Pemazyre®
(pemigatinib) tablets
13.5 mg • 9 mg • 4.5 mg

3+ YEARS

OF **CLINICAL EXPERIENCE** SINCE FDA APPROVAL WITH **1,000+ PATIENTS** TREATED[1,*]

*Commercially available in the US since 2020.

Target Patients in Second-Line Treatment

The *first FDA-approved treatment* for previously treated, unresectable locally advanced or metastatic cholangiocarcinoma (CCA) with an FGFR2 fusion or rearrangement as detected by an FDA-approved test[2]

FGFR=fibroblast growth factor receptor.

INDICATIONS AND USAGE

PEMAZYRE 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 as detected by an FDA-approved test.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

Ocular Toxicity

Retinal Pigment Epithelial Detachment (RPED): PEMAZYRE can cause RPED, which may cause symptoms such as blurred vision, visual floaters, or photopsia. Clinical trials of PEMAZYRE did not conduct routine monitoring including optical coherence tomography (OCT) to detect asymptomatic RPED; therefore, the incidence of asymptomatic RPED with PEMAZYRE is unknown.

Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, RPED occurred in 11% of patients, including Grade 3-4 RPED in 1.3%. The median time to first onset of RPED was 56 days. RPED led to dose interruption of PEMAZYRE in 3.1% of patients, and dose reduction and permanent discontinuation in 1.3% and in 0.2% of patients, respectively. RPED resolved or improved to Grade 1 levels in 76% of patients who required dosage modification of PEMAZYRE for RPED.

Perform a comprehensive ophthalmological examination including OCT prior to initiation of PEMAZYRE and every 2 months for the first 6 months and every 3 months thereafter during treatment. For onset of visual symptoms, refer patients for ophthalmologic evaluation urgently, with follow-up every 3 weeks until resolution or discontinuation of PEMAZYRE. Modify the dose or permanently discontinue PEMAZYRE as recommended in the prescribing information for PEMAZYRE.

Dry Eye: Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, dry eye occurred in 31% of patients, including Grade 3-4 in 1.6% of patients. Treat patients with ocular demulcents as needed.

Please see Important Safety Information on pages 18–19 for related and other risks.

FGFR2 fusions are actionable targets for treatment in iCCA[3-5]

~50% of patients with iCCA have actionable genomic alterations[3,6-8]

FGFR2 fusions are among the most common actionable genomic alterations in iCCA[3-5]

10%–16% of patients with iCCA have FGFR2 fusions[3-5]

- FGFR2 fusions are detectable early in disease progression and are key drivers of tumor growth[9,10]
- Molecular profiling is necessary to identify FGFR2 fusions or rearrangements

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Recommend molecular testing for patients with unresectable or metastatic cholangiocarcinoma[11,*,†,‡]

"Given emerging evidence regarding actionable targets for treating cholangiocarcinoma, molecular testing of unresectable and metastatic tumors is recommended."[11]

*See the Guidelines online at NCCN.org for the full recommendation.

†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.

‡Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Please see Important Safety Information on pages 18–19 for related and other risks.

Selecting an NGS test that identifies both known and unknown FGFR2 fusions is critical

A next-generation sequencing (NGS) assay should meet the following criteria to identify FGFR2 fusions or rearrangements:

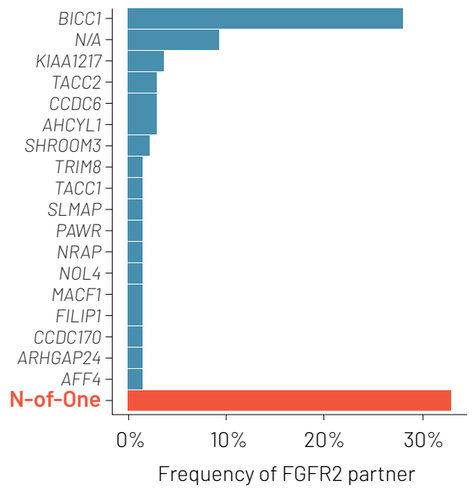
- Detects fusions with a wide range of fusion partners (whether known or unknown)
- Specifically detects FGFR2 fusions (distinct from FGFR2 mutations)

Not all next-generation sequencing-based (NGS) tests meet these criteria

Be sure to use an NGS test that can detect both known and unknown fusion partners

A high-sensitivity NGS-based assay, such as **FoundationOne® CDx**, can detect FGFR2 fusions, including those with known or unknown fusion partners

FGFR2 Fusion Partners in CCA[12]



N-of-One fusion partners are unique to a single patient

Adapted from Silverman IM, et al. Cancer Discovery. 2021;11:326-339.

