PrPEMAZYRE® has been issued conditional marketing authorization pending the results of studies to verify its clinical benefit. Patients should be advised of this conditional marketing authorization.

Pr Pemazyre® NEW
pemigatinib tablets
13.5 mg • 9 mg • 4.5 mg

Incyte

PEMAZYRE® RECOMMENDED DOSING AND ADMINISTRATION[1]

A guide for starting patients on PEMAZYRE®[1]

PEMAZYRE® (pemigatinib) is indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or other rearrangement.[1]

FGFR2: fibroblast growth factor receptor 2.

PEMAZYRE® patient selection[1]

Before initiating PEMAZYRE® treatment[1]

- ☑ Confirm the presence of an FGFR2 fusion or rearrangement using a validated test
- ☑ Perform ophthalmological exams including:
  - Visual acuity test
  - Slit-lamp examination
  - Fundoscopy
  - OCT

  Repeat these ophthalmological exams every 2 months for the first 6 months of treatment and every 3 months afterwards, and urgently at any time for visual symptoms.
- ☑ Verify the pregnancy status of female patients

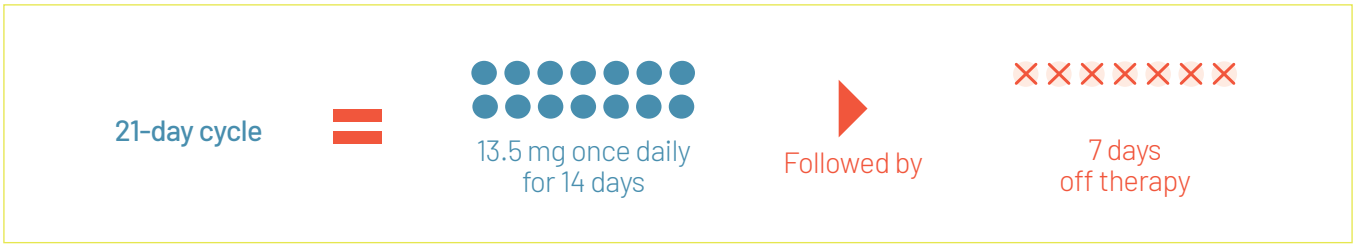
PEMAZYRE® may cause fetal harm and should not be used during pregnancy.

FGFR2: fibroblast growth factor receptor 2; OCT: optical coherence tomography.

Recommended PEMAZYRE® dosing and administration[1]

PEMAZYRE® offers the convenience of a daily oral tablet[1]

The recommended dosage of PEMAZYRE® is 13.5 mg orally once daily for 14 consecutive days followed by 7 days off therapy, in 21-day cycles. Continue treatment until disease progression or unacceptable toxicity.



PEMAZYRE® administration[1]

PEMAZYRE® can be taken with or without food.

PEMAZYRE® should not be taken with grapefruit, its juice, or grapefruit extract.

Pemazyre NEW pemigatinib tablets 13.5mg · 9mg · 4.5mg

Recommended PEMAZYRE® dosing and administration[1] (cont'd)

Missed dose[1]

If it has been ≥4 hours, advise patients not to take their missed dose and to resume their usual dosing schedule the next day.

If it has been <4 hours, advise patients to take their PEMAZYRE® right away.

If vomiting occurs any time after taking PEMAZYRE®, the next dose should be taken at the next scheduled time.

Please see the PEMAZYRE® Product Monograph for complete dosing and administration instructions.

PEMAZYRE® dose reductions and modifications[1]

PEMAZYRE® tablets are available in 3 strengths for convenient dose modifications: 13.5 mg, 9 mg, and 4.5 mg[1]

PEMAZYRE® 13.5 mg tablets are round, white to off-white debossed on one side with "I" and "13.5" on the other side.

PEMAZYRE® 9 mg tablets are oval, white to off-white debossed on one side with "I" and "9" on the other side.

PEMAZYRE® 4.5 mg tablets are round, white to off-white debossed on one side with "I" and "4.5" on the other side.

Recommended PEMAZYRE® dose reductions for adverse reactions[1]

Starting dose
13.5 mg once daily

First dose reduction
PEMAZYRE® 9 mg taken orally once daily, 14 days on, 7 days off therapy

Second dose reduction
PEMAZYRE® 4.5 mg taken orally once daily, 14 days on, 7 days off therapy

Permanently discontinue if unable to tolerate PEMAZYRE® 4.5 mg once daily

Please see the PEMAZYRE® Product Monograph for complete dosing and administration instructions.

