Indication	For the treatment of HER2 positive unresectable locally advanced, recurrent and/or metastatic gastric or oesophagogastric junction cancer histologically confirmed adenocarcinoma.
Treatment Intent	Palliative
Frequency and number of cycles	Cycle 1 to 8 repeat every 21 days CarboX with trastuzumab. Cycle 9 onwards, trastuzumab monotherapy. Continue until disease progression, unacceptable toxicity or patient choice.

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.
	• **DPD testing:** DPD testing must be undertaken in all patients before starting treatment; the result must be checked before treatment is started.
	• The use of trastuzumab is restricted to patients whose tumours significantly overexpress HER2 at the IHC 3+ level or greater or at the IHC 2+ level and a confirmatory SISH or FISH result.
	• At each nurse assessment patients should be assessed for signs of dyspnoea.
	• **Cardiac Function:**
	• Cardiac function should be monitored at baseline (ECHO/MUGA and ECG) and then every 6 months (ECHO or MUGA) during treatment, or as clinically indicated.
	• Record on KOMs Cardiac Monitoring Record.
	• Baseline LVEF must be >/= 55%.
	• It is the prescriber's responsibility to check that the ECHO/MUGA result is satisfactory before continuing treatment.
	• Caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.
	• **EDTA** should be used to measure GFR prior to cycle 1 or 2.
	• C+G may be used to estimate CrCl if delay in obtaining EDTA result.
	• **Haematological monitoring:**
	• **Cycles 1 to 8** Monitor FBC, U&E's, LFT's at each cycle.
	• **Day 1** If neuts 1.0-1.4 and PLT >/=100 d/w consultant. If neuts <1.0 or PLTS <100 delay treatment one week.
	• **Cycle 9 onwards**
	• FBC, U&Es and LFTs every 3 months.
	• **Hepatic impairment:** no recommended dose adjustment in hepatic impairment.
	• **Renal impairment:**
	  ○ Regimen contraindicated if CrCl <30ml/min.
	  ○ If CrCl < 50 ml/min dose reduce capecitabine. d/w consultant, consider 25% dose reduction of capecitabine (see SPC).
	• **Infusion-related reactions:**
	  ○ **Carboplatin:** Mild/moderate reactions (grade 1-2): If symptoms resolve after treatment with hydrocortisone and chlorphenamine, the infusion may be restarted at 50% rate for 30 mins, then, if no further reaction, increase to 100% rate.
	  If symptoms do not resolve after treatment with hydrocortisone and chlorphenamine, do not restart the infusion. At consultant's discretion, patients may be rechallenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider alternative treatment.
	  Severe (grade 3): Do not restart infusion. Consider alternative treatment.

	Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment. ○ **Trastuzumab:** Patients must be observed closely for infusion related adverse effects for 6 hours after the start of the loading dose of trastuzumab (iv), 2 hours after the start of the second dose of trastuzumab (iv) and one hour after the start of subsequent doses. ○ *If the first trastuzumab (iv) dose is well tolerated (no infusion related reactions), then the second and subsequent doses may be administered over the shorter infusion time of 30 minutes. ○ Infusion reactions, allergic-like reactions and hypersensitivity can occur. The majority of these events occur during or within 2.5 hours of the start of the first infusion. Interruption or slowing the rate of the infusion may help control such symptoms. The infusion may be resumed when symptoms subside. • **Management of adverse reactions and dose adjustments:** • Interrupt capecitabine in the event of >/= grade 2 non-haematological toxicity (with the exception of side effects such as alopecia, alteration in taste etc, considered to be not serious) until resolution of toxicity to grade 0-1. • Dose reduction should be considered if grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </= grade 1. • **Cardiac Dysfunction:** Trastuzumab should be withheld for at least 3 weeks in the event of signs and symptoms of CHF or drop in LVEF to less than 50% associated with a fall of >/=10% points below pre-treatment values. Trastuzumab may be resumed if the LVEF has recovered to >/=50% or to a difference of < 10% points below pre-treatment values. • **Skin reactions:** Capecitabine can induce severe skin reactions such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis. Patients should be informed of the possibility of such reactions and informed to seek urgent medical advice should any symptoms of a severe skin reaction occur. Treatment should be permanently discontinued in affected patients. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** ○ **Carboplatin:** Caution when used concurrently with other nephrotoxic or ototoxic drugs. ○ **Capecitabine** must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC. Monitor PT and INR regularly in patients taking coumarin-derivative anticoagulants. Monitor phenytoin levels with concomitant use. Caution with folinic acid or folic acid – potential for increased toxicity. Avoid concomitant allopurinol. • **Missed dose:** • If the patient misses a dose of trastuzumab by 1 week or less, then a dose of 6mg/kg should be given as soon as possible. • If the patient misses a dose of trastuzumab by more than one week, a re-loading dose of trastuzumab should be given over 90 minutes. • **Driving and operating machinery:** Dizziness, fatigue and nausea has been reported. Patients should be aware this may affect their ability to drive or operate machinery. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	ARIA regimen UGI-052 KMCC proforma UGI -052 V1

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

Cycle 1 only 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1	**TRASTUZUMAB** Loading dose	**8mg/kg**	IV	90 min	In 250ml sodium chloride 0.9%
	Patients must be observed closely for infusion related adverse effects for 6 hours after the start of trastuzumab				
	Dexamethasone	8mg	PO		
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15min	Sodium Chloride 0.9% 50ml
	CARBOPLATIN (AUC= 5)	**DOSE = AUC x (GFR + 25) Max dose 700mg**	IV	30min	In Glucose 5% 500ml
TTO	Drug	Dose	Route	Directions	
Day 1	**CAPECITABINE**	**1250mg/m^2/day** In 2 divided doses	PO	**Continuously for 21 days.** Take within 30 mins after food and approximately every 12 hours. Available as 500mg and 150mg tablets	
	Dexamethasone	6mg	PO	OM for 3 days	
	Metoclopramide	10mg	PO	10mg TDS for 3 days and then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.	

Cycle 2 to 8 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1	**TRASTUZUMAB**	**6mg/kg**	IV	30mins if previously tolerated See monitoring parameters above*	In 250ml sodium chloride 0.9%
	Patients must be observed closely for infusion related adverse effects for 2 hours after the start of the trastuzumab for cycle 2, then one hour from the start of the infusion for cycle 3 onwards				
	Dexamethasone	8mg	PO		
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15min	Sodium Chloride 0.9% 50ml
	CARBOPLATIN (AUC= 5)	**DOSE = AUC x (GFR + 25) Max dose 700mg**	IV	30min	In Glucose 5% 500ml
TTO	Drug	Dose	Route	Directions	
Day 1	**CAPECITABINE**	**1250mg/m^2/day** In 2 divided doses	PO	**Continuously for 21 days.** Take within 30 mins after food and approximately every 12 hours. Available as 500mg and 150mg tablets	
	Dexamethasone	6mg	PO	OM for 3 days	
	Metoclopramide	10mg	PO	10mg TDS for 3 days and then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.	

Cycle 9 onwards repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**TRASTUZUMAB**	**6mg/kg**	IV	30mins if previously tolerated See monitoring parameters above*	In 250ml sodium chloride 0.9%
	Patients must be observed closely for infusion related adverse effects for one hour after the start of trastuzumab				