In patients with CCA, FGFR2 fusions may have a wide variety of fusion partners, both known (frequently occurring) as well as unknown (rare, or patient-specific fusions), including those unique to a single patient.[12]

FGFR2 fusions are distinct from FGFR2 mutations.[12]

For more information on selecting an appropriate NGS assay, please visit hcp.pemazyre.com/fgfr2-fusion-testing or scan this code.

Pemazyre® (pemigatinib) tablets 13.5 mg · 9 mg · 4.5 mg

The first FDA-approved FGFR2-fusion-targeted therapy for CCA

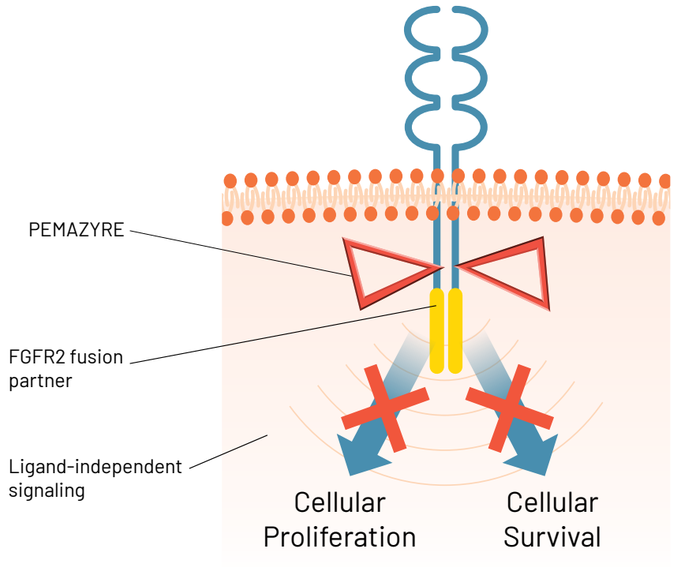
PEMAZYRE (pemigatinib) is the first FDA-approved treatment for patients with previously treated, unresectable locally advanced or metastatic CCA with an FGFR2 fusion or rearrangement.[2]

Select patients for the treatment of unresectable locally advanced or metastatic cholangiocarcinoma with PEMAZYRE based on the presence of an FGFR2 fusion or rearrangement as detected by an FDA-approved test[2]

Pemigatinib is a small-molecule kinase inhibitor of FGFR1, 2 and 3[2]

Constitutive FGFR signaling can support the proliferation and survival of malignant cells.[2]

Pemigatinib inhibits FGFR1–3 phosphorylation and signaling[2]



PEMAZYRE inhibits FGFR2 kinase activity, which may decrease tumor cell proliferation and survival in FGFR-driven tumors.[2]

PEMAZYRE was studied in the FIGHT-202 study[2]

FIGHT-202 was a multicenter, open-label, single-arm study in previously treated patients with locally advanced or metastatic cholangiocarcinoma (N=146).

- The efficacy population consisted of 107 patients with disease that had progressed on or after at least 1 prior therapy and who had an FGFR2 fusion or non-fusion rearrangement, as determined by a clinical trial assay (FoundationOne® CDx) performed at a central laboratory
- Patients received PEMAZYRE in 21-day cycles at a dosage of 13.5 mg orally once daily for 14 days, followed by 7 days off therapy administered until disease progression or unacceptable toxicity
- The major efficacy outcome measures were overall response rate (ORR) and duration of response (DoR), as determined by an independent review committee (IRC) according to RECIST v1.1
- All patients had received at least 1 prior line of systemic therapy, with some having 3 or more prior lines of therapy

NCCN Guidelines® recommend pemigatinib (PEMAZYRE) as a subsequent-line systemic therapy option for unresectable or metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements following disease progression[11,*,†,‡]

*See the Guidelines online at NCCN.org for the full recommendation.

†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.

‡Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

IMPORTANT SAFETY INFORMATION

Hyperphosphatemia and Soft Tissue Mineralization

PEMAZYRE can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcification, calcinosis, and non-uremic calciphylaxis. Increases in phosphate levels are a pharmacodynamic effect of PEMAZYRE. Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, hyperphosphatemia was reported in 93% of patients based on laboratory values above the upper limit of normal. The median time to onset of hyperphosphatemia was 8 days (range 1-169). Phosphate lowering therapy was required in 33% of patients receiving PEMAZYRE.

Monitor for hyperphosphatemia and initiate a low phosphate diet when serum phosphate level is > 5.5 mg/dL. For serum phosphate levels > 7 mg/dL, initiate phosphate lowering therapy and withhold, reduce the dose, or permanently discontinue PEMAZYRE based on duration and severity of hyperphosphatemia as recommended in the prescribing information.

