.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Mechanism of action and pharmacodynamics effects
TALZENNA is a potent inhibitor of PARP enzymes, PARP1, and PARP2. PARP enzymes are involved in cellular DNA damage response signaling pathways such as DNA repair, gene transcription, cell cycle regulation, and cell death. PARP inhibitors (PARPi) exert cytotoxic effects on cancer cells by 2 mechanisms, inhibition of PARP catalytic activity and by PARP trapping, whereby PARP protein bound to a PARPi does not readily dissociate from a DNA lesion, thus preventing DNA repair, replication, and transcription and ultimately leading to apoptosis and/or cell death.

Treatment of cancer cell lines that are harboring defects in DNA repair genes with talazoparib single agent leads to increased γH2AX level, which is a marker of double stranded DNA breaks, resulting in decreased cell proliferation and increased apoptosis. The potent cytotoxicity observed with talazoparib against multiple tumor cell lines harboring mutations in the DNA damage response (DDR) pathways, can be attributed to its inhibition of PARP catalytic activity and robust PARP trapping. Talazoparib anti-tumor activity was also observed in the patient-derived xenograft (PDX) BRCA-mutant breast cancer model that was previously treated with a platinum-based regimen. In the PDX model talazoparib decreased tumor growth and increased γH2AX level and apoptosis in the tumors.

Detection of BRCA mutation
Patients are eligible for TALZENNA treatment if they have a confirmed deleterious or suspected deleterious germline BRCA mutation (i.e., a mutation that disrupts normal gene function; detected using an appropriately validated test).

Clinical efficacy and safety

Randomized Phase 3 study EMBRACA
EMBRACA was an open-label, randomized, parallel, 2-arm multicenter study of TALZENNA versus chemotherapy (capecitabine, eribulin, gemcitabine, vinorelbine) in patients with germline BRCA-mutated HER2-negative locally advanced or metastatic breast cancer who 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 setting. 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.

A total of 431 patients were randomized 2:1 to receive TALZENNA 1 mg capsules once daily or chemotherapy at standard doses until progression or unacceptable toxicity. Of the 431 patients randomized onto EMBRACA, 287 were randomized to the TALZENNA arm and 144 to the chemotherapy arm. Randomization was stratified by prior use of chemotherapy for metastatic disease (0 versus 1, 2, or 3), by triple-negative disease status (triple-negative breast cancer [TNBC] versus non-TNBC), and history of central nervous system metastasis (yes versus no). The majority of patients 408/431 (95%) were selected using the BRAC*Analysis* test and BRCA mutation status (breast cancer susceptibility gene 1 [BRCA1] positive or breast cancer susceptibility gene 2 [BRCA2] positive) was similar across both treatment arms.

Patient demographic and baseline characteristics were generally similar between the study treatment arms. The median age of patients treated with TALZENNA was 45 years (range 27 to 84) and 50 years (range 24 to 88) among patients treated with chemotherapy. Of note, 63% versus 47% of patients were <50 years of age in the talazoparib and chemotherapy arms, respectively, 27% versus 47% were 50 to <65 years of age, and 9% versus 7% were ≥65 years of age. Among all randomized patients, 1% versus 2% were males, 66.9% versus 75.0% were White; 10.8% versus 11.1% were Asian, and 4.2% versus 0.7% were Black or African American in the

talazoparib and chemotherapy arms, respectively. Almost all patients (97.7%) in both arms had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Approximately 55.9% of patients had hormone receptor-positive (either estrogen receptor [ER]-positive or progesterone receptor [PR]-positive) disease; 44.1% of patients had triple-negative disease and the proportions were balanced across treatment arms. The median time from initial diagnosis of breast cancer to diagnosis of advanced breast cancer was 1.9 years (range 0 to 22) on the talazoparib arm and 2.7 years (range 0 to 24) on the chemotherapy arm. The reported disease-free interval (DFI) was <12 months in 37.6% of patients on the talazoparib arm and in 29.2% of patients on the chemotherapy arms. Among all patients enrolled, the median number of prior cytotoxic regimens for advanced breast cancer was 1 where 38.3% of patients received no prior regimens for advanced or metastatic disease, 37.4% received 1, 19.7% received 2, and 4.6% received ≥3 prior regimens, respectively. Sixteen percent of patients in the talazoparib arm and 20.8% of patients in the chemotherapy arm had received prior platinum treatment. 54.7% of patients had hormone receptor-positive disease in the talazoparib arm, of which 90.4% took a prior hormonal therapy, while 9.6% did not take any prior endocrine therapy. In the chemotherapy arm, 58.3% of patients had hormone receptor-positive disease, of which 83.3% took a prior hormonal therapy, while 16.7% did not take any prior endocrine therapy.

