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

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.

TARGET CHOLANGIOCARCINOMA WITH AN FGFR2 FUSION OR OTHER REARRANGEMENT[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]

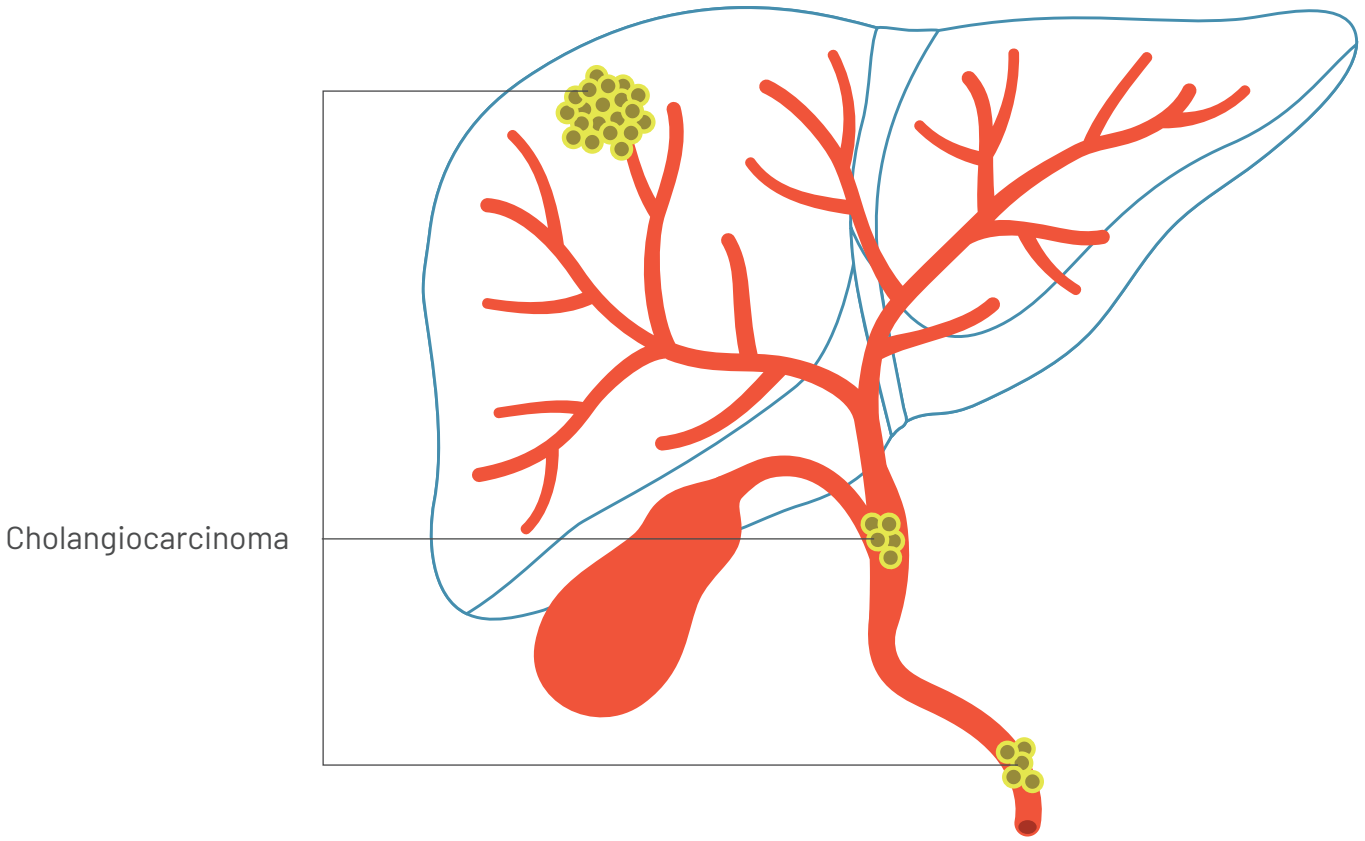
- **FIGHT-202 clinical trial:** In a non-randomized, open-label study, **35.5% of patients demonstrated ORR** (95% CI: 26.5–45.4) with a **median DoR of 9.1 months** (95% CI: 6.0–14.5).[1*]
- The **first protein kinase inhibitor** with an indication in cholangiocarcinoma available in Canada.[1-3†]
- 1,000+ patients treated in the United States.[4†]