Please see Important Safety Information on pages 18–19 for related and other risks.

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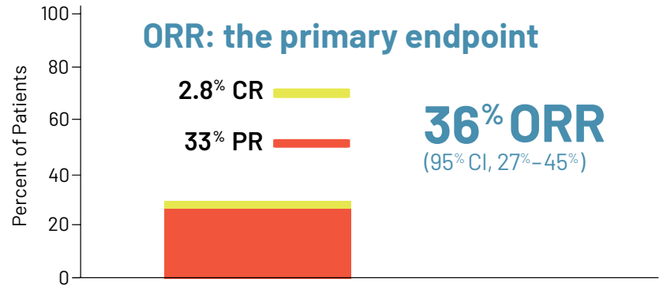
PEMAZYRE (pemigatinib) provided durable responses[2]

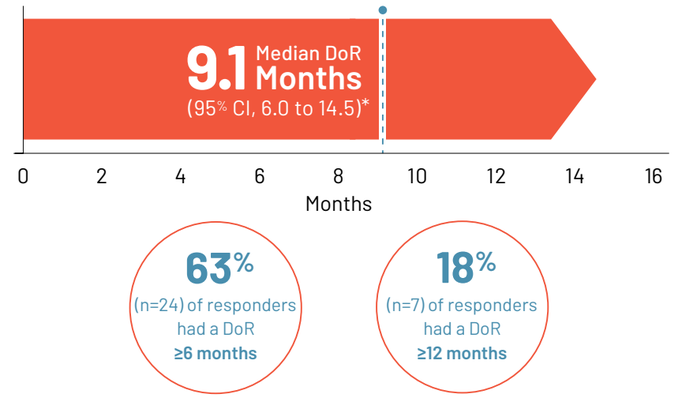
PEMAZYRE demonstrated a 36% ORR[2]



All evaluable patients N=107
Note: Data are from IRC per RECIST v1.1, and CR and PR are confirmed.

Median time to response was 2.7 months (range, 0.7–6.9 months)

Duration of response (DoR)[2]



CI, confidence interval; CR, complete response; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.
*The 95% CI was calculated using the Brookmeyer and Crowley's method.

IMPORTANT SAFETY INFORMATION

Embryo-Fetal Toxicity

Based on findings in an animal study and its mechanism of action, PEMAZYRE can cause fetal harm when administered to a pregnant woman. Oral administration of pemigatinib to pregnant rats during the period of organogenesis caused fetal malformations, fetal growth retardation, and embryo-fetal death at maternal exposures lower than the human exposure based on area under the curve (AUC) at the clinical dose of 13.5 mg.

Advise pregnant women of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the last dose.

FIGHT-202: Additional Endpoints

PEMAZYRE received accelerated approval from the FDA based on overall response rate and duration of response in a single arm study

- Progression-free survival, overall survival, and disease control rate were secondary endpoints that were studied in FIGHT-202 that are not reflected in the full Prescribing Information
- Due to the potential variability in the natural history of the disease, a single-arm study may not adequately characterize these time-to-event endpoints
- For this reason, a confirmatory Phase 3 study in cholangiocarcinoma is underway

Disease Control Rate (DCR)[13]

82% DCR
(95% CI, 74 to 89)

DCR was defined as CR+PR+SD[13]

- CR in 2.8% of patients (n=3); PR in 32.7% of patients (n=35); SD in 46.7% of patients (n=50)
- FIGHT-202 was a single-arm study[13]
  - In this setting, the DCR results reflect the natural history of cholangiocarcinoma in an individual patient, rather than the direct effect of treatment

IMPORTANT SAFETY INFORMATION

Adverse Reactions: Cholangiocarcinoma

Serious adverse reactions occurred in 45% of patients receiving PEMAZYRE (n=146). Serious adverse reactions in ≥2% of patients who received PEMAZYRE included abdominal pain, pyrexia, cholangitis, pleural effusion, acute kidney injury, cholangitis infective, failure to thrive, hypercalcemia, hyponatremia, small intestinal obstruction, and urinary tract infection. Fatal adverse reactions occurred in 4.1% of patients, including failure to thrive, bile duct obstruction, cholangitis, sepsis, and pleural effusion.

Permanent discontinuation due to an adverse reaction occurred in 9% of patients who received PEMAZYRE. Adverse reactions requiring permanent discontinuation in ≥1% of patients included intestinal obstruction and acute kidney injury.