The primary efficacy endpoint 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). The secondary objectives were objective response rate (ORR), overall survival (OS), safety, and PK. Exploratory objectives included duration of response (DOR), Clinical Benefit Rate at 24 weeks (CBR24), quality of life (QoL) assessed using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire – Core 30 (QLQ-C30)/EORTC Quality of Life Questionnaire – Breast Cancer Module (QLQ-BR23) and biomarker research.

The study met its primary objective of demonstrating a statistically significant improvement in PFS for TALZENNA compared with chemotherapy (hazard ratio [HR] 0.54; 95% confidence interval [CI]: 0.41, 0.71; p-value <0.0001). A sensitivity analysis of investigator-assessed PFS was consistent with the BICR-assessed PFS results. Efficacy data for EMBRACA are summarized in Table 4 and the Kaplan-Meier curves for PFS and OS are shown in Figures 1 and 3. Consistent results were observed across pre-specified patient subgroups (Figure 2).

Table 4. Summary of Efficacy Results – EMBRACA Study*

	Talazoparib	Chemotherapy
PFS by BICR	N=287	N=144
Events, number (%)	186 (65%)	83 (58%)
Median (95% CI), months	8.6 (7.2, 9.3)	5.6 (4.2, 6.7)
Hazard ratio (95% CI)	0.54 (0.41, 0.71)	
2-sided p-value[a]	p<0.0001	
OS (final analysis)[b]	N=287	N=144
Events, number (%)	216 (75.3%)	108 (75.0%)
Median (95% CI), months	19.3 (16.6, 22.5)	19.5 (17.4, 22.4)
Hazard ratio** (95% CI)	0.85 (0.67, 1.07)[b]	
2-sided p-value[a]	p=0.1693	
24-Month Survival Probability, % (95% CI)	42 (36, 47)	38 (30, 47)
36-Month Survival Probability, % (95% CI)	27 (22, 33)	21 (14, 29)
Objective Response by Investigator[c,d]	N=219	N=114
ORR, % (95% CI)	62.6 (55.8, 69.0)	27.2 (19.3, 36.3)
Odds ratio (95% CI)	4.99 (2.9, 8.8)	
2-sided p-value[e]	p<0.0001	
Duration of Response by Investigator[c]	N=137	N=31
Median (IQR), months	5.4 (2.8, 11.2)	3.1 (2.4, 6.7)

Abbreviations: BICR=blinded independent central review; CI=confidence interval; CMH=Cochran-Mantel-Haenszel; CR=complete response; IQR=interquartile range; ITT=intent-to-treat; ORR=objective response rate; OS=overall survival; PARP=poly (adenosine diphosphate [ADP] ribose) polymerase; PFS=progression-free survival; PR=partial response; RECIST 1.1=Response Evaluation Criteria in Solid Tumors version 1.1.

* PFS, ORR, and Duration of Response are based on the data cutoff date of 15 September 2017. OS is based on the data cutoff date 30 September 2019, and is based on a median follow up of 44.9 months (95% CI: 37.9, 47.0) in the talazoparib arm and 36.8 months (95% CI: 34.3, 43.0) in the chemotherapy arm.

** Hazard ratio was based on stratified Cox regression model with treatment as the only covariate (stratification factors: number of prior cytotoxic chemotherapy regimens, triple-negative status, history of central nervous system metastasis) and was relative to overall chemotherapy with <1 favoring talazoparib.

a. Stratified Log-rank test.

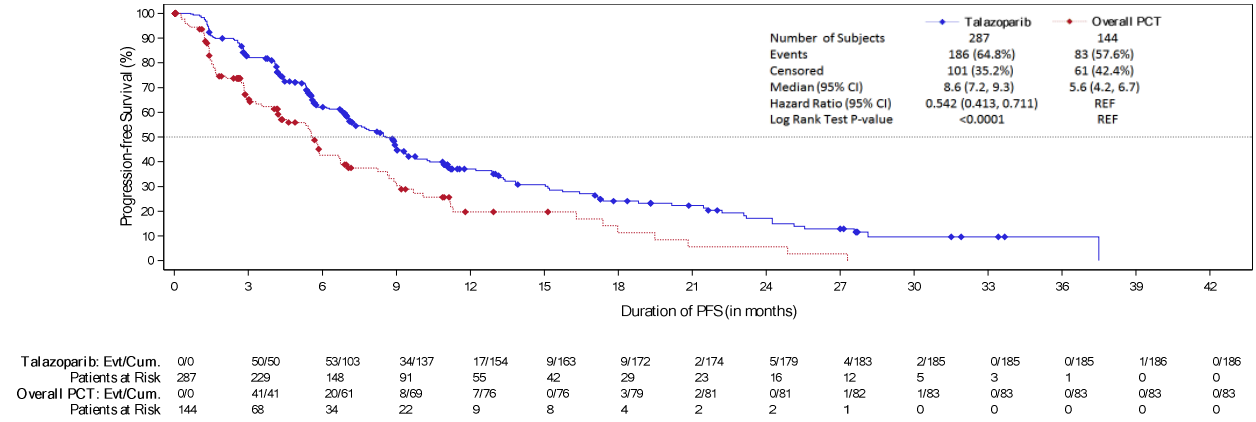
b. At the time of the final OS analysis, 46.3% versus 41.7% of patients randomized in the talazoparib and chemotherapy arms, respectively, received subsequently a platinum therapy, and 4.5% versus 32.6% received subsequently a PARP inhibitor treatment.

