



# Pfizer Receives Positive CHMP Opinion for TALZENNA® (talazoparib) for Patients with Inherited (Germline) BRCA-Mutated Locally Advanced or Metastatic Breast Cancer

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Positive opinion based on results from largest Phase 3 trial performed to date of a PARP inhibitor in gBRCA-mutated advanced breast cancer

Pfizer Inc. (NYSE: PFE) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending TALZENNA® (talazoparib), an oral poly (ADP-ribose) polymerase (PARP) inhibitor, be granted marketing authorization in the European Union (EU). The indication the CHMP adopted is for TALZENNA as monotherapy for the treatment of adult patients with germline breast cancer susceptibility gene (gBRCA)1/2-mutations, who have human epidermal growth factor receptor 2-negative (HER2-) locally advanced (LA) or metastatic breast cancer (MBC). Patients should have been previously treated with an anthracycline and/or a taxane in the (neo)adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor-positive (HR+) breast cancer should have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy.

The positive CHMP opinion of TALZENNA follows the medicine's approval by the U.S. Food and Drug Administration (FDA) in October 2018.1

“There is a pressing need for new, effective medicines that are specifically developed for patients with an inherited BRCA mutation who are often diagnosed at a younger age and have limited options for the treatment of advanced-stage disease,” said Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology, Pfizer Global Product Development. “Results from the EMBRACA trial provide evidence supporting the use of TALZENNA in these patients, and we look forward to working with the European Commission to potentially offer an alternative treatment option to chemotherapy.”

The CHMP’s opinion for TALZENNA, which was acquired as part of Pfizer’s acquisition of Medivation, will now be reviewed by the European Commission. The Marketing Authorization Application was submitted based on results from the EMBRACA trial, the largest Phase 3 trial performed to date of a PARP inhibitor in patients with gBRCA-mutated LA or MBC. This Phase 3, open-label, randomized trial evaluated once-daily TALZENNA compared to physician’s choice standard chemotherapy (capecitabine, eribulin, gemcitabine or vinorelbine) in patients with an inherited BRCA1/2 mutation and triple-negative or HR+/HER2- LA or MBC who may have received up to three prior cytotoxic chemotherapy regimens for their advanced disease. A total of 431 patients were enrolled at 145 sites in 16 countries, including 190 patients in European countries such as Belgium, France, Germany, Ireland, Italy, Poland, Spain and the United Kingdom.

#### About talazoparib

Talazoparib is an inhibitor of PARP enzymes, which play a role in DNA repair. Preclinical studies suggest that talazoparib may work by blocking PARP enzyme activity and trapping PARP at the site of DNA damage, leading to decreased cancer cell growth and cancer cell death. Talazoparib anti-tumor activity also was observed in mouse models of human breast cancer that expressed mutated or non-mutated BRCA1/2.<sup>1</sup>

In addition to gBRCA-mutated LA or MBC, talazoparib also is being evaluated in several ongoing clinical trials in breast and other cancers, including early triple-negative breast cancer and prostate cancer, as well as other novel combinations with targeted therapies and studies with immunotherapy in various solid tumors.

#### Indication in the U.S.

TALZENNA® (talazoparib) is approved in the U.S. for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (gBRCA)-mutated human epidermal growth factor receptor 2-negative (HER2-), locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for TALZENNA.<sup>1</sup>

## TALZENNA® (talazoparib) Important Safety Information from the U.S. Prescribing Information

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported in patients who received TALZENNA. Overall, MDS/AML have been reported in 2 out of 584 (0.3%) solid tumor patients treated with TALZENNA in clinical studies.

Myelosuppression consisting of anemia, leukopenia/neutropenia, and/or thrombocytopenia have been reported in patients treated with TALZENNA. Grade  $\geq 3$  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 ( $\geq 20\%$ ) 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%).

The most frequently reported Grade  $\geq 3$  adverse reactions ( $\geq 5\%$ ) for TALZENNA vs chemotherapy were anemia (39% vs 5%), neutropenia (21% vs 36%), and thrombocytopenia (15% vs 2%).

The most common lab abnormalities ( $\geq 25\%$ ) 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 co-administering 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. No dose adjustment is required for patients with mild renal impairment. TALZENNA has not been studied in patients with severe renal impairment or 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.

Please see full U.S. Prescribing Information and Patient Information for TALZENNA® (talazoparib) at [www.TALZENNA.com](http://www.TALZENNA.com).

## About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 18 approved innovative cancer medicines and biosimilars across more than 20 indications, including breast, prostate, kidney, lung and hematology. Pfizer Oncology is striving to change the trajectory of cancer.

Pfizer Inc: Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality,

safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at [www.pfizer.com](http://www.pfizer.com). In addition, to learn more, please visit us on [www.pfizer.com](http://www.pfizer.com) and follow us on Twitter at @Pfizer and @Pfizer\_News, LinkedIn, YouTube, and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

DISCLOSURE NOTICE: The information contained in this release is as of April 26, 2019. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about TALZENNA (talazoparib), including a potential indication in the EU and TALZENNA's potential benefits, that involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of TALZENNA; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when applications for TALZENNA may be filed in any other jurisdictions; whether and when the European Commission may approve the pending application for TALZENNA in the EU and whether and when any such other applications for TALZENNA that may be pending or filed may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether TALZENNA will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or

commercial potential of TALZENNA; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

1 TALZENNA® (talazoparib) Prescribing Information. New York, NY: Pfizer Inc: 2018.

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