Chemotherapy Protocol

CHOLANGIOCARCINOMA

PEMIGATINIB

Regimen

- Cholangiocarcinoma - Pemigatinib

Indication

Pemigatinib for locally advanced or metastatic cholangiocarcinoma which has a fibroblast growth factor receptor 2 gene fusion/rearrangement in patients with disease progression during or after previous systemic therapy where:

- The patient has a histologically or cytologically confirmed diagnosis of cholangiocarcinoma (that is intra-hepatic or extrahepatic in origin).
- The cholangiocarcinoma has been tested for fibroblast growth factor receptor 2 (FGFR2) gene fusion or rearrangement with a validated test and the result is positive.
- The patient has unresectable locally advanced or metastatic disease.
- The patient has previously been treated with systematic therapy for cholangiocarcinoma and the disease has progressed during or after such therapy.
- The patient has a ECOG performance status of 0, 1 or 2
- The patient either has no known brain metastases or if the patient has brain metastases, the patient is symptomatically stable prior to starting treatment with pemigatinib.
- Pemigatinib will be used as monotherapy.
- The patient will be treated until loss of benefit or excessive toxicity or patient choice to discontinue treatment, whichever is sooner.
- Pemigatinib can cause serous retinal detachment and therefore ophthalmological examination (including optical coherence tomography) should be arranged prior to initiation and then whilst on therapy.
- Pemigatinib can increase the risk of developing hyper-phosphataemia during treatment and the prescriber understands the following: requirement for monitoring of phosphate levels, the role of phosphate-lowering measures and the need to review such measures if pemigatinib treatment is deferred or discontinued.
- Patients should avoid taking proton pump inhibitors whilst taking pemigatinib.
- The 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.

Toxicity

Drug	Adverse Effect
Pemigatinib	Hyponatraemia, hyperphosphataemia, hypophosphataemia, dysgeusia, dry eyes, nausea, stomatitis, diarrhoea, constipation, dry mouth, palmer-planter erythrodysesthesia syndrome, nail toxicity, alopecia, dry skin, fatigue, arthralgia, creatinine increase, serous retinal detachment

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, U&Es (including phosphate and calcium) and LFTs every 28 days
- Ophthalmological examination (including optical coherence tomography) should be arranged prior to initiation of pemigatinib, then every 2 months for the first 6 months and every 3 months thereafter.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well. The toxicities below should be read in conjunction with the relevant Summary of Product Characteristics (www.medicines.org.uk).

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for SACT that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Dose reduction steps

Dose reduction steps	Dose
1	13.5mg once a day
2	9mg once a day
3	4.5mg once a day
4	Stop treatment

Haematological

Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L).

Discuss with prescriber if platelets $<75x10^9$/L or neutrophils $<1x10^9$/L as dose reduction may be required.

Hepatic Impairment

Dose adjustment is not required for patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. For patients with severe (Child Pugh C) hepatic impairment, the dose of patients taking 13.5mg pemigatinib once daily reduced to 9mg pemigatinib once daily and the dose of patients who are taking 9mg pemigatinib once daily reduced to 4.5mg pemigatinib once daily.

Renal Impairment

Dose adjustment is not required for patients with mild or renal impairment or end stage renal disease on haemodialysis. For patients with severe renal impairment (Circle <30ml/min), the dose of patients taking 13.5mg pemigatinib once daily should be reduced to 9mg pemigatinib once daily and the dose of patients who are taking 9mg pemigatinib once daily reduced to 4.5mg pemigatinib once daily.

Pemigatinib may increase serum creatinine by decreasing renal tubular secretion of creatinine, which may not affect glomerular function. Alternative markers of renal function should be considered if persistent elevations in serum creatinine are observed.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Hyperphosphataemia

All patients with a phosphate greater than 5.5mg/dL should be advised to adopt a low phosphate diet. Discontinuing phosphate-lowering therapy and diet should be considered during pemigatinib treatment breaks/discontinuing treatment or if serum phosphate levels fall below the normal range.

