Indication	For the treatment of previously treated unresectable locally advanced or metastatic triple negative, PDL1 positive* or negative breast cancer, following taxane based therapy (unless contraindicated) in patients who have: received 2 or more prior lines of systemic therapy for unresectable locally advanced or metastatic disease OR only had 1 line of systemic therapy for unresectable locally advanced or metastatic disease and have also previously received adjuvant or neoadjuvant systemic therapy. *PDL1 positive patients must have received 1st line atezolizumab or pembrolizumab unless the use of immunotherapy was contraindicated
Treatment Intent	Palliative
Frequency and number of cycles	Every 21 days Until disease progression or excessive toxicity or until the patient chooses to discontinue treatment. A formal medical review will be scheduled to occur at least by the end of the first 6 weeks of treatment to assess tolerability and whether treatment should continue or not.
Monitoring Parameters pre-treatment	• **Virology status checked prior to Cycle 1** • **Day 1**: FBC, U&Es and LFTs before every cycle. If neuts >/=1.5 and plts >/=100, proceed with treatment. • **Day 8:** FBC only. If neuts >/=1.0 and plts >/=100, proceed with treatment. • If blood parameters not met, delay day 1 by one week or omit day 8, as appropriate. • Administration of G-CSF and dose reduction may be required if severe neutropenia or febrile neutropenia occurs. Consider prophylactic G-CSF with subsequent doses. See table 1 below. • Confirm the patient has no symptomatically active brain metastases or leptomeningeal metastases. • **Hepatic impairment**: No adjustment required in mild hepatic impairment (bilirubin </= ULN and AST > ULN, or bilirubin > 1.0 to </= 1.5 ULN and AST of any level). Safety has not been established in moderate or severe hepatic impairment, clinical decision**.** It is not recommended in patients with bilirubin > 1.5 ULN or AST/ALT >3 ULN without liver metastases or AST/ALT > 5 ULN with liver metastases. • **Renal impairment:** No adjustment to the starting dose is required in patients with mild renal impairment. Sacituzumab has not been studied in patients with moderate or severe renal impairment (<60ml/min), or end-stage renal disease. ○ **Adverse reactions:** Dose modification may be required to manage adverse reactions (see table 1). If a dose reduction is required it should not be re-escalated once the reaction has resolved. ○ **Excessive cholinergic response*:** Patients who experience an excessive cholinergic response (e.g. abdominal cramping, diarrhoea, salivation, etc.) to the first dose of sacituzumab govitecan may require prophylactic atropine before subsequent doses. ○ **Diarrhoea:** Severe diarrhoea has been reported during treatment with sacituzumab, patients should be advised of the risk of diarrhoea and instructed to report any episodes immediately. Dose interruption and reduction may be required, see table 1. At the onset of diarrhoea, and if no infectious cause can be identified, promptly initiate loperamide 4 mg initially followed by 2 mg with every episode of diarrhoea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhoea resolves. In patients with infectious diarrhoea, initiate anti-infective treatment as clinically indicated. Additional supportive measures (e.g. fluid and electrolyte substitution) may also be employed as clinically indicated. ○ **Neutropenia:** See table 1

	• **Patients with reduced UGT1A1 activity:** Patients who are homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1) 28 allele are at increased risk of severe neutropenia, severe diarrhoea, febrile neutropenia, and anaemia and may be at increased risk for other adverse reactions following initiation of treatment. Patients with known reduced UGT1A1 activity should be closely monitored for adverse reactions. Withhold or permanently discontinue sacituzumab based on clinical assessment of the onset, duration and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 activity. • **Infusion-related reactions and dose modification:** • Patients should be premedicated prior to infusion, patients should be closely monitored throughout the infusion and for 30 minutes after completion. The infusion rate should be slowed down or infusion interrupted if the patient develops an infusion-related reaction. Treatment should be permanently discontinued if life-threatening infusion-related reactions occur. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** No interaction studies have been performed. SN-38 (the small molecule moiety of sacituzumab govitecan) is primarily metabolised via UGT1A1, so the following guidance should be considered. o Concomitant use with UGT1A1 inhibitors (e.g. propofol, ketoconazole, EGFR tyrosine kinase inhibitors) may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Use with caution and monitor patients closely. o Concomitant use with UGT1A1 inducers (e.g. carbamazepine, phenytoin, rifampicin, protease inhibitors) may significantly reduce exposure to SN-38, use with caution and monitor patients closely. • **Driving:** Dizziness has been reported as a side effect, patients should be cautious when driving or operating machinery.
References	SPC accessed online 18.07.2022 BlueTeq form accessed online 18.07.2022

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1: Recommended dose modifications for adverse reactions

Adverse Reaction	**Occurrence**	**Dose Modification**
Severe Neutropenia		
Grade 4 (<0.5 x 10^9 /L) neutropenia >/= 7 days, OR Grade 3 febrile neutropenia (ANC -<1.0 x 10^9 /L and fever >/= 38.5°C), OR At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing by 2 or 3 weeks for recovery to </= Grade 1 (1.5 x 10^9 /L – LLN)	First	25% dose reduction and administer granulocyte-colony stimulating factor (G-CSF)
	Second	50% dose reduction
	Third	Discontinue treatment
At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to </= Grade 1 (1.5 x 10^9 /L – LLN)	First	Discontinue treatment
Severe Non-Neutropenic Toxicity		
Grade 4 non-haematological toxicity which recovers to </= Grade 1 within 3 weeks, OR Any Grade 3-4 nausea, vomiting or diarrhoea due to treatment that is not controlled with antiemetics and anti-diarrheal agents, OR Other Grade 3-4 non-haematological toxicity persisting > 48 hours despite optimal medical management, OR At time of scheduled treatment, Grade 3-4 non-neutropenic haematological or non- haematological toxicity, which delays dose by 2 or 3 weeks for recovery to </= Grade 1	First	25% dose reduction
	Second	50% dose reduction
	Third	Discontinue treatment
In the event of Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, Grade 3 nausea or Grade 3-4 vomiting, which does not recover to </= Grade 1 within 3 weeks	First	Discontinue treatment

Grading according to NCI-CTCAE v.4.03

NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events

Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1 & Day 8	Famotidine	40mg	PO		Take 4-2 hours before chemotherapy
	Dexamethasone	12mg	IV	bolus	Given at least 30 minutes before the sacituzumab infusion
	Ondansetron	< 75yrs 16mg >/=75yrs 8mg	IV	15 min In 50ml sodium chloride 0.9%	
	Chlorphenamine	10mg	IV	bolus	
	Paracetamol	1000mg	PO		
	Atropine	0.25mg	SC		If required for acute cholinergic syndrome (diarrhoea, abdominal cramps, salivation etc). See notes above
	SACITUZUMAB GOVITECAN	**10mg/kg**	**IV**	1st infusion: over 3 hours. Subsequent infusions: over 1 to 2 hours if prior infusions were tolerated.	Sodium Chloride 0.9% 250ml-500ml* Diluted to achieve a concentration of 1.1 mg/mL to 3.4 mg/mL
	Observe closely for signs of infusion-related reaction during infusion and for at least 30 minutes after completion.				
	*For patients whose body weight exceeds 170 kg, divide the total dosage equally between two 500 mL infusion bags and infuse sequentially via slow infusion				
TTO	Drug	Dose	Route	Directions	
	Dexamethasone	6mg	PO	OM for 3 days after Day 1 and Day 8.	
	Loperamide	2mg-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day.	
	Metoclopramide	10mg	PO	3 times a day as required after Day 1 and Day 8. Do not take for more than 5 days continuously.	