PEMIGATINIB (Pemazyre)

INDICATION (ICD10) C22

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (PEMIG1)

1. Pemigatinib monotherapy for locally advanced or metastatic unresectable cholangiocarcinoma which has a fibroblast growth factor receptor 2 gene fusion/rearrangement in patients with disease progression during or after previous systemic therapy Either has no known brain metastases or if the patient has brain metastases, the patient is symptomatically stable prior to starting treatment with pemigatinib. PS 0, 1 or 2. (TA722)

REGIMEN

Days 1 to 14 PEMIGATINIB 13.5mg orally daily followed by a 7 day rest

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days until disease progression.
A first formal medical review as to whether treatment with pemigatinib should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment.

ADMINISTRATION

Available as 4.5mg, 9mg and 13.5mg tablets
Swallowed whole with water with or without food.

ANTI-EMETICS

Minimal emetic risk

CONCURRENT MEDICATION REQUIRED

Pemigatinib	Ocular demulcents to prevent or treat dry eye.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC and U&E, Ca^{++} and PO_4^{3+} every cycle
LFTs every cycle
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥75
Creatinine every cycle
Baseline weight and every cycle
Ophthalmological examination, including optical coherence tomography (OCT) should be performed prior to initiation of therapy and every 2 months for the first 6 months of treatment, every 3 months afterwards, and urgently at any time for visual symptoms.

MAIN TOXICITES AND ADVERSE REACTIONS

Pemigatinib	Diarrhoea Dry eye Hyperphosphataemia Hyponatraemia Hypophosphataemia Mucositis Serous retinal detachment

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

Pemigatinib	Concomitant use of pemigatinib with proton pump inhibitors should be avoided. Concomitant use of pemigatinib with strong CYP3A4 inhibitors should be avoided. Patients should be advised to avoid eating grapefruit or drinking grapefruit juice while taking pemigatinib. Concomitant use of pemigatinib with strong or moderate CYP3A4 inducers is not recommended.

DOSE MODIFICATIONS
Pemigatinib

Recommended dose	13.5mg once daily
First dose adjustment	9mg once daily
Second dose adjustment	4.5mg once daily

Non-haematological

Hyperphosphataemia (1mg/dl≡3.1mmol/l)

>5.5-≤7mg/dL	• pemigatinib should be continued at current dose.
>7-≤10mg/dL	• pemigatinib should be continued at current dose, phosphate-lowering therapy should be initiated, serum phosphate should be monitored weekly, dose of phosphate lowering therapy should be adjusted as needed until level returns to <7mg/dL. • pemigatinib should be withheld if levels do not return to <7mg/dL within 2 weeks of starting a phosphate lowering therapy. pemigatinib and phosphate-lowering therapy should be restarted at the same dose when level returns to <7mg/dL. • Upon recurrence of serum phosphate at >7mg/dL with phosphate-lowering therapy, pemigatinib should be reduced 1 dose level.
>10mg/dL	• pemigatinib should be continued at current dose, phosphate-lowering therapy should be initiated, serum phosphate should be monitored weekly and dose of phosphate lowering therapy should be adjusted as needed until level returns to <7mg/dL. • pemigatinib should be withheld if levels continue >10mg/dL for 1 week. pemigatinib and phosphate-lowering therapy should be restarted 1 dose level lower when serum phosphate is <7mg/dL. • If there is recurrence of serum phosphate >10mg/dL following 2 dose reductions, pemigatinib should be permanently discontinued.

Hypophosphataemia

Discontinuing phosphate-lowering therapy and low phosphate diet should be considered during the 7 day pemigatinib breaks, or if serum phosphate level falls below the normal range

Serous retinal detachment

Asymptomatic	• pemigatinib should be continued at current dose. Monitoring should be performed.
Moderate decrease in visual acuity (best corrected visual acuity 20/40 or better or ≤3 lines of decreased vision from baseline); limiting instrumental activities of daily living	• pemigatinib should be withheld until resolution. If improved on subsequent examination, pemigatinib should be resumed at the next lower dose level. • If it recurs, symptoms persist or examination does not improve, permanent discontinuation of pemigatinib should be considered based on clinical status.
Marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or >3 lines decreased vision from baseline up to 20/200); limiting activities of daily living	• pemigatinib should be withheld until resolution. If improved on subsequent examination, pemigatinib may be resumed at 2 dose levels lower. • If it recurs, symptoms persist or examination does not improve, permanent discontinuation of pemigatinib should be considered, based on clinical status.
Visual acuity worse than 20/200 in affected eye; limiting activities of daily living	• pemigatinib should be withheld until resolution. If improved on subsequent examination, pemigatinib may be resumed at 2 dose levels lower. • If it recurs, symptoms persist or examination does not improve, permanent discontinuation of pemigatinib should be considered, based on clinical status.

Hepatic impairment

Pemigatinib

No dose adjustment necessary in patients with mild or moderate (Child Pugh A or B) hepatic impairment.

For patients with severe hepatic impairment, the pemigatinib dose should be reduced.

Renal impairment

Pemigatinib

No dose adjustments are necessary in patients with CrCl ≥30ml/min, or mild or moderate renal impairment or in patients with end-stage renal disease and on haemodialysis.

For patients with CrCl <30ml/min and not on dialysis, the pemigatinib dose should be reduced.

REFERENCES

1. Abou-Alfa, G et al; Lancet 2020; 21 (5): 671-684