Indication	For the treatment of breast cancer in patients with HER2-positive locally advanced, unresectable or metastatic (stage IV) breast cancer who have previously received trastuzumab and a taxane or trastuzumab and capecitabine, either separately or in combination.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 21 days. Continue until disease progression unless progression is within the CNS alone, unacceptable toxicity or patient's choice.
Monitoring Parameters	• **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. • The use of trastuzumab emtansine is restricted to patients whose tumours significantly overexpress HER2 at the 3+ level or greater, or a ratio of $\geq$ 2.0 by ISH • FBC, U&Es and LFTs should be monitored at baseline and prior to each cycle. • At the start of each cycle ensure PLT>/= 100 and neuts >/=1.5, otherwise d/w consultant. • Patients with thrombocytopenia (≤ 100 x 10^9/l) and patients on anti-coagulant treatment should be monitored closely while on trastuzumab emtansine, cases of haemorrhage have been reported. See table 1 for further guidance on thrombocytopenia. • Blood pressure before every cycle. • Cardiac function should be monitored at baseline (ECHO/MUGA and ECG) and then every 3 to 4 months (ECHO or MUGA) during treatment or as clinically indicated. • Record on KOMs Cardiac Monitoring Record. • It is the prescribers' responsibility to check that the ECHO/MUGA result is satisfactory before starting and continuing treatment. LVEF should be >/=50% at baseline. See **Table 1** for dose modifications**.** • **Hepatic Impairment:** No adjustment to the starting dose is required for patients with mild or moderate hepatic impairment. Trastuzumab emtansine has not been studied in patients with severe hepatic impairment. Treatment of patients with hepatic impairment should be undertaken with caution due to known hepatotoxicity observed with trastuzumab emtansine. • **Renal Impairment:** No adjustment to the starting dose is needed in patients with mild or moderate renal impairment (CrCl >/=30ml/min and <90ml/min). Use with caution in patients with severe renal impairment (CrCl<30ml/min). • **Dose modification** • If a dose reduction is required the first should be to 3mg/kg and the second to 2.4mg/kg. No further dose reduction is permitted. Do not re-escalate a previously reduced dose. Treatment should be discontinued if symptoms persist. See table 1 modification guidelines. o Trastuzumab emtansine should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until resolution to ≤ Grade 2. At retreatment a dose reduction may be considered. • **Infusion rates and infusion related reaction:** o Patients must be observed closely for infusion related adverse effects during the infusion and for at least 90 minutes following the first infusion and (if tolerated) for subsequent doses, during the infusion and for at least 30 minutes after the end of the infusion.

	○ If the first dose is well tolerated (no infusion related reactions), then the second and subsequent doses may be administered over 30 minutes (no pre-medication required). ○ The infusion site should be closely monitored for possible subcutaneous infiltration during administration, cases of delayed epidermal injury or necrosis following extravasation have been observed. • **Interstitial lung disease (ILD),** including pneumonitis, has been reported in patients treated with trastuzumab emtansine. At each nurse assessment assess for dyspnoea, cough & fatigue. It is recommended that treatment be permanently discontinued in patients who are diagnosed with ILD or pneumonitis. • **Peripheral neuropathy,** has been reported in patients treated with trastuzumab emtansine. Dose interruption and reduction may be required see table 1. • **<u>Common drug interactions</u>: (for comprehensive list refer to BNF/SPC)** • Concomitant use of strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, and voriconazole) should be avoided if possible. • **Missed dose:** If a dose is missed, it should be administered as soon as possible and the schedule adjusted to maintain a 3 weekly interval between doses. • **Contraception:** Women of childbearing potential should use effective contraception during treatment and for 7 months following the last dose of trastuzumab emtansine. Male patients or their female partners should also use effective contraception. • **Driving and machinery:** Fatigue, headache, dizziness and blurred vision have been reported in some patients receiving trastuzumab emtansine, therefore patients should be advised to be cautious when driving or operating machines.
References	KMCC protocol BRE-037 V4 SPC accessed online 29.07.2025 CDF list V1.368

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

Table 1

Dose Modifications for Patients with MBC		
Adverse reaction	**Severity**	**Treatment modification**
Thrombocytopenia	Grade 3 ($25x10^9$/L to < $50x10^9$/L)	Do not administer trastuzumab emtansine until platelet count recovers to ≤ Grade 1 (≥ 75 x 10^9/L), and then treat at the same dose level
	Grade 4 (< 25 $x10^9$/L)	Do not administer trastuzumab emtansine until platelet count recovers to ≤ Grade 1 (≥75 x 10^9/L), and then reduce one dose level
Increased Transaminase (AST/ALT)	Grade 2 (> 2.5 to ≤ 5× the ULN)	Treat at the same dose level
	Grade 3 (> 5 to ≤ 20× the ULN)	Do not administer trastuzumab emtansine until AST/ALT recovers to Grade ≤ 2 (</=2.5 to 5 x the ULN), and then reduce one dose level
	Grade 4 (> 20× the ULN)	Discontinue trastuzumab emtansine
Hyperbilirubinemia	Grade 2 (> 1.5 to ≤ 3× the ULN)	Do not administer trastuzumab emtansine until total bilirubin recovers to Grade ≤ 1 (≤1.5 xULN), and then treat at the same dose level.
	Grade 3 (> 3 to ≤ 10× the ULN)	Do not administer trastuzumab emtansine until total bilirubin recovers to Grade ≤ 1 (≤ 1.5 x ULN) and then reduce one dose level.
	Grade 4 (> 10× the ULN)	Discontinue trastuzumab emtansine
Drug Induced Liver Injury (DILI)	Serum transaminases > 3 x ULN and concomitant total bilirubin > 2× ULN	Permanently discontinue trastuzumab emtansine in the absence of another likely cause for the elevation of liver enzymes and bilirubin, e.g. liver metastasis or concomitant medication
Nodular Regenerative Hyperplasia (NRH)	All grades	Permanently discontinue trastuzumab emtansine.
Left Ventricular Dysfunction	Symptomatic CHF	Discontinue trastuzumab emtansine
	LVEF <40%	Do not administer trastuzumab emtansine. Repeat LVEF assessment within 3 weeks. If LVEF <40% is confirmed, discontinue trastuzumab emtansine
	LVEF 40% to ≤ 45% and decrease is ≥ 10% points from baseline	Do not administer trastuzumab emtansine. Repeat LVEF assessment within 3 weeks. If the LVEF has not recovered to within 10% points from baseline, discontinue trastuzumab emtansine.
	LVEF 40% to ≤ 45% and decrease is < 10% points from baseline	Continue treatment with trastuzumab emtansine. Repeat LVEF assessment within 3 weeks.
	LVEF > 45%	Continue treatment with trastuzumab emtansine.
Pulmonary Toxicity	Interstitial lung disease (ILD) or pneumonitis	Permanently discontinue trastuzumab emtansine
Peripheral Neuropathy	Grade 3-4	Do not administer trastuzumab emtansine until resolution ≤ Grade 2.

ALT = alanine transaminase; AST = aspartate transaminase, CHF = congestive heart failure, LVEF = left ventricular ejection fraction, LVSD = left ventricular systolic dysfunction, TBILI = Total Bilirubin, ULN = upper limit of normal

* Prior to starting trastuzumab emtansine treatment.

Repeat every 21 days.

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**TRASTUZUMAB EMTANSINE (Kadcyla®)**	**3.6mg/kg**	IV	90 min for first infusion. See notes for subsequent infusions	In 250ml sodium chloride 0.9% with 0.22micron in-line PES filter