* Data are from IRC per RECIST v1.1, and CR and PR are confirmed. The 95% CI for DoR was calculated using the Brookmeyer and Crowley method. Refer to page 6 for the FIGHT-202 study parameters.
† Clinical significance is unknown.
FGFR2: fibroblast growth factor receptor 2; ORR: objective response rate; CI: confidence interval; DoR: duration of response; IRC: independent review committee; RECIST: Response Evaluation Criteria in Solid Tumors; CR: complete response; PR: partial response.

Incyte

Unresectable locally advanced or metastatic **cholangiocarcinoma (CCA)** with an **FGFR2 fusion or other rearrangement**[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.

Genomic profiling and the FGFR2 gene[1,3,5,6]

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]

Genetic alterations in FGFR genes result in activation of FGFR signaling that supports the proliferation and survival of malignant cells.

Identifying and testing for FGFR2 fusions or rearrangements requires a method that can:

- Specifically detect FGFR2 fusions, which are distinct from FGFR2 point mutations.[5]
- Identify fusions with a range of fusion partners.[1,3,5,6]

NCCN Guidelines recommend comprehensive molecular profiling for patients with unresectable or metastatic CCA who are candidates for systemic therapy. A comprehensive panel including the targets listed below may optimize the chance of identifying a targetable aberration:[1,3]*

- *NTRK* gene fusion
- MSI-H/dMMR
- TMB-H
- *BRAF* V600E mutation
- *FGFR2* fusion or rearrangement
- *IDH1* mutation
- HER2 (*ERBB2*) overexpression and/or amplification
- *RET* gene fusion
- *KRAS* G12C mutation

Testing your patients for FGFR2 fusions or rearrangements is critical to identifying those who may be considered for treatment with PEMAZYRE®.[1,3,5]

* Refer to the complete NCCN Guidelines for full recommendations and information. NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

FGFR: fibroblast growth factor receptor; NCCN: National Comprehensive Cancer Network.

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PEMAZYRE® is the **first protein kinase inhibitor** with an indication in cholangiocarcinoma available in Canada[1-3]*

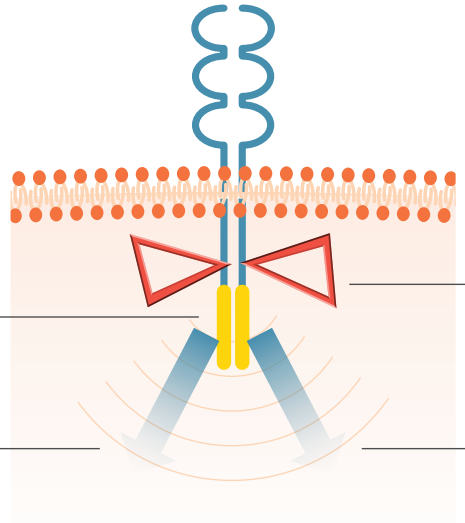
PEMAZYRE® (pemigatinib) is a small molecule kinase inhibitor of FGFR1, 2 and 3[1†]

PEMAZYRE® **selectively decreases cell viability in cancer cell lines with activating FGFR genetic alterations,** including:[1]

1. Point mutations,
2. Amplifications, and
3. Fusions or rearrangements.

These FGFR genetic alterations result in the activation of FGFR signaling, supporting the proliferation and survival of malignant cells.[1]

PEMAZYRE® inhibits FGFR phosphorylation and signaling[1,7]



Adapted from the PEMAZYRE® Product Monograph and Boilly *et al.*[1,7]

In FGFR-activated cancer cell lines, the concentration required for 50% inhibition (IC_{50}) was less than 2 nM.[1]

* Clinical significance is unknown.
† 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.
MOA: mechanism of action; FGFR: fibroblast growth factor receptor.