c. Conducted in ITT with measurable disease population who had an objective response. The complete response rate was 5.5% for talazoparib compared to 0% for the chemotherapy arm.

d. Per RECIST 1.1, confirmation of CR/PR was not required.

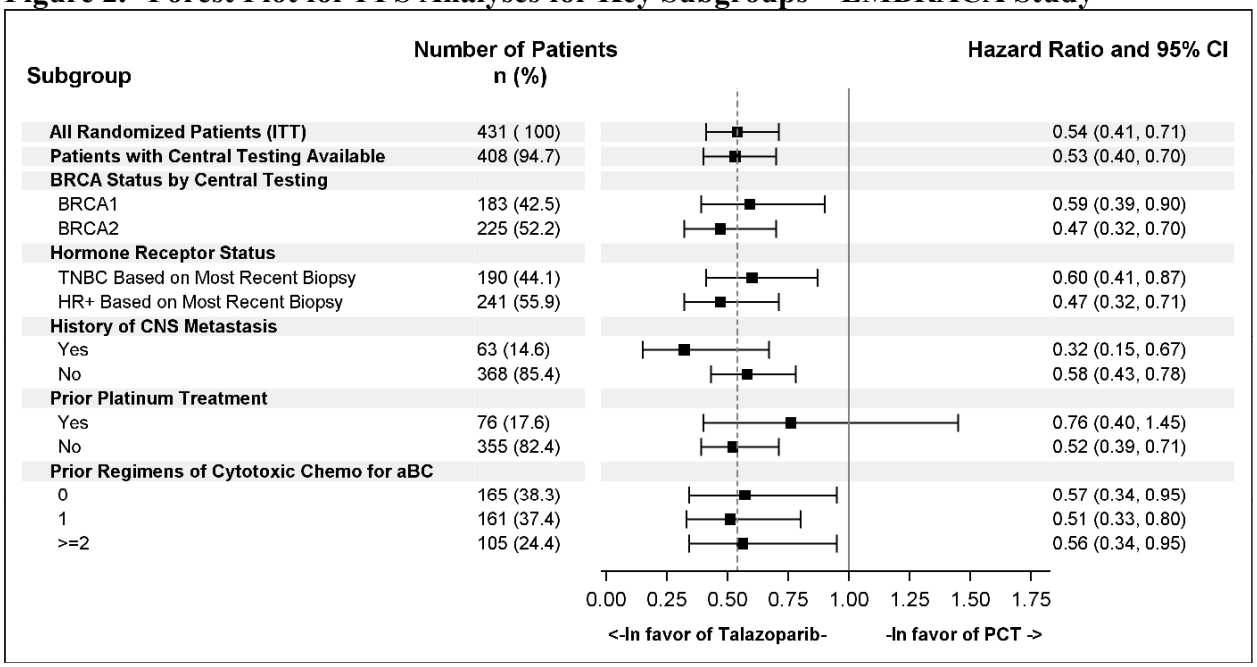
e. Stratified CMH test.