PEMAZYRE® dose reductions and modifications[1] (cont'd)

PEMAZYRE® dose modifications for toxicities[1]

Adverse Reaction	PEMAZYRE® Dose Modifications
Hyperphosphatemia 	**>5.5 mg/dL – ≤7 mg/dL** • **Continue** PEMAZYRE® at the current dose. • **Initiate** a low phosphate diet. **>7 mg/dL – ≤10 mg/dL** • **Continue** PEMAZYRE® at the current dose, continue a low phosphate diet, and initiate phosphate-binding therapy. • **Monitor** serum phosphate levels weekly and adjust the dose of phosphate lowering therapy as needed until levels return to <7 mg/dL. • **Withhold** PEMAZYRE® if serum phosphate levels do not return to <7 mg/dL within 2 weeks of starting a phosphate lowering therapy. **Restart** PEMAZYRE® at the same dose when serum phosphate levels return to <7 mg/dL. • If serum phosphate levels return to >7 mg/dL with phosphate-lowering therapy, **reduce** PEMAZYRE® 1 dose level. **>10 mg/dL** • **Continue** PEMAZYRE® at the current dose, continue a low phosphate diet, and adjust phosphate-binding therapy. • **Monitor** serum phosphate levels weekly and adjust the dose of phosphate lowering therapy as needed until levels return to <7 mg/dL. • **Withhold** PEMAZYRE® if serum phosphate levels continue >10 mg/dL for 1 week. • **Restart** PEMAZYRE® 1 dose level lower when serum phosphate is <7 mg/dL. • If serum phosphate levels return to >10 mg/dL following 2 dose reductions, **permanently discontinue** PEMAZYRE®.

Adapted from the PEMAZYRE® Product Monograph.[1]

Refer to **page 12** for more information on PEMAZYRE® risk management and monitoring for adverse reactions.

Adverse Reaction	PEMAZYRE® Dose Modifications
Serous retinal detachment (SRD) 	Educational material to assist healthcare professionals with diagnosis and management of SRD is available through the manufacturer. **Asymptomatic and stable on serial examination** • **Continue** PEMAZYRE® at the current dose. **Symptomatic or worsening on serial examination** • **Withhold** PEMAZYRE®. • If asymptomatic and improved on next examination, **resume** PEMAZYRE® at next lower dose. • If symptoms persist, consider **permanent discontinuation** of PEMAZYRE®.
Other adverse reactions	**Grade 1 or 2** • **Continue** PEMAZYRE® and treat the toxicity; monitor as medically indicated. **Grade 3** • **Interrupt** PEMAZYRE® up to 2 weeks (14 days) until the toxicity has resolved to ≤Grade 1. • **Restart** PEMAZYRE® at the next lower dose if adverse reaction resolves within 2 weeks; continue to monitor as indicated. • **Permanently discontinue** PEMAZYRE® if adverse reaction does not resolve within 2 weeks. • **Permanently discontinue** PEMAZYRE® for recurrent Grade 3 adverse reactions after **2** dose reductions. **Grade 4** • **Permanently discontinue** PEMAZYRE®.

Adapted from the PEMAZYRE® Product Monograph.[1]

Please see the PEMAZYRE® Product Monograph for complete dosing and administration instructions.

PEMAZYRE® dose reductions and modifications[1] (cont'd)

Dose modifications for renal and hepatic impairment[1]

Severe renal impairment (GFR <30 mL/min)
- Reduce the starting dose of PEMAZYRE® to 9 mg.

Mild or moderate renal impairment (GFR ≥30 to <90 mL/min)
- No PEMAZYRE® dose modifications are needed.

Severe hepatic impairment (total bilirubin >3 x ULN with any AST)
- Reduce the starting dose of PEMAZYRE® to 9 mg.

Mild (total bilirubin >ULN–1.5 x ULN or AST >ULN) **or moderate hepatic impairment** (total bilirubin >1.5–3 x ULN with any AST)
- No PEMAZYRE® dose modifications are needed.

Dose modifications for CYP3A4 inhibitors and CYP3A inducers[1]

- Avoid co-administration of PEMAZYRE® with strong or moderate CYP3A4 inhibitors
- If co-administration cannot be avoided adjust the PEMAZYRE® dosage as follows:

If the patient is taking this dose...	Reduce the dose to this
PEMAZYRE® 13.5 mg once daily	PEMAZYRE® 9 mg once daily
PEMAZYRE® 9 mg once daily	PEMAZYRE® 4.5 mg once daily

Avoid co-administration of PEMAZYRE® with strong or moderate CYP3A inducers.