The safety profile and efficacy of PEMAZYRE® were studied in **FIGHT-202**[1]

A multicenter, non-randomized, open-label, multi-cohort, Phase 2 study[1]

N=107

Patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement

- Qualifying in-frame fusions and other rearrangements were predicted to have a breakpoint within intron 17/exon 18 of the FGFR2 gene, leaving the FGFR2 kinase domain intact
- FGFR mutation status for screening and enrolment of patients was determined by a validated clinical trial assay

- Patients received 13.5 mg PEMAZYRE® orally once daily for 14 days followed by no therapy for 7 days in 3-week cycles (21 days)
- **PEMAZYRE® was administered until disease progression or unacceptable toxicity**

Major efficacy outcome measures:[1]

- ORR (CR+PR)
- DoR

As determined by an IRC according to RECIST v1.1.

FGFR: fibroblast growth factor receptor; ORR: objective response rate; CR: complete response; PR: partial response; DoR: duration of response; IRC: independent review committee; RECIST: Response Evaluation Criteria in Solid Tumors.

FGFR mutation status for screening and enrolment of patients was determined by a validated clinical trial assay[1]

FGF/FGFR genetic alterations identified by central genomics laboratory in ≥2 participants[1]

FGF/FGFR alteration, n	Cohort A (N=107)
FGFR2-BICC1	31
FGFR2-N/A*	5
FGFR2-KIAA1217	4
FGFR2-AHCYL1	3
FGFR2-ARHGAP24	2
FGFR2-AFF4	2
FGFR2-CCDC6	2
FGFR2-MACF1	2
FGFR2-NOL4	2
FGFR2-NRAP	2
FGFR2-PAWR	2
FGFR2-SLMAP	2

Adapted from the PEMAZYRE® Product Monograph.[1]

- Patients had locally advanced or metastatic cholangiocarcinoma that had progressed on or after at least 1 prior therapy and who had an FGFR2 fusion or rearrangement.[1]
- Qualifying in-frame fusions and other rearrangements were predicted to have a breakpoint within intron 17/exon 18 of the FGFR2 gene, leaving the FGFR2 kinase domain intact.[1]
- Of 146 patients enrolled, 107 patients had centrally-confirmed FGFR2 fusions or rearrangements. Of these 107 patients, 56 different partners were identified, 42 (75%) of which were unique to individual patients.[6]

The median duration of therapy was 6.0 months; the median duration of efficacy follow-up was 15.4 months.[1]

* FGFR2 rearrangement confirmed but gene partner not identified/available.
FGFR: fibroblast growth factor receptor; FGF: fibroblast growth factor; N/A: not applicable.

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Summary of patient demographics[1]

Variable	Cohort A* N=107 (%)
Age (years)	55.3 (12.02)
Mean (STD)	56.0
Median (range)	26–77
Age group, n (%)	
<65 years	82 (76.6)
≥65 years	25 (23.4)
Sex, n (%)	
Male	42 (39.3)
Female	65 (60.7)
Race, n (%)	
White	79 (73.8)
Black or African American	7 (6.5)
Asian	11 (10.3)
Other†	4 (3.7)
Missing	6 (5.6)
ECOG status at baseline, n (%)	
0	45 (42.1)
1	57 (53.3)
2	5 (4.7)

Variable	Cohort A* N=107 (%)
Renal impairment grade at baseline‡	
Normal	42 (39.3)
Mild	47 (43.9)
Moderate	18 (16.8)
Severe	0
Hepatic impairment grade at baseline§	
Normal	48 (44.9)
Mild	52 (48.6)
Moderate	7 (6.5)
Cholangiocarcinoma location	
Intrahepatic	105 (98.1)
Extrahepatic	1 (0.9)
Other	0
Missing	1 (0.9)¶
Metastatic disease**	88 (82.2)
Locally advanced disease	16 (15.0)

Adapted from the PEMAZYRE® Product Monograph.[1]