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



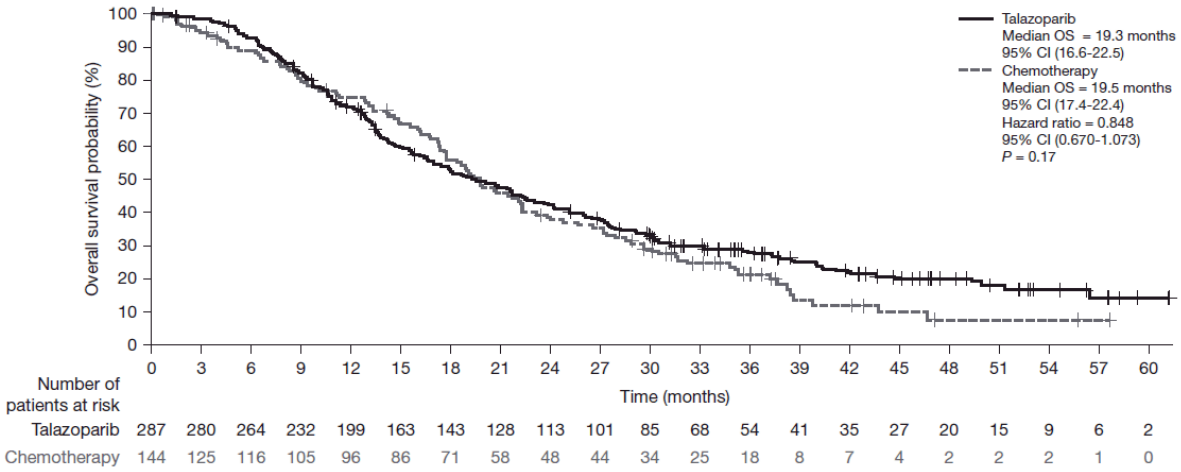
Abbreviations: CI=confidence interval; Cum=cumulative; Evt=event; PFS=progression-free survival; PCT=physician's choice treatment (chemotherapy); REF=reference treatment group.
Primary analysis p-value was based on a stratified log-rank test.

Figure 2. Forest Plot for PFS Analyses for Key Subgroups – EMBRACA Study



Abbreviations: aBC=advanced breast cancer; BRCA=breast cancer susceptibility gene; CI=confidence interval; CNS=central nervous system; HR+ =hormone receptor-positive; ITT=intent-to-treat; PCT=physician's choice treatment (chemotherapy); PFS=progression-free survival; TLZ=talazoparib; TNBC=triple-negative breast cancer.

Figure 3 Kaplan-Meier Curves of OS – EMBRACA Study



Abbreviations: CI=confidence interval; PCT=physician's choice treatment (chemotherapy); OS=overall survival.
Primary analysis' p-value was based on a stratified log-rank test.

Patient-reported symptoms were assessed using the EORTC QLQ-C30 and its EORTC QLQ-BR23. A total of 262 patients in the talazoparib arm and 114 patients in the chemotherapy arm completed the questionnaire at baseline and at least 1 postbaseline visit.

A significantly greater overall improvement from baseline in global health status (GHS)/QoL was observed in the talazoparib arm (3.0 [95% CI: 1.2, 4.8]) compared to the chemotherapy arm (-5.4 [95% CI: -8.8, -2.0]) (p<0.0001). A significantly greater delay in time to clinically meaningful (≥10 point decrease from baseline) definitive deterioration in GHS/QoL was observed in the talazoparib arm compared with chemotherapy [(HR: 0.38 [95% CI: 0.26, 0.55]; p<0.0001), median 24.3 months versus 6.3 months].

A significantly greater overall improvement from baseline in breast symptoms was observed in the talazoparib arm (-5.1 [95% CI: -6.7, -3.5]) compared to the chemotherapy arm (-0.1 [95% CI: -2.9, 2.6]) (p=0.002). A significantly greater delay in time to clinically meaningful (≥10 point increase from baseline) definitive deterioration in breast symptoms was observed in the talazoparib arm compared with chemotherapy (HR of 0.39 [95% CI: 0.20, 0.78]; p=0.005, median times not reached [NR]).

A significantly greater overall improvement from baseline was observed in the talazoparib arm compared to the chemotherapy arm in role functioning [12.4, 95% CI: (7.1, 17.7) (p<0.0001)] and the following symptoms: fatigue [-12.3, 95% CI: (-17.2, -7.5) (p<0.0001)], pain [-13.3, 95% CI: (-18.5, -8.1) (p<0.0001)] and appetite loss [-11.7, 95% CI: (-17.6, -5.7) (p=0.0001)].

A significantly greater delay in time to clinically meaningful deterioration in the following symptoms was observed in the talazoparib arm compared to the chemotherapy arm for fatigue, [(HR: 0.40 [95% CI: 0.28, 0.56]; p<0.0001), median 17.1 months versus 7.1 months], pain, [(HR: 0.34 [95% CI: 0.23, 0.50]; p<0.0001), median 22.7 months versus 7.5 months], appetite loss, [(HR: 0.32 [95% CI: 0.21,

0.49]; p<0.0001), median NR versus 9.0 months], systemic therapy side effects, [(HR: 0.33 [95% CI: 0.22, 0.51]; p<0.0001), median 24.6 months versus 7.9 months], arm symptoms, [(HR: 0.46 [95% CI: 0.29, 0.73]; p=0.0008), median NR versus 13.2 months]. A significantly greater delay in time to clinically meaningful deterioration was observed in the talazoparib arm compared to the chemotherapy arm for role functioning, [(HR: 0.36 [95% CI: 0.25, 0.52]; p<0.0001), median 20.5 months versus 5.6 months].