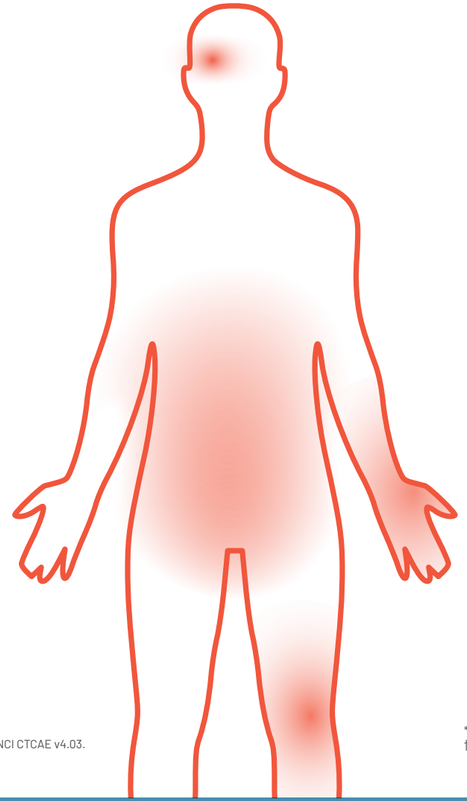
Refer to the PEMAZYRE® Product Monograph for more information on special populations, recommended doses and dose adjustments.

GFR: glomerular filtration rate; ULN: upper limit of normal; AST: aspartate aminotransferase.

Adverse reactions of all grades (≥15%) in patients receiving PEMAZYRE® in FIGHT-202[1]

Adverse Reaction N=146 All Grades (%)*		
Eye disorders	Dry eye (35%)†	
Metabolic and blood chemistry	Hyperphosphatemia (60%)‡ Hypophosphatemia (23%)§ Decreased appetite (33%)	Dehydration (15%) Hypercalcemia (15%)
Nervous system disorders	Dysgeusia (40%) Headache (16%)	
Gastrointestinal disorders	Diarrhea (47%) Nausea (40%) Constipation (35%) Stomatitis (35%)	Dry mouth (34%) Vomiting (27%) Abdominal pain (23%)
General disorders	Fatigue (42%) Edema peripheral (18%)	

Adapted from the PEMAZYRE® Product Monograph.[1]



Adverse Reaction N=146 All Grades (%)*	
Skin disorders	Alopecia (49%) Nail toxicity (43%)† Dry skin (20%) Palmar-plantar erythrodysaesthesia syndrome (15%)
Musculoskeletal and connective tissue disorders	Arthralgia (25%) Back pain (20%) Pain in extremity (19%)
Infections and Infestations	Urinary tract infection (16%)
Investigations	Weight decreased (16%)

Adapted from the PEMAZYRE® Product Monograph.[1]

* Graded per NCI CTCAE 4.03.
† Includes dry eye, keratitis, lacrimation increased, pinguecula, and punctate keratitis.
‡ Includes hyperphosphatemia and blood phosphorous increased; graded based on clinical severity and medical interventions taken according to the "investigations-other, specify" category in NCI CTCAE v4.03.
§ Includes hypophosphatemia and blood phosphorous decreased.

* Graded per NCI CTCAE 4.03.
† Includes nail toxicity, nail disorder, nail discoloration, nail dystrophy, nail hypertrophy, nail ridging, nail infection, onychalgia, onychoclasis, onycholysis, onychomadesis, onychomycosis, and paronychia.

PEMAZYRE® risk management and monitoring[1]

Risk management for hyperphosphatemia[1]

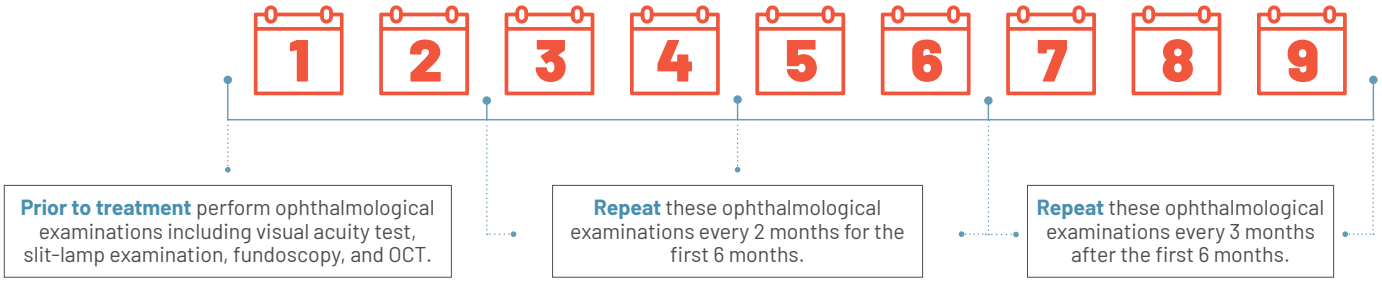
Start all patients on a low phosphate diet when their phosphate level is **>5.5 mg/dL** and consider adding a phosphate lowering therapy when a patient's level is **>7 mg/dL**.[1]