The median time to response was 2.7 months (range: 0.7–6.9 months).[1]

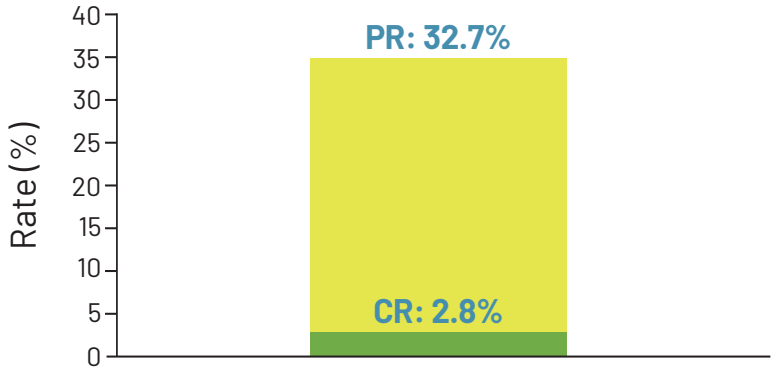
* Cohort determination is based on tumor FGF/FGFR status from central genomics laboratory. Cohort A = FGFR2 rearrangements or fusions.
† Includes Hispanic, Latino, or Spanish or not reported.
‡ Baseline renal impairment grade (normal, mild, moderate, or severe) based on eGFR (calculated using the MDRD equation): normal renal function = eGFR ≥90 mL/min/1.73 m^2; mild renal impairment = eGFR ≥60 and 90 mL/min/1.73 m^2; moderate renal impairment = eGFR ≥30 to <60 mL/min/1.73 m^2; severe renal impairment = eGFR <30 mL/min/1.73 m^2.
§ Degree of hepatic impairment based on National Cancer Institute Hepatic Working Group Criteria.
¶ At baseline, this participant had stage 4 cholangiocarcinoma (T3 N0 M1), presumed intrahepatic, with current sites of disease in liver, omentum, and peritoneum.
** Metastatic information was not able to be confirmed for one participant and missing for two participants.
FGF: fibroblast growth factor; FGFR: fibroblast growth factor receptor; STD: standard deviation; eGFR: estimated glomerular filtration rate; MDRD: Modification of Diet in Renal Disease Study.

Efficacy profile in the FIGHT-202 clinical trial[1]

ORR in cohort A (FGFR2 fusion or rearrangement) efficacy evaluable population (N=107)[1*]

35.5% of patients achieved ORR

(95% CI: 26.5–45.4)



DoR in cohort A (FGFR2 fusion or rearrangement) efficacy evaluable population[1†]

Median DoR was 9.1 months

(95% CI: 6.0–14.5)[‡]

(N=107)

* Data are from IRC per RECIST v1.1, and CR and PR are confirmed.
† Data are from IRC per RECIST v1.1.
‡ The 95% CI was calculated using the Brookmeyer and Crowley method.
ORR: objective response rate; PR: partial response; CR: complete response; CI: confidence interval; DoR: duration of response; FGFR2: fibroblast growth factor receptor 2; IRC: independent review committee; RECIST: Response Evaluation Criteria in Solid Tumors.

PEMAZYRE® demonstrated a generally well-tolerated adverse reaction profile[1]

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

Adverse reaction	PEMAZYRE® (N=146)	
	All Grades (%)*	Grades ≥3 (%)†
Metabolism and nutrition disorders		
Hyperphosphatemia‡	60	0
Hypophosphatemia§	23	12
Decreased appetite	33	1.4
Dehydration	15	2.1
Hypercalcemia	15	2.1
Skin and subcutaneous tissue disorders		
Alopecia	49	0
Nail toxicity¶	43	2.1
Dry skin	20	0.7
Palmar-plantar erythrodysaesthesia syndrome	15	4.1
Gastrointestinal disorders		
Diarrhea	47	2.7
Nausea	40	2.1
Constipation	35	0.7
Stomatitis	35	5.5
Dry mouth	34	0
Vomiting	27	1.4
Abdominal pain	23	4.8