5.2. Pharmacokinetic properties

Talazoparib exposure generally increased proportionally with dose across the range of 0.025 mg to 2 mg after daily administration of multiple doses. Following repeated daily dosing of 1 mg talazoparib to patients, the geometric mean area under the plasma concentration-time curve (AUC) and maximum observed plasma concentration (C_{max}) of talazoparib at steady-state was in the range of 126 ng•hr/mL to 208 ng•hr/mL and 11.4 ng/mL to 19.1 ng/mL, respectively. Following repeated daily dosing, talazoparib plasma concentrations reached steady-state within 2 to 3 weeks. The median accumulation ratio of talazoparib following repeated oral administration of 1 mg once daily was in the range of 2.33 to 5.15.

Absorption

Following oral administration of talazoparib, the median time to C_{max} (T_{max}) was generally between 1 to 2 hours after dosing. The absolute bioavailability study has not been conducted in humans. However, based on urinary excretion data the absolute bioavailability is at least 54.6% with fraction absorbed of at least 68.7% (see Elimination).

The effect of food

Food intake decreased the rate but not the extent of talazoparib absorption. Following a single oral dose of talazoparib with high-fat, high-calorie food (approximately 827 calories, 57% fat), the mean C_{max} of talazoparib was decreased by approximately 46%, the median T_{max} was delayed from 1 to 4 hours, while the AUC_{inf} was not affected. Based on these results, TALZENNA can be administered with or without food.

Distribution

The population mean apparent volume of distribution (V_{ss}/F) of talazoparib was 420 L. *In vitro*, talazoparib is approximately 74% bound to plasma proteins with no concentration dependence over the concentration range of 0.01 µM to 1 µM. Renal or hepatic impairment does not appear to impact talazoparib protein binding as there was no obvious trend in the mean talazoparib fraction of unbound drug (f_u) in human plasma *in vivo* with worsening renal or hepatic function.

Metabolism

Talazoparib undergoes minimal hepatic metabolism in humans. Following oral administration of a single 1 mg dose of [^{14}C]talazoparib to humans, no major circulating metabolites were identified in plasma, and talazoparib was the only circulating drug-derived entity identified. No metabolites that individually represented more than 10% of the administered dose were recovered in the urine or feces. The identified metabolic pathways of talazoparib in humans include: 1) mono-oxidation;

2) dehydrogenation; 3) cysteine conjugation of mono-desfluoro-talazoparib; and 4) glucuronide conjugation.

In vitro, talazoparib was not an inhibitor of cytochrome (CYP)1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4/5 or inducer of CYP1A2, CYP2B6, or CYP3A4 at clinically relevant concentrations.

In vitro, talazoparib did not inhibit any of the major intestinal, hepatic or renal membrane transporters (P-gp, BCRP, organic anion transporting polypeptide [OATP]1B1, OATP1B3, organic cationic transporter [OCT]1 OCT2, organic anion transporter [OAT]1, OAT3, bile salt export pump [BSEP], multidrug and toxin extrusion [MATE]1 and MATE2-K) at clinically relevant concentrations.

In vitro, talazoparib did not inhibit any of the major uridine-diphosphate glucuronosyltransferase (UGT) isoforms (1A1, 1A4, 1A6, 1A9, 2B7, and 2B15) at clinically relevant concentrations.

Elimination

The mean terminal plasma half-life of talazoparib was 89.8 hours and the population mean apparent oral clearance (CL/F) was 6.45 L/h in cancer patients. In 6 female patients with advanced solid tumors given a single oral dose of [^{14}C]talazoparib, a mean of 68.7% and 19.7% of the total administered radioactive dose was recovered in urine and feces, respectively. Excretion of unchanged talazoparib in urine was the major route of elimination accounting for 54.6% of the administered dose, while unchanged talazoparib recovered in the feces accounted for 13.6%.

Age, sex, race, and body weight

A population PK analysis was conducted using data from 490 patients with cancer to evaluate the impact of age (ranging from 18 to 88 years), sex (53 males and 437 females), race (361 White, 41 Asian, 16 Black, 9 Others, and 63 Not reported), and body weight (ranging from 35.7 kg to 162 kg) on the PK of talazoparib. The results have shown that age, sex, race, and body weight had no clinically relevant effect on the PK of talazoparib.

Pediatric population

Pharmacokinetics of talazoparib have not been evaluated in patients <18 years of age.

Elderly population

Of the 494 patients who received TALZENNA, 85 patients were ≥65 years of age. No overall differences in safety or effectiveness of TALZENNA were observed between these patients and younger patients but greater sensitivity of some older individuals cannot be ruled out.

