Pemigatinib Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
As monotherapy for the treatment of adults with locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that have progressed after at least one prior line of systemic therapy.	C22	00889a	N/A

* This applies to post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Pemigatinib is administered orally once daily on day 1-14 of a 21 day cycle. Treatment should be continued until disease progression or unacceptable toxicity.

Day	Drug	Dose	Route	Cycle
1-14	Pemigatinib	13.5mg once daily	PO	Every 21 days
The tablets should be taken at approximately the same time every day. Patients should not crush, chew, split 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 is commonly available as 4.5mg, 9mg and 13.5mg tablets				

ELIGIBILITY:

- Indication as above
- ECOG 0-2
- *FGFR2* fusion or rearrangement as confirmed by a validated test method

CAUTIONS:

- Untreated brain or CNS metastases
- Patients with clinically significant medical eye disorders

EXCLUSIONS:

- Hypersensitivity to pemigatinib or to any of the excipients
- Prior treatment with FGFR inhibitor
- Pregnancy
- Breastfeeding

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Phosphate, calcium
- Ophthalmological assessment

Regular tests:

- FBC, renal and liver profile
- Phosphate, calcium
- Ophthalmological assessment every 2 months for the first 6 months of treatment and every 3 months afterwards as clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Dose modifications or interruption of dosing should be considered for the management of toxicities.
- Pemigatinib dose reduction levels are summarised in table 1
- Dose modifications for hyperphosphataemia, serous retinal detachment and renal/hepatic impairment are provided in tables 2, 3 and 4 respectively

Table 1: Recommended pemigatinib dose reduction levels

Dose	Dose reduction levels	
	First	Second
13.5 mg taken orally once daily for 14 days followed by 7 days off therapy	9 mg taken orally once daily for 14 days on, followed by 7 days off therapy	4.5 mg taken orally once daily for 14 days on, followed by 7 days off therapy

* Treatment should be permanently discontinued if patient is unable to tolerate 4.5 mg pemigatinib once daily.

Table 2: Dose modifications for hyperphosphataemia

Adverse reaction	Dose modification
>5.5 mg/dL - ≤7 mg/dL	• Pemigatinib should be continued at current dose.
>7 mg/dL - ≤10 mg/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 <7 mg/dL. • Upon recurrence of serum phosphate at >7 mg/dL with phosphate-lowering therapy, pemigatinib should be reduced 1 dose level.
>10 mg/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 <7 mg/dL. • Pemigatinib should be withheld if levels continue >10 mg/dL for 1 week. Pemigatinib and phosphate-lowering therapy should be restarted 1 dose level lower when serum phosphate is <7 mg/dL. • If there is recurrence of serum phosphate >10 mg/dL following 2 dose reductions, pemigatinib should be permanently discontinued.

Table 3: Dose modifications for serous retinal detachment

Adverse reaction	Dose modification
Asymptomatic	• Pemigatinib should be continued at current dose. Monitoring should be performed as described in the baseline and regular tests sections above. .
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.

Renal and Hepatic Impairment:

Table 4: Dose modifications in renal and hepatic impairment

Renal Impairment		Hepatic Impairment	
CrCl (mL/min)	**Dose**	Child-Pugh A/B or Mild/moderate	No dose adjustment is needed
≥30	No dose adjustment is needed	Child Pugh C or Severe	Reduce dose from 13.5mg once daily to 9mg once daily and from 9mg once daily to 4.5mg once daily
<30	Reduce dose from 13.5mg once daily to 9mg once daily and from 9mg once daily to 4.5 mg once daily		
Haemodialysis	No dose adjustment is needed		
Recommendations from Giraud et al, 2023			

Dose Modification for use with CYP3A inhibitors/inducers:

- Concurrent use of strong CYP3A4 inhibitors, including grapefruit juice, should be avoided during treatment with pemigatinib
- If co-administration with a strong CYP3A4 inhibitor or a moderate to strong inducer the dose of pemigatinib should be reduced as descried in Table 5

Table 5: Management of potential pemigatinib interactions with CYP3A inhibitors/inducers

Inhibitors	Dose	Dose modification
Strong CYP3A4 inhibitors	13.5mg once daily	Reduce dose to 9mg once daily
	9mg once daily	Reduce dose to 4.5mg once daily
Strong or moderate CYP3A4 inducers	Co-administration not recommended	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting Available on the NCCP website

Minimal to low (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

- No specific recommendations

OTHER SUPPORTIVE CARE:

- Low phosphate diet in all patients should be initiated when serum phosphate level is > 5.5 mg/dL and adding a phosphate-lowering therapy should be considered when level is > 7 mg/dL. The dose of phosphate-lowering therapy should be adjusted until serum phosphate level returns to < 7 mg/dL. Discontinuing phosphate-lowering therapy and diet should be considered during treatment breaks or if serum phosphate level falls below normal range.
- Both diarrhoea and constipation are common side effects associated with pemigatinib treatment. Patients may require either laxatives or anti-diarrhoeals
- Refer to local skin care policy for management of skin adverse reactions
- Patients should use ocular demulcents, in order to prevent or treat dry eye, as needed.
- Women of childbearing potential and male patients with female partners of childbearing potential should be advised to use effective contraception during treatment with pemigatinib and for 1 week after the last dose.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.
- This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions

REGIMEN SPECIFIC COMPLICATIONS

- **Hyperphosphataemia:** Hyperphosphataemia is a pharmacodynamic effect expected with pemigatinib administration. Prolonged hyperphosphataemia can cause precipitation of calcium-phosphate crystals that can lead to hypocalcaemia, soft tissue mineralisation, anaemia, secondary hyperparathyroidism, muscle cramps, seizure activity, QT interval prolongation, and arrhythmias. Soft tissue mineralization, including cutaneous calcification, calcinosis and non-uraemic calciphylaxis have been observed with pemigatinib treatment. Recommendations for management of hyperphosphataemia include dietary phosphate restriction, administration of phosphate-lowering therapy, and dose modification when required, please refer to Table 2.
- **Ocular toxicity:** Pemigatinib can cause serous retinal detachment reactions, which may present with symptoms such as blurred vision, visual floaters, or photopsia. 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. For serous retinal detachment reactions, the dose modification guidelines should be followed as outline in Table 3. Careful consideration should be taken with patients that have clinically significant medical eye disorders, such as retinal disorders, including but not limited to, central serous retinopathy, macular/retinal degeneration, diabetic retinopathy, and previous retinal detachment. Pemigatinib can cause dry eye, patients should use ocular demulcents, in order to prevent or treat dry eye, as needed.

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

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Abou-Alfa, GK et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. Lancet Oncol. 2020 Mar 20;21(5):671–684
2. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis Version 2.2024 – September 27, 2024. Accessed June 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf
4. Pemigatinib (Pemazyre®) Summary of Product Characteristics. Last updated 12/9/2023. Accessed December 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/pemazyre-epar-product-information_en.pdf#

Version	Date	Amendment	Approved By
1	20/01/2025		Prof Maccon Keane

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