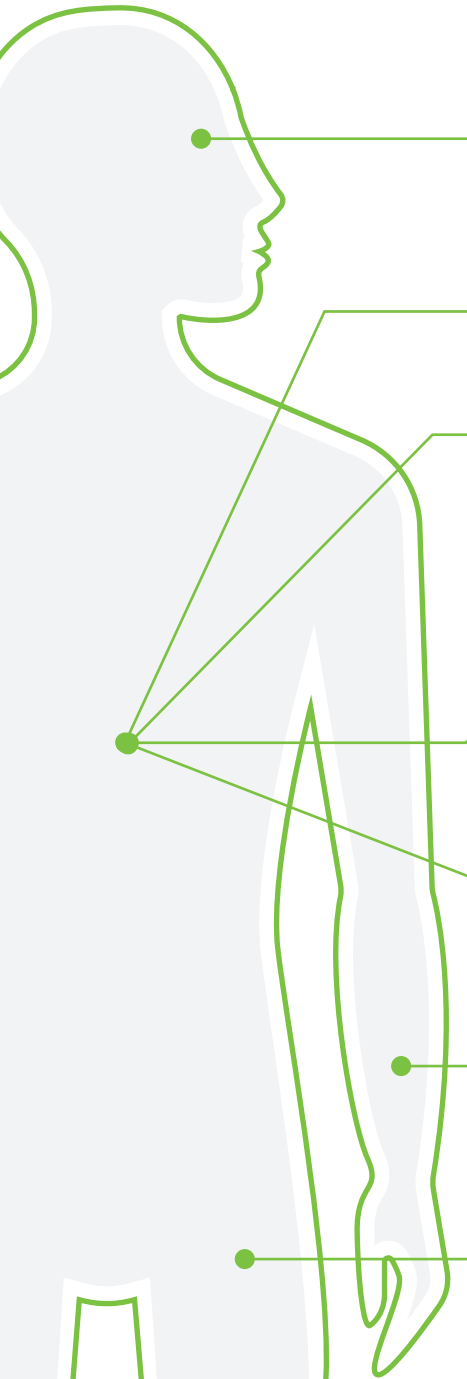
Pemigatinib ▼ adverse event management and dosing guide

Pemigatinib has a conditional marketing authorisation 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[1]

Please see SmPC for full details of special warnings and precautions for pemigatinib before prescribing



Adverse events[1,2]*	% (n)†	Serious adverse events[1,2]*	% (n)†
Eye disorders			
Dry eye	27.9 (41)	Retinal detachment	0.7 (1)
Serous retinal detachment	4.8 (7)	Non-arteritic optic ischaemic neuropathy	0.7 (1)
		Retinal artery occlusion	0.7 (1)
Metabolic and blood chemistry			
Hyperphosphataemia	60.5 (89)	Hyponatraemia	2.0 (3)
Hypophosphataemia	23.8 (35)	Increased blood creatinine	1.4 (2)
Nervous system			
Dysgeusia	36.1 (53)		
Gastrointestinal			
Diarrhoea	47.6 (70)		
Nausea	41.5 (61)		
Stomatitis	38.1 (56)		
Constipation	36.7 (54)		
Dry mouth	34.0 (50)		
Constitutional			
Fatigue	43.5 (64)		
Skin disorders			
Alopecia	49.7 (73)		
Nail toxicity	44.9 (66)		
Dry skin	21.8 (32)		
Palmar-plantar erythrodysesthesia syndrome	16.3 (24)		
Musculoskeletal			
Arthralgia	29.9 (44)		

Patient monitoring and management[1]

Serous retinal detachment

- Ophthalmological examination, including optical coherence tomography prior to initiation and every 2 months for the first 6 months, every 3 months afterwards and urgently at any time for visual symptoms

Dry eye

- Patients should use ocular demulcents in order to prevent or treat dry eye, as needed

Hyper/hypophosphataemia

- Recommendations for management of hyperphosphataemia include dietary phosphate restriction, administration of phosphate-lowering therapy and dose modification when required (see overleaf for specific guidance)
- For hypophosphataemia, discontinuation of phosphate-lowering therapy and diet should be considered during pemigatinib treatment breaks or if serum phosphate level falls below normal range
- For patients presenting with hyperphosphataemia or hypophosphataemia, additional close monitoring and follow-up is recommended regarding dysregulation of bone mineralisation

Dose reduction: see overleaf[1]

- May be required to mitigate adverse events
- See overleaf for specific guidance on eye disorders and hyperphosphataemia

1. PEMAZYRE® (pemigatinib). Summary of Product Characteristics. 2023 (data cutoff: 08 July 2021).
2. Incyte Data on File.

*Adverse events were reported in the FIGHT-202 registrational trial (N=147).[1,2]
†Patient numbers for adverse/serious adverse events are taken from Incyte Data on File.[2]

Pemigatinib dose-reduction steps[1]

Recommended dose	Level 1 reduction	Level 2 reduction	
13.5 mg once daily (14 days on/7 days off)	9 mg once daily (14 days on/7 days off)	4.5 mg once daily (14 days on/7 days off)	Discontinue if patient unable to tolerate pemigatinib 4.5 mg once daily

Serous retinal detachment[1]

Moderate decrease in visual acuity (BCVA of 20/40 or better or ≤3 lines of decreased vision from baseline; limiting instrumental activities of daily living).	Withhold until resolution; if improved resume at next lower dose level.	**Consider discontinuation if condition recurs, or if symptoms persist or do not improve on examination**
Marked decrease in visual acuity (BCVA worse than 20/40 or >3 lines decreased vision from baseline up to 20/200; limiting activities of daily living).	Withhold until resolution; if improved resume at two dose levels lower.	
Visual acuity worse than 20/200 in affected eye; limiting activities of daily living.	Withhold until resolution; if improved resume at two dose levels lower.	