Renal impairment

Data from a PK trial in advanced cancer patients with varying degrees of renal impairment indicate that talazoparib total exposure (AUC_{0-24}) after multiple talazoparib once-daily doses increased by 12%, 43%, and 163% in patients with mild (eGFR 60 - 89 mL/min/1.73 m^2), moderate (eGFR 30 - 59 mL/min/1.73 m^2), and severe (eGFR 15 - 29 mL/min/1.73 m^2) renal impairment, respectively, relative to patients with normal renal function (eGFR ≥90mL/min/1.73 m^2). Talazoparib C_{max}

increased by 11%, 32%, and 89% in patients with mild, moderate, and severe renal impairment, respectively, relative to patients with normal renal function. Consistent with these findings, a population PK analysis that included 490 patients, where 132 patients had mild renal impairment (60 mL/min ≤ CrCL < 90 mL/min), 33 patients had moderate renal impairment (30 mL/min ≤ CrCL < 60 mL/min), and 1 patient had severe renal impairment (CrCL <30 mL/min), showed that talazoparib CL/F was decreased by 14.4% and 37.1% in patients with mild and moderate renal impairment, corresponding to 17% and 59% increase in AUC, respectively, when compared to patients with normal renal function (CrCL ≥90 mL/min). The PK of talazoparib has not been studied in patients requiring hemodialysis.

Hepatic impairment
Based on a population PK analysis that included 490 patients, where 118 patients had mild hepatic impairment (total bilirubin ≤1.0 × ULN and AST >ULN, or total bilirubin >1.0 to 1.5 × ULN and any AST), mild hepatic impairment had no effect on the PK of talazoparib. The PK of talazoparib in patients with normal hepatic function, mild hepatic impairment, moderate hepatic impairment (total bilirubin >1.5 to 3.0 × ULN and any AST), or severe hepatic impairment (total bilirubin >3.0 × ULN and any AST) was studied in a PK trial. Population PK analysis using data from this PK trial indicated that mild, moderate, or severe hepatic impairment had no significant impact on the PK of talazoparib.

Cardiac electrophysiology
The effect of talazoparib on cardiac repolarization was evaluated using time-matched electrocardiograms (ECGs) in assessing the relationship between the change of the QT interval corrected for heart rate (QTc) from baseline and the corresponding plasma talazoparib concentrations in 37 patients with advanced solid tumors. Talazoparib did not have a clinically relevant effect on QTc prolongation at the maximum clinically recommended dose of 1 mg once daily.

5.3. Preclinical safety data

Carcinogenicity
Carcinogenicity studies have not been conducted with talazoparib.

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

Repeat-dose toxicity
In repeat-dose toxicity studies of up to 13-week duration, talazoparib was clinically tolerated in rats at 0.04 mg/kg/day and in dogs at 0.01 mg/kg/day and the AUC_{24} exposure margins at the no adverse effect level are 0.2-fold the relevant human exposure. The main findings at subtherapeutic exposures included bone marrow hypocellularity with dose-dependent decrease in hematopoietic cells, depletion of lymphoid tissue in multiple organs and atrophy and/or degenerative changes in testes,

epididymis, and seminiferous tubules. Additional findings at higher exposures included dose-dependent increase in apoptosis/necrosis in the gastrointestinal (GI) tract, liver, and ovary. Most of the histopathologic findings were generally reversible while the testes findings were partially reversible after 4 weeks of dosing cessation. These toxicity findings are consistent with the pharmacology of talazoparib and its tissue distribution pattern.

Reproductive toxicology
In an embryo-fetal development study in rats, talazoparib resulted in embryo-fetal death, fetal malformation (depressed eye bulge, small eye, split sternebra, fused cervical vertebral arch) and structural variations in bones at a maternal systemic AUC_{24} exposure approximately 0.09-fold the relevant human exposure at the recommended dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Talazoparib capsules content
Silicified microcrystalline cellulose (sMCC)

Capsule shell

White body shell
Hypromellose (HPMC)
Titanium dioxide (E171)

Ivory cap
Hypromellose (HPMC)
Yellow iron Oxide (E172)
Titanium dioxide (E171)

Light red cap
Hypromellose (HPMC)
Red iron oxide (E172)
Yellow iron oxide (E172)
Titanium dioxide (E171)

Printing ink
Shellac
Propylene glycol
Ammonium hydroxide
Black iron oxide
Potassium hydroxide

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

Refer to outer carton for expiration date.

6.4. Special precautions for storage

Store at or below 30°C.

6.5. Nature and contents of container

TALZENNA 0.25 mg hard capsules
High-density polyethylene (HDPE) bottle and polypropylene (PP) closure with heat induction seal (HIS) liner, containing 30 or 60 or 90 hard capsules.

Polyvinyl chloride/polyvinylidene chloride (PVC/PVdC) blister with an aluminum peel off foil lidding in cartons of 30 × 1, or 60 × 1, or 90 × 1 hard capsules.

