Indication	Monotherapy for the treatment of HER2 negative, locally advanced or metastatic breast cancer with germline BRCA1/2 mutations, previously treated with an anthracycline and/or taxane in the adjuvant/neoadjuvant/advanced disease setting. No prior treatment with a PARP inhibitor is permitted unless the patient has received adjuvant olaparib and this was completed without disease progression during therapy or within 12 months of its completion or olaparib was commenced for this locally advanced or metastatic indication and had to be stopped within 6 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression. NB Patients with hormone receptor (HR)-positive breast cancer should also have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days. Until disease progression, unacceptable toxicity or patient choice to discontinue. A formal medical review as to how talazoparib is being tolerated and whether talazoparib should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • Monitor FBC, U&Es and LFTS at baseline then at the beginning of each cycle. • Prior to cycle 1: If Hb >/=100g/L, Neuts >/=1.5 and PLTS >/=75 proceed with treatment. • During treatment see table 1. • **Hepatic impairment:** No dose adjustment required in mild, moderate or severe hepatic impairment. • **Renal impairment:** • No dose adjustment is required in mild renal impairment (CrCl 60-89ml/min), in moderate impairment (CrCl 30-59ml/min), the recommended starting dose is 0.75 mg OD. In severe renal impairment (CrCl 15-29 ml/min), the recommended starting dose is 0.5 mg once daily. Talazoparib has not been studied in patients with CrCl <15ml/min or patients requiring haemodialysis no data available. • **Management of adverse reactions and dose adjustments:** • Interruption of treatment or dose reduction may be required to manage adverse reactions (see table 1) • Grade 3 or 4 non-haematology adverse reaction, withhold treatment. • The recommended first dose reduction is to 0.75mg OD, second dose reduction 0.5mg OD and if required a further final dose reduction to 0.25mg OD. NB see below for dose adjustment when co-administered with strong P-gp inhibitors. • **Myelodysplastic syndrome/Acute Myeloid Leukaemia (MDS/AML)** have been reported in patients who received poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitors, including talazoparib. If MDS/AML is confirmed, talazoparib should be discontinued.

	• **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** • Concomitant use of strong P-gp inhibitors (e.g. amiodarone, carvedilol, clarithromycin, erythromycin, indinavir, itraconazole, ketoconazole, quinidine, and verapamil) should be avoided. If co-administration with a strong P-gp inhibitor is unavoidable, talazoparib dose should be reduced to the next lower dose, when the strong inhibitor is discontinued, increase to the dose of talazoparib prior to the initiation of the strong P-gp inhibitor (after 3-5 half lives). • Co-administration of talazoparib with strong BCRP inhibitors (e.g. cyclosporin) may increase talazoparib exposure and should be avoided. If co-administration of strong BCRP inhibitors cannot be avoided, patient should be monitored for potential increased adverse reactions. • **Missed dose:** If the patient vomits or misses a dose, an additional dose should not be taken. Patients should take their next normal dose at its scheduled time. • **Driving and machinery:** Talazoparib may cause fatigue/asthenia or dizziness, patients should be made aware and advised if affected to not drive or operate machinery**.** • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	CDF list V1.342 accessed on line 14.01.2025 SPC Talzenna® accessed online 19.02.2025

<u>Table 1 Dose modification and management</u>

	Withhold until levels resolve to	**Resume Talazoparib**
Haemoglobin < 80g/L	>/= 90g/L	Resume at next lower dose
Platelet count < 50	>/= 75	
Neutrophil count < 1	>/= 1.5	
Non-haematologic adverse reaction Grade 3 or Grade 4	</= Grade 1	Consider resuming at next lower dose or discontinue

<u>Repeat every 28 days</u>

TTO	Drug	Dose	Route	Directions
Day 1	**TALAZOPARIB TOSYLATE**	**1mg**	PO	OD Capsules should be swallowed whole, not chewed, opened or dissolved. Available as 0.25mg and 1mg capsules Dispense original packs (30 capsules).
	Metoclopramide	10mg	PO	TDS PRN Do not take for more than 5 days continuously. (dispense 28 tablets on cycle 1, then only if specified)
	Loperamide	2-4mg	PO	Take 4mg initially then 2mg after each loose stool when required (max 16mg a day) (dispense 1x op on cycle 1, then when required)

Protocol No	BRE-100	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V3	Written by	M.Archer
Supersedes version	V2	Checked by	C. Waters V2 P. Chhabhaiya V1 V2 / V3 updated in line with commissioning criteria change only
Date	26.02.2025	Authorising consultant (usually NOG Chair)	J. Glendenning V1