Indication	HER2-positive unresectable locally advanced, recurrent and/or metastatic gastric cancer or oesophagogastric junction cancer histologically confirmed adenocarcinoma. NB: Trastuzumab is not licensed for use in combination with oxaliplatin, therefore Trust policy regarding the use of unlicensed treatments must be followed.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 21 days Maximum of 8 cycles of OX with trastuzumab followed by maintenance trastuzumab. Maintenance trastuzumab: Continue until disease progression, intolerance 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. • **Cardiotoxicity:** • Caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris. • ECG prior to cycle 1. • ECHO should be monitored at baseline and then every 6 months during treatment or as clinically indicated. • **Trastuzumab:** o 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 o At each nurse assessment patients should be assessed for signs of dyspnoea. • FBC, U&Es and LFTs should be monitored prior to each cycle of cytotoxic chemotherapy and then every 3 months. • If neuts 1.0-1.4 and/or Plts 75-100 d/w consultant. • If neuts <1.0 or PLT <75 defer 1 week. • Before starting treatment GFR (C+G) should be >/= 50ml/min. • **Renal Impairment:** If CrCl <50ml/min dose reduce capecitabine (see SPC) and if CrCl <30ml/min consider dose reduction of oxaliplatin. Capecitabine is contraindicated if CrCl <30ml/min. There are no recommendations for dose adjustments of trastuzumab in renal impairment. • **Hepatic Impairment:** no recommended dose adjustment in hepatic impairment for trastuzumab, oxaliplatin or capecitabine. • **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 prescribers' responsibility to check that the ECHO/MUGA result is satisfactory before continuing treatment.** • 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.

	• Trastuzumab must not be given within 3 weeks of an anthracycline, therefore it must be started a minimum of 3 weeks after administration of the final dose of anthracycline therapy. • **Dose Modification:** ○ Dose reduction of cytotoxic chemotherapy 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. ○ **Oxaliplatin** Refer to Table 1 for oxaliplatin induced neuropathy guidance. ○ **Capecitabine** Interrupt 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. ○ **Trastuzumab:** No recommended dose modifications. • **Infusion related reactions:** ○ **Trastuzumab:** ➢ Patients must be observed closely for infusion related adverse effects for 6 hours after the start of the first dose, 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. • **Common drug interactions: (for comprehensive list refer to BNF/SPC)** ○ **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. ○ **Oxaliplatin** Caution is advised when oxaliplatin is co-administered with other medicinal products known to cause QT interval prolongation. Caution is advised when oxaliplatin treatment is administered concomitantly with other medicinal products known to be associated with rhabdomyolysis. ○ **Trastuzumab** No formal drug interaction studies have been performed. • **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. • **Driving and operating machinery:** Dizziness, fatigue, nausea and somnolence have been reported during treatment, patients should be aware this may affect their ability to drive or operate machinery. • **Missed dose:** 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. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	UGI-070 V1 SPC accessed online 26.07.2023

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

Cycle 1 only: 21 day cycle

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**TRASTUZUMAB** Loading dose	**8mg/kg**	IV	90 mins	In 250ml sodium chloride 0.9%
	Patients must be observed closely for infusion related adverse effects for 6 hours after the start of trastuzumab				
2	Dexamethasone	8mg	PO		
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IV	15 min	NaCl 0.9% 50ml
	Flush with 5% glucose before and after administration of oxaliplatin				
	OXALIPLATIN	**130mg/ m²**	IV	2-6 hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml)
TTO	Drug	Dose	Route	Directions	
	CAPECITABINE	**1250mg/m²/day** **In 2 divided doses**	PO	**For 21 days** (the 1st dose will be taken as the evening dose on day 1 and the last dose is taken the morning of day 22). Take within 30 minutes after food, and approximately every 12 hours. **Available as 150mg and 500mg tablets**	
	Dexamethasone	6mg	PO	OM for 3 days	
	Metoclopramide	10mg	PO	10mg TDS for 3 days then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.	