TALZENNA 1 mg hard capsules
High-density polyethylene (HDPE) bottle and polypropylene (PP) closure with heat induction seal (HIS) liner, containing 30 hard capsules.

Polyvinyl chloride/polyvinylidene chloride (PVC/PVdC) blister with an aluminum foil lidding in cartons of 30 × 1 hard capsules.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. NAME AND ADDRESS OF PRODUCT OWNER

Pfizer Inc
New York,
United States

TAL-SIN-1123/0
Date of last revision: November 2023

Package leaflet: Information for the patient

TALZENNA 0.25 mg hard capsules
TALZENNA 1 mg hard capsules
talazoparib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What TALZENNA is and what it is used for

What TALZENNA is and how it works
TALZENNA contains the active substance talazoparib. It is a type of anticancer medicine known as a 'PARP (poly-ADP ribose polymerase) inhibitor'.

Patients with changes (mutations) in genes called BRCA are at risk of developing some forms of cancer. TALZENNA works by blocking PARP, which is an enzyme that repairs damaged DNA in certain cancer cells. As a result, the cancer cells can no longer repair themselves and they die.

What TALZENNA is used for
TALZENNA is used to treat adults with breast cancer of a type known as HER2-negative breast cancer who have an abnormal inherited BRCA gene.

TALZENNA is used when the cancer has spread beyond the original tumor or to other parts of the body.

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

If you have any questions about how TALZENNA works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you take TALZENNA

Do not take TALZENNA
- If you are allergic to talazoparib or any of the other ingredients of this medicine (listed in section 6).
- If you are breast-feeding.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking TALZENNA and during your treatment if you experience signs or symptoms described in this section.

Low blood cell counts
TALZENNA lowers your blood cell counts, such as your red blood cell count (anaemia), white blood cell count (neutropenia), or blood platelet count (thrombocytopenia). Signs and symptoms you need to look out for include:
- **Anaemia:** Being short of breath, feeling very tired, pale skin, or fast heartbeat – these may be signs of a low red blood cell count
- **Neutropenia:** Infection, developing chills or shivering, or fever – these may be signs of a low white blood cell count
- **Thrombocytopenia:** Bruising or bleeding for longer than usual if you hurt yourself – these may be signs of a low blood platelet count

You will have regular blood tests during treatment with TALZENNA to check your blood cells (white blood cells, red blood cells, and platelets).

Serious problems with the bone marrow
Rarely, low blood cell counts may be a sign of more serious problems with the bone marrow such as myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML). Your doctor may want to test your bone marrow to check for these problems.

Male and female contraception
Women who can become pregnant and men with partners who are or can become pregnant should use effective contraception.

Please see section "Male and female contraception" below.

Children and adolescents
TALZENNA is not to be used in children or adolescents (under 18 years of age).

Other medicines and TALZENNA
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines. This is because TALZENNA can affect the way some other medicines work. Also some medicines can affect the way TALZENNA works.

In particular, the following may increase the risk of side effects with TALZENNA:
- Amiodarone, carvedilol, dronedarone, propafenone, quinidine, ranolazine and verapamil – generally used to treat heart problems.
- Clarithromycin and erythromycin antibiotics – used to treat bacterial infections.
- Itraconazole and ketoconazole – used to treat fungal infections.

- Cobicistat, darunavir, indinavir, lopinavir, ritonavir, saquinavir, telaprevir and tipranavir – used to treat HIV infections/AIDS.
- Cyclosporin – used in organ transplantation to prevent rejection.
- Lapatinib – used to treat patients with certain types of breast cancer.
- Curcumin (e.g. found in turmeric root) in some medicines (see also section TALZENNA with food and drink below).
- Other products such as valspodar.

The following medicines may reduce the effect of TALZENNA:
- Carbamazepine and phenytoin – anti-epileptics used to treat seizures or fits.
- St. John's wort (*Hypericum perforatum*) – a herbal remedy used to treat mild depression and anxiety.

TALZENNA with food and drink
Do not use curcumin in food supplements while you are taking TALZENNA as it may increase TALZENNA's side effects. Curcumin is found in turmeric root and you should not use large amounts of turmeric root, but using spices in food is not likely to cause a problem.

Pregnancy
TALZENNA may harm an unborn baby. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Your doctor will perform a pregnancy test prior to starting TALZENNA. TALZENNA is not recommended during pregnancy or for women of childbearing potential not using contraception.

- You should not use TALZENNA if you are pregnant.
- You should not become pregnant while taking TALZENNA.
- Discuss contraception with your doctor if there is any possibility that you or your partner may become pregnant.