Adverse reaction	PEMAZYRE® (N=146)	
	All Grades (%)*	Grades ≥3 (%)†
General disorders		
Fatigue	42	4.8
Edema peripheral	18	0.7
Nervous system disorders		
Dysgeusia	40	0
Headache	16	0
Eye disorders		
Dry eye**	35	0.7
Musculoskeletal and connective tissue disorders		
Arthralgia	25	6.2
Back pain	20	2.7
Pain in extremity	19	2.1
Infections and Infestations		
Urinary tract infection	16	3.4
Investigations		
Weight decreased	16	2.1

Adapted from the PEMAZYRE® Product Monograph.[1]

* Graded per NCI CTCAE 4.03.
† Only Grades 3–4 were identified.
‡ 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.
¶ Includes nail toxicity, nail disorder, nail discoloration, nail dystrophy, nail hypertrophy, nail ridging, nail infection, onychalgia, onychoclasis, onycholysis, onychomadesis, onychomycosis, and paronychia.
** Includes dry eye, keratitis, lacrimation increased, pinguecula, and punctate keratitis.

PEMAZYRE® can cause serous retinal detachment (SRD)[1]

SRD may cause symptoms such as blurred vision, visual floaters, or photopsia. Clinical trials did not conduct routine monitoring, including optical coherence tomography (OCT), to detect asymptomatic SRD; therefore, the incidence of asymptomatic SRD is unknown. SRD events occurred in 7.5% of all patients treated with PEMAZYRE® and included SRD, retinal detachment, detachment of retinal pigmented epithelium, retinal thickening, subretinal fluid, chorioretinal folds, chorioretinal scar, and maculopathy.[1]

Serious adverse events[1]

Serious adverse events were reported in 45% of patients. The most common serious adverse events (≥2%) were:[1]

- Abdominal pain (4.8%)
- Pyrexia (4.8%)
- Cholangitis (3.4%)
- Pleural effusion (3.4%)
- Acute kidney injury (2.1%)
- Cholangitis infective (2.1%)
- Failure to thrive (2.1%)
- Hypercalcemia (2.1%)
- Hyponatremia (2.1%)
- Small intestinal obstruction (2.1%)
- Urinary tract infection (2.1%)

Fatal adverse reactions occurred in 4.1% of patients, including failure to thrive (2 patients, 1.4%), and bile duct obstruction, cholangitis, sepsis, and pleural effusion (1 patient each, 0.7%).[1]

Dose interruptions and dose reductions[1]

Dose interruptions and dose reductions of PEMAZYRE® due to adverse events occurred in 43% and 14% of patients, respectively.[1]

Dose modifications (interruptions and/or reductions) due to adverse events were most commonly due to stomatitis (7.5%), palmar-plantar erythrodysesthesia syndrome (5.5%), arthralgia (4.8%), and fatigue (4.1%).

Permanent discontinuation of PEMAZYRE® due to adverse events occurred in 8.9% of patients, most commonly (≥1%) due to intestinal obstruction and acute kidney injury (2 patients each, 1.4%).

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

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

Recommended dose[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.[1]

13.5 mg once daily for 14 days

Follow by 7 days off therapy

Advise patients of the following

- Take PEMAZYRE® exactly as prescribed (see recommended dosing schedule above)
- PEMAZYRE® can be taken with or without food
- Take PEMAZYRE® at about the same time each day
- Swallow tablets whole – do not crush, chew, split, or dissolve tablets
- In the event of a missed dose
  - ≥4 hours or if vomiting occurs any time after taking the dose: do NOT make up the dose. Skip it and continue with the next dose at the usual time. Do not take an extra dose the next day to make up for the missed dose.
  - <4 hours: take the dose as soon as possible. Continue with the next dose at the usual time.

Dose reductions are required in patients with severe renal or hepatic impairment. Please refer to the Product Monograph for more information.[1]

PEMAZYRE® dosage form, strengths, and packaging[1]

Tablets are available in 3 strengths for 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.	