Consider discontinuing phosphate lowering therapy during PEMAZYRE® treatment breaks or if phosphate level falls below normal.[1]

Serum phosphate[1]

Phosphate concentrations should be assessed **14 days after initiating PEMAZYRE®** and then monitored **every 2 cycles** (approximately 6 weeks) after.

Monitoring and managing ocular events with PEMAZYRE®[1]



PEMAZYRE® can cause SRD events, which may present with symptoms such as:

- Blurred vision
- Visual floaters
- Photopsia

OCT: optical coherence tomography.

The Incyte Solutions™ Support Program

At Incyte Biosciences Canada, we want to help provide support for patients. That is why Incyte Solutions™ is available to provide resources for patients who have been prescribed PEMAZYRE®.

Through this program, eligible patients have direct access to additional support to help them throughout treatment.

Incyte Solutions™
SUPPORT PROGRAM

Phone: **1-84-INCYTE-00** (1-844-629-8300)

Email: **support@incytesolutions.ca**

Fax: **1-84-INCYTE-01** (1-844-629-8301)

PEMAZYRE® safety information[1]

Indication and clinical use:

PEMAZYRE® (pemigatinib) is indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement.

Clinical effectiveness of PEMAZYRE® is based on overall response rate (ORR) and duration of response (DoR) from a single-arm Phase 2 trial in patients with specific FGFR2 rearrangements.

Treatment with PEMAZYRE® should be initiated following confirmation of a FGFR2 fusion or rearrangement using a validated test.

Pediatrics (18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

Contraindications:

- PEMAZYRE® is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

Relevant warnings and precautions:

- If patients experience symptoms affecting their vision, it is recommended that they do not drive or use machines until the effect subsides.
- Soft tissue mineralization, including cutaneous calcification, calcinosis, and non-uremic calciphylaxis may be associated with hyperphosphatemia and has been observed with PEMAZYRE® treatment.
- Hypophosphatemia has been observed with PEMAZYRE®.
- Phosphate concentrations should be assessed 14 days after initiating PEMAZYRE® treatment and then monitored every 6 weeks thereafter.
- Opthalmological exams including the visual acuity test, slit-lamp exam, fundoscopy, and optical coherence tomography should be performed prior to initating treatment with PEMAZYRE® and throughout treatment.
- Pemigatinib may increase serum creatinine due to a blockade of tubular secretion via renal transporters OCT2 and MATE1.
- PEMAZYRE® can cause serous retinal detachment events, which may present with symptoms such as blurred vision, visual floaters, or photopsia.
- PEMAZYRE® may cause fetal harm and potential loss of pregnancy. Advise females of reproductive potential to use effective contraception during treatment with PEMAZYRE® and for 1 month after the last dose.
- Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PEMAZYRE® and for 1 month after the last dose.
- Advise women not to breastfeed during treatment with PEMAZYRE® and for 1 month after the final dose.

For more information:

Please consult the Product Monograph at bit.ly/Pemazyre for important information relating to monitoring and laboratory tests, adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling 1-833-309-2759 or contacting medinfocanada@incyte.com.

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PEMAZYRE® tablets are available in 3 strengths for convenient dose modifications: 13.5 mg, 9 mg, and 4.5 mg.

Visit our resource hub for additional resources and information on how to enroll your patients in the Incyte Solutions™ Support Program: **www.IncyteOnco.ca**.

Phone: **1-84-INCYTE-00** (1-844-629-8300)
Email: **support@incytesolutions.ca**
Fax: **1-84-INCYTE-01** (1-844-629-8301)

Reference: 1. PEMAZYRE® Product Monograph. Incyte Corporation. September 8, 2021.

REVIEWED BY PAAB

MEMBER OF INNOVATIVE MEDICINES CANADA

Incyte