Male and female contraception
Women who are able to become pregnant should use effective birth control (contraception) during treatment with TALZENNA and for at least 7 months after the last dose of TALZENNA. Since the use of hormonal contraception is not recommended if you have breast cancer, you should use two non-hormonal contraception methods.

Talk to your healthcare provider about birth control methods that may be right for you.

Men with female partners who are pregnant or able to become pregnant should use effective birth control (contraception), even after a vasectomy, during treatment with TALZENNA and for at least 4 months after the last dose.

Breast-feeding
You should not breast-feed while taking TALZENNA and for at least 1 month after the last dose. It is not known if TALZENNA passes into breast milk.

Fertility
Male and female fertility may be compromised by treatment with TALZENNA.

Driving and using machines
TALZENNA may have a minor influence on the ability to drive and use machines. If you feel dizzy, weak, or tired (these are very common side effects of TALZENNA), you should not drive or use machines.

3. How to take TALZENNA

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take
The recommended dose is one 1-mg capsule taken by mouth once daily.

If you get certain side effects while you are taking TALZENNA (see section 4), your doctor may lower your dose or stop treatment, either temporarily or permanently. The dose may be lowered to 0.75 mg (taken as three 0.25-mg capsules) once daily, or 0.5 mg (two 0.25-mg capsules) once daily, or 0.25 mg (one 0.25-mg capsule) once daily.

Swallow the capsule whole with a glass of water. Do not chew or crush the capsules. You can take TALZENNA with food or between meals. Do not open the capsules. Contact with the capsule content should be avoided.

If you take more TALZENNA than you should
If you have taken more TALZENNA than your normal dose, contact your doctor or nearest hospital right away. Urgent treatment may be necessary.

Take the carton and this leaflet so that the doctor knows what you have been taking.

If you forget to take TALZENNA
If you miss a dose or vomit, take your next dose as scheduled. Do not take a double dose to make up for the forgotten or vomited capsules.

If you stop taking TALZENNA
Do not stop taking TALZENNA unless your doctor tells you to.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor straight away if you notice any of the following symptoms which could be a sign of serious blood disorder:

Very common (may affect more than 1 in 10 people)
- Being short of breath, feeling very tired, having pale skin, or fast heartbeat – these may be signs of a low red blood cell count (anaemia).
- Infection, developing chills or shivering, or fever or feeling hot – these may be signs of a low white blood cell count (neutropenia, leukopenia).
- Bruising or bleeding for longer than usual if you hurt yourself – these may be signs of a low blood platelet count (thrombocytopenia).

Talk to your doctor if you get any other side effects. These can include:

Very common (may affect more than 1 in 10 people)
- Low counts of white blood cells, red blood cells, and blood platelets
- Decreased appetite
- Feeling dizzy
- Headache
- Feeling sick (nausea)
- Being sick (vomiting)
- Diarrhoea
- Pain in the abdomen
- hair loss (alopecia)
- Tiredness

Common (may affect up to 1 in 10 people)
- Low levels of lymphocytes.
- Alteration in taste (dysgeusia)
- Indigestion
- Mouth inflammation

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store TALZENNA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the bottle or blister after EXP. The expiry date refers to the last day of that month.

Store at or below 30°C.

Do not use this medicine if the pack is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What TALZENNA contains
- The active substance is talazoparib. TALZENNA hard capsules come in different strengths.
- TALZENNA 0.25 mg hard capsules: each capsule contains talazoparib tosylate equivalent to 0.25 mg talazoparib.
- TALZENNA 1 mg hard capsules: each capsule contains talazoparib tosylate equivalent to 1 mg talazoparib.

The other ingredients are:
- Capsule content: silicified microcrystalline cellulose (sMCC) (microcrystalline cellulose and silicone dioxide).
- 0.25 mg capsule shell: hypromellose (HPMC), yellow iron oxide (E172), and titanium dioxide (E171)
- 1 mg capsule shell: hypromellose (HPMC), yellow iron oxide (E172), titanium dioxide (E171), and red iron oxide (E172)

Printing ink: shellac, propylene glycol, ammonium hydroxide, black iron oxide, and potassium hydroxide.

What TALZENNA looks like and contents of the pack
TALZENNA 0.25 mg is supplied as opaque, approximately 14.30 mm x 5.32 mm hard capsule with an ivory cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.25” in black).

TALZENNA 1 mg is supplied as opaque, approximately 14.30 mm x 5.32 mm hard capsule with a light red cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 1” in black).

TALZENNA 0.25 mg is available in blister packs of 30 x 1, or 60 x 1, or 90 x 1 hard capsules and in plastic bottles of 30 or 60 or 90 hard capsules.

TALZENNA 1 mg is available in blister pack of 30 x 1 hard capsule and in plastic bottles of 30 hard capsules.

Not all pack sizes may be marketed.

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