ZANIDATAMAB (Ziihera)

INDICATION (ICD10) C22.1

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/ (ZANI1)

1. Zanidatamab monotherapy for the treatment of IHC3+.HER2-positive locally advanced or metastatic biliary tract cholangiocarcinoma cancer after 1 or more lines of systemic treatment (patients who have progressed <6 months from completion of adjuvant therapy will be considered as having received 1 prior line of therapy for advanced disease). Has no known brain metastases or if the patient has brain metastases, the patient is symptomatically stable prior to starting treatment with zanidatamab. PS 0 or 1. (TA833)

REGIMEN

Day 1 Premedication 30-60 minutes prior to infusion:

Dexamethasone	8mg IV bolus
Chlorphenamine	10 mg IV bolus
Paracetamol	1000mg oral
ZANIDATAMAB	20mg/kg in #ml sodium chloride 0.9% IV infusion over *minutes

diluent and diluent volume for dose prescribed as per national standardised product specification

*Administer first dose over 120-150 minutes,
the second dose over at least 90 minutes,
if previous infusions were tolerated and subsequent doses over at least 60 minutes, if previous infusions were tolerated.
Patients should be monitored for signs and symptoms of IRRs during administration and for 30 minutes post completion of infusion. Appropriate emergency medicine and equipment to treat IRRs should be available for immediate use, and IRRs should be managed as specified in dose modifications section.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 14 days until disease progression

ANTI-EMETICS

Minimal risk

CONCURRENT MEDICATION REQUIRED

Zanidatamab	Ensure premedication given before zanidatamab. Lopoeramide if required.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Zanidatamab -

Administer set with 0.2-0.22micron filter
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs, creatinine every dose
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.
LVEF at baseline and at regular intervals during treatment.
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Zanidatamab	Infusion related reactions Left ventricular dysfunction Pneumonitis

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Zanidatamab	-

DOSE MODIFICATIONS

Non-haematological

Zanidatamab
Infusion related reactions

Mild (grade 1)	• Reduce infusion rate by 50%. • Subsequent infusions should start at this reduced rate. • Infusion rate for subsequent infusions may be increased gradually to the rate prior to symptoms, as tolerated.
Moderate (grade 2)	• Hold infusion immediately. • Treat with appropriate therapy. • Resume infusion at 50% of previous infusion rate once symptoms resolve. • Infusion rate for subsequent infusions may be increased gradually to the rate prior to symptoms, as tolerated.
Severe (grade 3)	• Hold infusion immediately. • Promptly treat with appropriate therapy. • Resume infusion at the next scheduled dose at 50% of previous infusion rate once symptoms resolve. • Permanently discontinue for recurrent grade 3 symptoms.
Life threatening (grade 4)	• Hold infusion immediately. • Promptly treat with appropriate therapy. • Permanently discontinue.

Left ventricular dysfunction (LVEF)

Absolute decrease of ≥16% points in LVEF from pre-treatment baseline LVEF value below 50% and absolute decrease of ≥10% points below pre-treatment baseline	• Withhold treatment for at least 4 weeks. • Repeat LVEF assessment within 4 weeks. • Resume treatment within 4 to 8 weeks, if LVEF returns to normal limits and the absolute decrease is ≤15% points from baseline. • If LVEF has not recovered to within 15% points from baseline, permanently discontinue.

Pneumonitis

Confirmed grade ≥2	• Permanently discontinue.

Hepatic impairment
Zanidatamab
Dose adjustments are not required for patients with mild hepatic impairment (total bilirubin ≤ULN and AST >ULN or total bilirubin 1-1.5xULN and any AST).
Zanidatamab has not been evaluated in patients with moderate (total bilirubin >1.5-≤3xULN and any AST) to severe (total bilirubin >3xULN and any AST) hepatic impairment. However due to minor involvement of hepatic processes in the clearance of zanidatamab, no dose adjustment is recommended for patients with hepatic impairment as no difference in exposure is expected.

Renal impairment.
Zanidatamab
Dose adjustments are not required for patients with mild or moderate renal impairment (eGFR 30-89mL/min estimated using the CKD-EPI).
Zanidatamab has not been evaluated in patients with severe renal impairment or with end-stage renal disease with or without dialysis. However, due to minor involvement of renal processes in the clearance of zanidatamab, no dose adjustment is recommended for patients with renal impairment as no difference in exposure is expected.

REFERENCES
1 CDF list