GEMCITABINE CAPECITABINE

INDICATION (ICD10) C25

1. Advanced or metastatic adenocarcinoma of the pancreas with a PS 0, 1 or 2, where first line chemotherapy is to be used (unlicensed)
2. Adjuvant pancreatic cancer where either microscopic clearance (R0) or microscopic infiltration (R1) of the margins has been achieved following surgical resection. Treatment should commence within 12 weeks of surgery and continue for six months (unlicensed)

REGIMEN

Day 1 GEMCITABINE 1000mg/m^2 infusion in #ml sodium chloride 0.9% IV infusion over 30 minutes

Days 1 to 21 CAPECITABINE 830mg/m^2 twice daily (1660mg/m^2/day) tablets followed by a 7 day rest

Days 8 and 15 GEMCITABINE 1000mg/m^2 infusion in #ml sodium chloride 0.9% IV infusion over 30 minutes

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

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days for up to 6 cycles

ADMINISTRATION

Tablets should be taken 12 hours apart.
Swallowed with water within 30 minutes after a meal, or dissolve in 200ml luke warm water, stir thoroughly (squash may be added if unpalatable).

ANTI-EMETICS

Low risk days 1 to 21

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Gemcitabine	None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Gemcitabine – neutral

No filters required
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC every dose, U&E, LFTs and creatinine every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Baseline weight and every cycle
DPYD (dihydropyrimidine dehydrogenase) test

MAIN TOXICITES AND ADVERSE REACTIONS

Capecitabine	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function (consider ECG at baseline). To minimise risk of anthracycline induced cardiac failure signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. All patients should be told to report any cardiac symptoms immediately and should be told to stop the medication immediately if any suspicion of cardiac problems. Stomatitis
Gemcitabine	Diarrhoea – see dose modifications, treat with loperamide or codeine Mucositis – see dose modifications, use routine mouthcare

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Capecitabine	Brivudine and analogues should be avoided Warfarin Phenytoin Allopurinol

DOSE MODIFICATIONS
DPYD variant identified follow national or local DPD dose modification guidelines.

Haematological
Capecitabine
Neutrophils <0.5x10^9/L and platelets <50x10^9/L discuss with consultant about continuing capecitabine.

Gemcitabine

Neutrophils >1.5x10^9/L and platelets >100x10^9/L	give 100% dose
Neutrophils 1.0-1.5x10^9/L or platelets 75-100x10^9/L	Discuss with consultant
Neutrophils <1.0x10^9/L or platelets <100x10^9/L	delay treatment (day 1) or omit treatment (day 8)

Non-haematological

Capecitabine

Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction).

Once the dose has been reduced it should not be increased at a later time.

When capecitabine is stopped for toxicity, the doses are omitted and not delayed.

Toxicity grades	Dose changes within a treatment cycle	Dose adjustment for next cycle/dose (% of starting dose)
Grade 2 - 1st appearance	Interrupt until resolved to grade 0-1	100%
Grade 2 - 2nd appearance	Interrupt until resolved to grade 0-1	75%
Grade 2 - 3rd appearance	Interrupt until resolved to grade 0-1	50%
Grade 2 - 4th appearance	Discontinue treatment permanently	Not applicable
Grade 3 - 1st appearance	Interrupt until resolved to grade 0-1	75%
Grade 3 - 2nd appearance	Interrupt until resolved to grade 0-1	50%
Grade 3 - 3rd appearance	Discontinue treatment permanently	Not applicable
Grade 4 - 1st appearance	Discontinue permanently OR if physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50%
Grade 4 - 2nd appearance	Discontinue treatment permanently	Not applicable

Gemcitabine

Diarrhoea and/or mucositis grade 2 toxicity	omit until toxicity resolved then restart at 100% dose
Diarrhoea and/or mucositis grade 3	omit until toxicity resolved then restart at 75% dose
Diarrhoea and/or mucositis grade 4	omit until toxicity resolved then restart at 50% dose

Hepatic impairment

Capecitabine

Bilirubin of >3xULN or ALT/AST >2.5xULN	Interrupt Capecitabine Treatment may be resumed when bilirubin decreases to <3xULN or hepatic aminotransferases decrease to <2.5xULN.

Gemcitabine

Bilirubin >27µmol/L	initiate treatment with 80% dose

Renal impairment

Capecitabine

CrCl (ml/min) >50	give 100% dose
CrCl (ml/min) 30-50	give 75% dose
CrCl (ml/min) <30	contraindicated

Gemcitabine
No need for dose adjustment

REFERENCES

1. Gemcap trial arm 2
2. ESPAC4