Indication	For the treatment of HER-2 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 CarboF 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.
	• **It is the prescriber's responsibility to check that the ECHO/MUGA result is satisfactory before continuing treatment.**
	• Record on KOMs Cardiac Monitoring Record.
	• Baseline LVEF must be >/= 55%.
	• 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 and 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.
	• **Day 8 & 15** continue 5FU provided neuts >/=0.5 and PLT >/=75
	• **Cycle 9 onwards**
	• FBC, U&Es and LFTs cycle 9 then every 3 months.
	• **Hepatic impairment:**
	  ○ Carboplatin – no dose adjustment required.
	  ○ 5FU – caution is advised, dose reduction may be required. In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%. If the bilirubin is >85umol/L and / or AST >180 fluorouracil is contra-indicated.
	• **Renal impairment:**
	  ○ If CrCl <30ml/min stop platinum.
	  ○ 5FU - caution is advised, dose reduction may be required in severe renal impairment.
	• **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 first dose, for 2 hours after the start of the second dose and one hour after the start of subsequent doses. *If the first trastuzumab 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. As with the 90 minute schedule, no pre-medication is required. ○ 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:** • 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. • **Missed doses:** ○ 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. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** In patients receiving phenytoin, levels may be affected. ○ **Carboplatin:** Caution when used concurrently with other nephrotoxic or ototoxic drugs. ○ **5-FU:** If used concomitantly with warfarin monitor INR and prothrombin time closely. Caution with folinic acid or folic acid – potential for increased 5FU toxicity. 5FU must not be given with concurrent sorivudine or derivatives (e.g. brivudine), see SPC. • **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.
References	ARIA regimen UGI-053 KMCC protocol UGI-008 V6

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

Cycle 1 only 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
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				
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	Sodium Chloride 0.9% 50ml
	Dexamethasone	8mg	PO		
	CARBOPLATIN AUC=5	**DOSE = (GFR + 25) x AUC Max dose 700mg**	IV	30 min	Glucose 5% 500ml
	5-FLUOROURACIL prescribe for a total of 7 days	**300mg/m^2/ day i.e. 2100mg/m^2/7 days**	IV	7 days	Continuous infusion pump
8	**5-FLUOROURACIL** prescribe for a total of 7 days	**300mg/m^2/ day i.e. 2100mg/m^2/7 days**	IV	7 days	Continuous infusion pump
15	**5-FLUOROURACIL** prescribe for a total of 7 days	**300mg/m^2/ day i.e. 2100mg/m^2/7 days**	IV	7 days	Continuous infusion pump

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone	6mg	PO	OM for 3 days
	Metoclopramide	10mg	PO	10mg TDS for 3 days, then 10mg up to TDS PRN. Do not take for more than 5 days continuously.

Cycle 2 to 8 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**TRASTUZUMAB**	**6mg/kg**	IV	30min 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				
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	Sodium Chloride 0.9% 50ml
	Dexamethasone	8mg	PO		
	CARBOPLATIN AUC=5	**DOSE = (GFR + 25) x AUC Max dose 700mg**	IV	30 min	Glucose 5% 500ml
	5-FLUOROURACIL prescribe for a total of 7 days	**300mg/m^2/ day i.e. 2100mg/m^2/7 days**	IV	7 days	Continuous infusion pump
8	**5-FLUOROURACIL** prescribe for a total of 7 days	**300mg/m^2/ day i.e. 2100mg/m^2/7 days**	IV	7 days	Continuous infusion pump
15	**5-FLUOROURACIL** prescribe for a total of 7 days	**300mg/m^2/ day i.e. 2100mg/m^2/7 days**	IV	7 days	Continuous infusion pump

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone	6mg	PO	OM for 3 days
	Metoclopramide	10mg	PO	10mg TDS for 3 days, then 10mg up to TDS PRN. 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 1 hour after the start of trastuzumab				