Cycles 2 –8 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**TRASTUZUMAB**	**6mg/kg**	IV	30 mins (see note above)*	In 250ml sodium chloride 0.9%
	Start oxaliplatin after the end of the trastuzumab observation period (ie 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	15 min	NaCl 0.9% 50ml
	Flush with 5% glucose before and after administration of oxaliplatin				
	OXALIPLATIN	**130mg/ m²**	IV	2-6 hrs	250-500ml 5% glucose (to give a concentration between 0.2 mg/ml and 0.70 mg/ml)
TTO	Drug	Dose	Route	Directions	
Day 1	**CAPECITABINE**	**1250mg/m²/day** **In 2 divided doses**	PO	**For 21 days** (the 1st dose will be taken as the evening dose on day 1 and the last dose is taken the morning of day 22). Take within 30 minutes after food, and approximately every 12 hours. **Available as 150mg and 500mg tablets**	
	Dexamethasone	6mg	PO	OM for 3 days	
	Metoclopramide	10mg	PO	10mg TDS for 3 days 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 Details
1	**TRASTUZUMAB** Maintenance dose	**6mg/kg**	IV	**Over 30 mins if tolerated (see monitoring parameters)**	In 250ml sodium chloride 0.9%

TABLE 1: Introduction

- Use the neuropathy assessment tool on KOMS at each pre-chemo review.
- Symptoms of sensory or functional neuropathy may include tingling or numbness which may persist to the next pre-chemotherapy assessment.
- This guidance is for patients receiving treatment outside the context of a clinical trial. For patients being treated within a clinical trial setting, follow trial protocol (using assessment below as far as possible).
- Do not assess oxaliplatin induced neuropathy using CTC toxicity criteria.
- Dysaesthesia in the jaw is an unpleasant sensation and/or pain in the jaw.
- Laryngopharyngeal spasm is a sensation of difficulty in swallowing / breathing.

Normal occurrence / Caution	**Symptoms**	**Action at nurse assessment**	**Consultant review required / Action by consultant**
Normal occurrence with oxaliplatin	Dysaesthesia (tingling in hands and feet) occurring with and up to 72 hours after infusion	No action required.	
	Dysaesthesia in the jaw (during infusion) and cold induced laryngopharyngeal spasm up to 48 hrs after infusion.	Advise patients to avoid cold drinks / cold weather. Consider administering next oxaliplatin infusion over 6 hours (SmPC).	
First caution / warning sign	Tingling persisting beyond 72 hours or painful cold-induced neuropathy	d/w consultant or clinicians authorised to prescribe chemotherapy Close monitoring at each subsequent cycle. Ask the following specific questions at each nursing assessment: 1. Is the dysaesthesia (during the infusion) and / or cold induced laryngopharyngeal spasm more severe? 2. Has the tingling continued for longer than during the previous cycle and / or is tingling still present when next cycle is due?	1. If yes, consultant review required. For consideration of DR at next cycle or omission of oxaliplatin. 2. If yes, consultant review required, for consideration of DR at next cycle or omission of oxaliplatin
Serious caution	Numbness in hands or feet Severe excitability channel neuropathy during infusion (very rare) seen as severe pain and numbness on infusion Painful neuropathy	Must be reviewed by a consultant Must be reviewed by a consultant Must be reviewed by a consultant	Consider DR or omission of oxaliplatin. Repeat consultant review before next cycle Consider DR or omission of oxaliplatin. Repeat consultant review before next cycle Consider Duloxetine. Starting at 30mg-60mg OD where available on Trust formulary. Alternatively, d/w pain management specialist.
Other cautions	A cumulative dose of 700-800mg/m^2 oxaliplatin has been reached	Must be reviewed by a consultant	

	All patients restarting oxaliplatin based chemotherapy after a break in treatment (this may be due to an intervention such as rectal cancer patients having surgery)	Must be reviewed by a consultant to assess for delayed onset neuropathy

Assessment and action

Notes

- Neurology referral should be considered in severe cases.
- Initial dose reductions should be at a 25% level. If there is no improvement or worsening symptoms, based on an assessment of risk and benefit, consider further dose reduction. Once reduced, doses should not be re-escalated.