Dosage interruptions due to an adverse reaction occurred in 43% of patients who received PEMAZYRE. Adverse reactions requiring dosage interruption in ≥1% of patients included stomatitis, palmar-plantar erythrodysesthesia syndrome, arthralgia, fatigue, abdominal pain, AST increased, asthenia, pyrexia, ALT increased, cholangitis, small intestinal obstruction, alkaline phosphatase increased, diarrhea, hyperbilirubinemia, electrocardiogram QT prolonged, decreased appetite, dehydration, hypercalcemia, hyperphosphatemia, hypophosphatemia, back pain, pain in extremity, syncope, acute kidney injury, onychomadesis, and hypotension.

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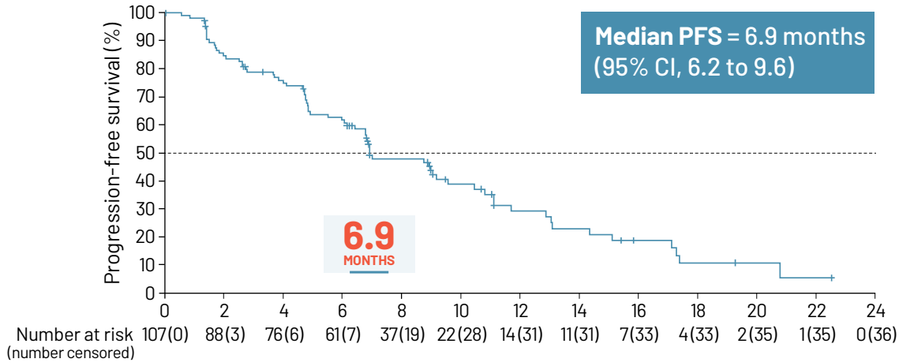
FIGHT-202: Additional Endpoints *(continued)*

Progression-free survival (PFS)[13]

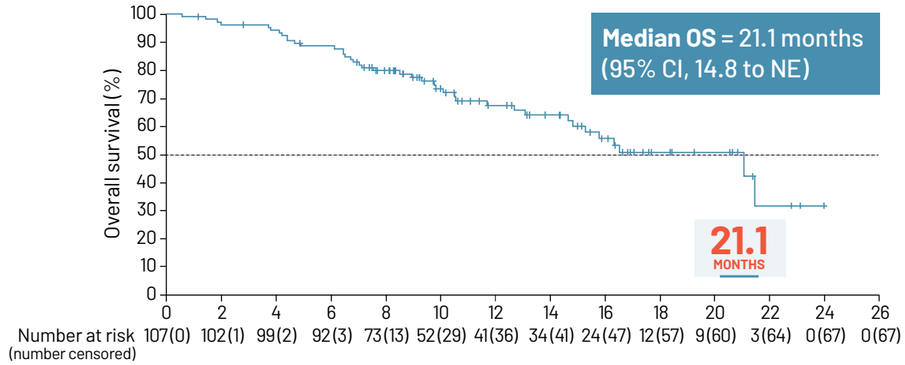
Kaplan-Meier estimate of PFS (N=107)



- Median follow-up at time of data cutoff was 15.4 months.[13]

Overall Survival (OS)[13]

Kaplan-Meier estimate of OS (N=107)



- At time of data cutoff: Median follow-up was 15.4 months; the OS data were not mature; a total of 40 patients (37%) had died.[13]

IMPORTANT SAFETY INFORMATION

Adverse Reactions: Cholangiocarcinoma *(continued)*

Dose reductions due to an adverse reaction occurred in 14% of patients who received PEMAZYRE. Adverse reactions requiring dosage reductions in ≥1% of patients who received PEMAZYRE included stomatitis, arthralgia, palmar-plantar erythrodysesthesia syndrome, asthenia, and onychomadesis.

Clinically relevant adverse reactions occurring in ≤10% of patients included fractures (2.1%). In all patients treated with pemigatinib, 0.5% experienced pathologic fractures (which included patients with and without cholangiocarcinoma [N = 635]). Soft tissue mineralization, including cutaneous calcification, calcinosis, and non-uremic calciphylaxis associated with hyperphosphatemia were observed with PEMAZYRE treatment.

The safety of PEMAZYRE (pemigatinib) was evaluated in FIGHT 202[2]

The safety of PEMAZYRE was evaluated in 146 patients with previously treated, locally advanced or metastatic cholangiocarcinoma. Patients were treated orally with PEMAZYRE 13.5 mg once daily for 14 days on followed by 7 days off therapy until disease progression or unacceptable toxicity. The median duration of treatment was 181 days (range: 7 to 730 days).