PEMAZYRE® tablets are available as a 14-day supply provided in convenient blister packs (14 tablets) designed to help facilitate adherence to the dosing regimen.[1]

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

Recommended dose modifications for adverse reactions[1]

PEMAZYRE® offers multiple dosage strengths to allow for dose modifications in patients with adverse events[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 the patient is unable to tolerate PEMAZYRE® 4.5 mg once daily

Risk management for hyperphosphatemia[1]

In all patients, initiate a low phosphate diet when phosphate level is **>5.5 mg/dL** and consider adding a phosphate lowering therapy when level is **>7 mg/dL**. Adjust the dose of phosphate lowering therapy until phosphate level returns to **<7 mg/dL**.

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

Refer to the PEMAZYRE® **Dosage and Administration Brochure** or the **Product Monograph** for more information on dose recommendations in special populations and modifications for toxicities.

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 may have access to financial assistance and additional support to help them throughout treatment. The Program will collect, use, disclose and store patient information to provide the following services:

- Nursing and/or pharmacists' support
- Assessment of eligibility to financial assistance
- Assistance in communicating with drug plan administrators, managers or insurance companies to aid in securing reimbursement coverage for the patient's prescription
- Reporting on the patient's insurance coverage to the prescribing healthcare professional (HCP)
- Regular communications on the patient's therapy and support program offerings, where applicable
- Other services as offered from time to time.

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)

Consider providing your patient information on the following patient support organizations

- **Cholangiocarcinoma Foundation®** – www.cholangiocarcinoma.org
- **Canadian Cholangiocarcinoma Collaborative (C3)** – www.cholangio.ca
- **Cholangio-Hepatocellular Carcinoma Canada** – www.mychcc.ca

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 OCT 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 SRD 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 pdf.hres.ca/dpd_pm/00062968.PDF 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.

References

1. PEMAZYRE® Product Monograph. Incyte Corporation. September 8, 2021. **2.** Incyte Corporation. Letter of attestation for PEMAZYRE®'s classification. June 11, 2024. **3.** National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Biliary Tract Cancers. Version 2.2025. July 2, 2025. **4.** Incyte Corporation. Letter of attestation for PEMAZYRE®: Patients treated. June 11, 2024. **5.** Lowery *et al*. Comprehensive molecular profiling of intra- and extrahepatic cholangiocarcinomas: potential targets for intervention. *Clin Cancer Res*. 2018;24(17):4154–4161. **6.** Abou-Alfa *et al*. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. *Lancet Oncol*. 2020;21(5):671–684. **7.** Boilly *et al*. FGF signals for cell proliferation and migration through different pathways – Cytokine. *Growth Factor Rev*. 2000;11:295–302.

PEMAZYRE® is the **first protein kinase inhibitor** with an indication in cholangiocarcinoma available in Canada[1-3]*

Test for FGFR2 fusions or other rearrangements to consider **treating** with PEMAZYRE®.

Target cholangiocarcinoma with an FGFR2 fusion or other rearrangement[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]

- FIGHT-202 clinical trial: In a non-randomized, open-label study, 35.5% of patients demonstrated ORR (95% CI: 26.5–45.4) with a median DoR of 9.1 months (95% CI: 6.0–14.5)[1†]
- PEMAZYRE® demonstrated a generally well-tolerated safety profile[1]
  - The most common adverse reactions (≥40%; all Grades) included hyperphosphatemia (60%), alopecia (49%), nail toxicity (43%), diarrhea (47%), nausea (40%), fatigue (42%), and dysgeusia (40%)

- PEMAZYRE® offers the convenience of a daily oral tablet[1]
  - Tablets are available in 3 strengths for 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)

* Clinical significance is unknown.
† Data are from IRC per RECIST v1.1, and CR and PR are confirmed. The 95% CI for DoR was calculated using the Brookmeyer and Crowley method.
FGFR2: fibroblast growth factor receptor 2; ORR: objective response rate; CI: confidence interval; DoR: duration of response; IRC: independent review committee; RECIST: Response Evaluation Criteria in Solid Tumors; CR: complete response; PR: partial response.

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