Adverse reaction	Pemigatinib dose modification
Greater than 5.5mg/dL to less than or equal to 7mg/dL	• Pemigatinib should be continued at current dose
Greater than 7mg/dL to less than or equal to 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 until level returns to less than 7mg/dL • Pemigatinib should be withheld if level do not return to less than 7mg/dL within 2 weeks of starting phosphate lowering therapy. Pemigatinib and phosphate-lowering therapy should be restarted at the same dose when level returns to less than 7mg/dL. • Upon recurrence of serum phosphate at greater than 7mg/dL with phosphate lowering therapy, pemigatinib should be reduced by 1 dose level.

Greater than 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 until level returns to less than 7mg/dL • Pemigatinib should be withheld if level continue greater than 10mg/dL for 1 week. Pemigatinib and phosphate-lowering therapy should be restarted 1 dose level lower when serum phosphate is less than 7mg/dL. • If there is a recurrence of serum phosphate greater than 10mg/dL following 2 dose reductions, pemigatinib should be permanently discontinued.

Serous retinal detachment

Pemigatinib can cause serous retinal detachment, which may present with symptoms such as blurred vision, visual floaters or photopsia. This can moderately influence the ability to drive and operate machinery.

Adverse reaction	Pemigatinib dose modification
Asymptomatic	• Pemigatinib should be continued at current dose. • Continue to monitor.
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 recurs, symptoms persist or examination doses not improve, permanent discontinuation should be considered.
Marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or >3 lines decreased from baseline up to 20/200); limiting activities of daily living.	• Pemigatinib should be withheld until resolution. If improved on subsequent examination, pemigatinib should be resumed at 2 dose levels lower. • If recurs, symptoms persist or

	examination doses not improve, permanent discontinuation should be considered.
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 should be resumed at 2 dose levels lower. • If recurs, symptoms persist or examination doses not improve, permanent discontinuation should be considered.

Dry eye

Pemigatinib can cause dry eyes and patients should use ocular demulcents in order to prevent or treat dry eyes as required.

Regimen

21 day cycle continued as long as clinical benefit is observed or until unacceptable toxicity occurs (12 cycles will be set in Aria)

Drug	Dose	Days	Administration
Pemigatinib	13.5mg once a day	1-14.	Oral

Dose Information

- Pemigatinib is available as 13.5mg, 9mg and 4.5mg tablets.

Administration Information

- Pemigatinib should be taken at approximately the same time every day.
- Pemigatinib tablets should be swallowed whole, patients should not crush, chew or dissolve the tablets.
- Pemigatinib may be taken with or without food.
- If a dose of pemigatinib is missed by 4 or more hours or vomiting occurs after taking a dose, an additional dose should not be administered, and dosing should be resumed with the next scheduled dose.
- Pemigatinib has moderate influence on the ability to drive and use machines. Adverse reactions such as fatigue and visual disturbances have been associated with pemigatinib. Therefore, caution should be recommended when driving or operating machines.

Additional Therapy

- Metoclopramide 10mg three times a day when required oral. This will not be included in the regimen in ARIA. It can be added from favourites.

- Mouthwashes according to local or national policy on the treatment of mucositis

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to pemigatinib.

- It must be made clear to all staff, including those in the community, that pemigatinib should only be prescribed under the supervision of an oncologist.

- Pemigatinib interact with many other agents. Always check for drug interactions.

References
1. Incyte Biosciences UK Ltd (2022). Pemazyre 13.5mg tablets summary of product characteristics. Available from: www.medicines.org.uk. Accessed 7/7/2022.
2. Abou-Alf et al (2020). Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study (FIGHT-202). The Lancet Oncology. 21 (5): 671-684.

REGIMEN SUMMARY

Pemigatinib

Day 1

Take Home Medicines

1. Pemigatinib 13.5mg once a day for 14 days oral
   Administration Instructions
   Oral SACT

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2022	None	Alexandra Pritchard Pharmacist	

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols are only one source of information. They should be read in conjunction with the latest Summary of Product Characteristics and published information.