PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

TALZENNA (TALAZOPARIB)

Marketing Authorization Number 67141

Hard capsules 0.25 mg, 1 mg

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LIST OF ABBREVIATIONS

AML	Acute Myeloid Leukaemia
BICR	Blinded independent central review
BRCA	Breast cancer susceptibility gene
DDR	DNA Damage Repair
EPAR	European Public Assessment Report
EMA	European Medicines Agency
HER2	Human Epidermal Growth Factor Receptor 2
mCRPC	metastatic Castration Resistant Prostate Cancer
MDS	Myelodysplastic Syndrome
PCT	Physician's Choice Treatment
RMP	Risk Management Plan
(r)PFS	(radiographic) Progression Free Survival
SmPC	Summary of Product Characteristics (Europe)
SPM	Second primary malignancy

OVERVIEW

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary for talazoparib is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g., by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of talazoparib in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer is fully responsible for the accuracy and correctness of the content of the published RMP summary of talazoparib.

SUMMARY OF RISK MANAGEMENT PLAN FOR TALAZOPARB

Summary of the risk management plan for Talzenna (Talazoparib)

This is a summary of the Risk Management Plan (RMP) for Talzenna. The RMP details important risks of Talzenna, how these risks can be minimised, and how more information will be obtained about Talzenna's risks and uncertainties (missing information).

Talzenna's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how talazoparib should be used.

I. The Medicine and What it is Used for

Talzenna monotherapy is authorised for the treatment of adult patients with germline BRCA mutated HER2-negative locally advanced or metastatic breast cancer (see SmPC for the full indication). The recommended dose of talazoparib monotherapy is 1 mg capsule taken orally once daily, for which 1 mg hard capsules are available. Talzenna is also available as 0.25 mg hard capsules to allow dose reductions to 0.75 mg, 0.5 mg, and 0.25 mg Talzenna.

Talzenna is proposed to be used in combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated.

The recommended dose of Talzenna when used in combination with enzalutamide is 0.5 mg.

Further information about the evaluation of Talzenna's benefits can be found in Talzenna's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Talzenna, together with measures to minimise such risks and the proposed studies for learning more about Talzenna's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the public (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

If important information that may affect the safe use of Talzenna is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Talzenna are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken.

Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of talazoparib. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected.

Table 1. List of Important Risks and Missing Information

Important Identified Risks	None
Important Potential Risks	Second primary malignancies (other than MDS/AML)
	Reproductive and developmental toxicity
Missing Information	None

II.B. Summary of Important Risks

Table 2. Important Potential Risk 1: Second Primary Malignancies (other than MDS/AML)

Evidence source and strength of evidence	During the clinical development, amongst patients who received Talzenna at the proposed starting dose of 1 mg once daily, there were 6 patients who experienced 7 second primary malignancy adverse events (excluding MDS/AML), and none amongst patients who received Talzenna at doses other than 1 mg once daily. In comparison, 1 case of second primary malignancy (Malignant melanoma) was reported in the PCT arm (N=126; 0.8%) of pivotal study 673 301 (EMBRACA). In the pivotal mCRPC study there were 14 events of SPM in patients treated with talazoparib in combination with enzalutamide: two (2) in part 1 of the study, and 12 in randomized part 2 of the study. In comparison, 20 events of SPM were observed in part 2 of mCRPC study in the placebo/enzalutamide arm. Overall, as of 16 August 2022, Second primary malignancy has been reported in 26 out of 1199[1] (2.1%) solid tumour patients treated at any dose with Talzenna in clinical studies. Evidence is confounded by prior exposure to other chemotherapeutic agents that may increase risk, and the inability to rule out the possibility of occurrence of second primary malignancies (other than MDS/AML) unrelated to treatment with Talzenna.
Risk factors and risk groups	Potential contributing factors for the development of second primary malignancies (other than MDS/AML) include previous platinum-containing chemotherapy, other DNA damaging agents, or radiotherapy. The incidences of second primary malignancies (other than MDS/AML) after first primary breast cancer are higher than the general population and have been estimated in several cohort studies, where rates range from 0.24 to 0.83 per 100 Patient-Years. Rates may vary due to various factors, including malignancy type definitions, cancer sites included, patient inclusion criteria, treatment patterns, and clinical approaches to follow up. There are no known specific preventive measures to reduce the risk of second primary malignancies (other than MDS/AML) in patients treated with Talzenna. Patients being treated with talazoparib should be monitored for new onset malignancies as per standard clinical practice.
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC Section 5.3 which provides in-vitro and in-vivo mutagenesis results <u>Additional risk minimisation measures:</u> None

[1] Of the participants who initiated treatment in MDV3800-13 at Talzenna doses other than 1 mg/day, 5 initiated treatment with Talzenna 1 mg/day in the originating study and are also represented in the talazoparib 1 mg population.

Table 2. Important Potential Risk 1: Second Primary Malignancies (other than MDS/AML)

Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: None Additional pharmacovigilance activities: None

Table 3. Important Potential Risk 2: Reproductive and Developmental Toxicity

Evidence source and strength of evidence	Based on findings from animal studies, Talzenna can cause embryo-foetal harm and may compromise male and female fertility. There are no available clinical data on Talzenna use in pregnant women or any clinical effects on fertility to inform a drug-associated risk.
Risk factors and risk groups	Risk factors and risk groups include women of childbearing potential, pregnant women, and lactating women. Women of childbearing potential should be advised to avoid becoming pregnant while receiving Talzenna. A highly effective method of contraception is required for patients and partners of patients during treatment with Talzenna.
Risk minimisation measures	Routine risk minimisation measures: - SmPC Section 4.4, 4.6 where advice is given regarding use of contraception in male and female patients as well as in male patients with female partners of reproductive potential or pregnant partners. - Package leaflet Section 2. Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: Pregnancy follow-up questionnaires (Exposure During Pregnancy Supplemental Forms) will be utilized to collect further data on this safety concern. Additional pharmacovigilance activities: None

II.C. Post-Authorisation Development Plan

Not applicable

II.C.1. Studies Which are Conditions of the Marketing Authorisation

The following study is condition of the marketing authorisation (obligation to conduct post-authorisation measures):

- Study C3441021 (TALAPRO-2): A Phase 3, Randomized, Double Blind, Placebo Controlled Study of Talazoparib With Enzalutamide in Metastatic Castration Resistant Prostate Cancer.

  Purpose of the study: to demonstrate that talazoparib in combination with enzalutamide is superior to placebo in combination with enzalutamide in prolonging BICR assessed rPFS, in patients with mCRPC unselected for DDR status (Cohort 1) and in patients with mCRPC harbouring DDR deficiencies (Cohort 2).

II.C.2. Other Studies in Post-Authorisation Development Plan

There are no studies required for Talzenna.