BCVA, best corrected visual acuity.

Hyperphosphataemia[1]

Serum phosphate >5.5 to ≤7 mg/dL	Pemigatinib should be continued at current dose.
Serum phosphate >7 to ≤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 <7 mg/dL. Pemigatinib should be withheld if levels do not return to <7 mg/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.
Serum phosphate >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.

1. PEMAZYRE® (pemigatinib). Summary of Product Characteristics. 2023 (data cutoff: 08 July 2021).
2. Incyte Data on File.

PRESCRIBING INFORMATION

PEMAZYRE®▼(pemigatinib) 4.5, 9, 13.5 mg tablets
contains Microcrystalline cellulose (E-460), Sodium starch glycolate (Type A), Magnesium stearate (E-572).

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See below for how to report adverse reactions.

Indication: Pemazyre monotherapy is indicated 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.

Dosage and administration: The recommended dose is 13.5 mg pemigatinib taken once daily for 14 days followed by 7 days off therapy. Therapy should be initiated by a physician experienced in biliary tract cancer. Confirm FGFR2 positive status prior to starting treatment. Treatment should be continued as long as the patient does not show evidence of disease progression or unacceptable toxicity.

Contraindications: Hypersensitivity to pemigatinib or excipients. Concomitant use of pemigatinib with St John's wort.

Warnings and precautions: Consult the Summary of Product Characteristics (SmPC) for full details of potential toxicities and drug interactions, as well as information on monitoring and management, including recommended dose modifications.

Hyperphosphataemia: Hyperphosphataemia is a pharmacodynamic effect expected with pemigatinib. Effective management strategies for hyperphosphataemia include dietary phosphate restriction, phosphate-lowering therapy and dose modification. Consult the SmPC for full details.

Hypophosphataemia: Consider discontinuing phosphate-lowering therapy and increasing dietary phosphate if hypophosphataemia occurs. Consult the SmPC for full details.

Serous retinal detachment: Pemigatinib can cause serous retinal detachment reactions. Symptoms can include blurred vision, visual floaters, or photopsia. Ophthalmological examination, including optical coherence tomography (OCT) should be performed prior to starting pemigatinib and throughout treatment. Consult the SmPC for full details of OCT requirements and dose modification guidelines for serous retinal detachment reactions.

Dry eye: Pemigatinib can cause dry eye. Treat with ocular demulcents as needed.

Blood creatinine increase: Pemigatinib may increase serum creatinine by decreasing renal tubular secretion of creatinine. Alternative markers of renal function should be considered if persistent elevations in serum creatinine are observed.

Hepatic or renal impairment: Dose adjustment is recommended when administering pemigatinib to patients with severe hepatic or renal impairment.

Central nervous system (CNS) metastasis: Since untreated or progressing brain/CNS metastasis were not allowed in the study, efficacy in this population has not been evaluated and no dose recommendations can be made, however the blood-brain barrier penetration of pemigatinib is expected to be low.

Driving and operating machinery: Adverse reactions of fatigue and symptoms associated with retinal detachment may influence the ability to drive and operate machinery.

Drug interactions: If concurrent use of strong CYP3A4 inhibitors is necessary, the daily dose of pemigatinib should be reduced. Consult the SmPC for full details and for information on all potential drug interactions.

Pregnancy and breast-feeding: Pemigatinib can cause foetal harm when administered during pregnancy. Women of childbearing potential, including partners of male patients, should use effective contraception during treatment with pemigatinib and for 1 week after the last dose. Discontinue breast-feeding during treatment with pemigatinib and for 1 week following last dose.

Undesirable effects: The most common adverse drug reactions (ADRs) were hyperphosphataemia, alopecia, diarrhoea, nail toxicity, fatigue, nausea, dysgeusia, stomatitis, constipation, dry mouth, dry eye, arthralgia, hypophosphataemia, dry skin, and palmar-plantar erythrodysaesthesia syndrome. The most common serious adverse reactions were hyponatraemia and blood creatinine increase (see SmPC for details of all ADRs).

Quantities and marketing authorisation numbers:
4.5 mg dose (14 or 28 tablets) EU/1/21/1535/001 002, PLGB 42338/0008
9 mg dose (14 or 28 tablets) EU/1/21/1535/003 004, PLGB 42338/0009
13.5 mg dose (14 or 28 tablets) EU/1/21/1535/005 006, PLGB 42338/0010

Cost (ex. VAT): 4.5 mg x 14 tablets £7,159; 9 mg x 14 tablets £7,159; 13.5 mg x 14 tablets £7,159.

Legal categorisation: POM (prescription only medicine).

Marketing authorisation holder:
Great Britain: Incyte Biosciences UK Ltd, First Floor Q1, The Square, Randalls Way, Leatherhead, KT22 7TW, UK.
United Kingdom (Northern Ireland): Incyte Biosciences Distribution B.V. Paasheuvelweg 25, 1105 BP Amsterdam, Netherlands.

Date of preparation: April 2021. UK/PEMA/P/21/0005

Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Incyte by calling 03301003677 (Great Britain)
00-800-0002-7423 (United Kingdom (Northern Ireland)).

UK/PEMA/P/23/0037
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