- The most common adverse reactions (incidence ≥20%) were hyperphosphatemia, alopecia, diarrhea, nail toxicity, fatigue, dysgeusia, nausea, constipation, stomatitis, dry eye, dry mouth, decreased appetite, vomiting, arthralgia, abdominal pain, hypophosphatemia, back pain, and dry skin.
- Serious adverse reactions occurred in 45% of patients receiving PEMAZYRE (n=146). Serious adverse reactions in ≥2% of patients who received PEMAZYRE included abdominal pain, pyrexia, cholangitis, pleural effusion, acute kidney injury, cholangitis infective, failure to thrive, hypercalcemia, hyponatremia, small intestinal obstruction, and urinary tract infection. Fatal adverse reactions occurred in 4.1% of patients, including failure to thrive, bile duct obstruction, cholangitis, sepsis, and pleural effusion.

Adverse reactions leading to permanent discontinuation occurred in 9% of patients[2]

For more information on the monitoring and management of adverse reactions, please visit hcp.pemazyre.com or scan this code.

Please see Important Safety Information on pages 18–19 for related and other risks.

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Adverse reactions (≥15%) in patients receiving PEMAZYRE (pemigatinib) in FIGHT-202[2]

PEMAZYRE N=146 Adverse Reaction	All Grades, %[a]	Grades 3 or 4, %[b]
Metabolism and nutrition disorders		
Hyperphosphatemia[c]	60	0
Decreased appetite	33	1.4
Hypophosphatemia[d]	23	12
Dehydration	15	3.4
Skin and subcutaneous tissue disorders		
Alopecia	49	0
Nail toxicity[e]	43	2.1
Dry skin	20	0.7
Palmar-plantar erythrodysesthesia syndrome	15	4.1
Gastrointestinal disorders		
Diarrhea	47	2.7
Nausea	40	2.1
Constipation	35	0.7
Stomatitis	35	5
Dry mouth	34	0
Vomiting	27	1.4
Abdominal pain	23	4.8

PEMAZYRE N=146 Adverse Reaction	All Grades, %[a]	Grades 3 or 4, %[b]
General disorders		
Fatigue	42	4.8
Edema peripheral	18	0.7
Nervous system disorders		
Dysgeusia	40	0
Headache	16	0
Eye disorders		
Dry eye[f]	35	0.7
Musculoskeletal and connective tissue disorders		
Arthralgia	25	6
Back pain	20	2.7
Pain in extremity	19	2.1
Infections and infestations		
Urinary tract infection	16	2.7
Investigations		
Weight loss	16	2.1

[a]Graded per NCI CTCAE 4.03.

[b]Only Grades 3 to 4 were identified.

[c]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.

[d]Includes hypophosphatemia and blood phosphorous decreased.

[e]Includes nail toxicity, nail disorder, nail discoloration, nail dystrophy, nail hypertrophy, nail ridging, nail infection, onychalgia, onychoclasis, onycholysis, onychomadesis, onychomycosis, and paronychia.

[f]Includes dry eye, keratitis, lacrimation increased, pinguecula, and punctate keratitis.

Clinically relevant adverse reactions occurring in ≤10% of patients included fractures (2.1%). In all patients treated with pemigatinib, 0.5% experienced pathologic fractures (which included patients with and without cholangiocarcinoma [N=635]). Soft tissue mineralization, including cutaneous calcification, calcinosis, and non-uremic calciphylaxis associated with hyperphosphatemia were observed with PEMAZYRE treatment.

Please see Important Safety Information on pages 18–19 for related and other risks.

Select laboratory abnormalities (≥10%) worsening from baseline in patients receiving PEMAZYRE in FIGHT-202[2]

PEMAZYRE[a] N=146 Laboratory Abnormality	All Grades, %[b]	Grades 3 or 4, %
Hematology		
Decreased hemoglobin	43	6
Decreased lymphocytes	36	8
Decreased platelets	28	3.4
Increased leukocytes	27	0.7
Decreased leukocytes	18	1.4
Chemistry		
Increased phosphate[c]	94	0
Decreased phosphate	68	38
Increased alanine aminotransferase	43	4.1
Increased aspartate aminotransferase	43	6
Increased calcium	43	4.1
Increased alkaline phosphatase	41	11
Increased creatinine[d]	41	1.4
Decreased sodium	39	12
Increased glucose	36	0.7
Decreased albumin	34	0
Increased urate	30	10
Increased bilirubin	26	6
Decreased potassium	26	5
Decreased calcium	17	2.7
Increased potassium	12	2.1
Decreased glucose	11	1.4

[a]The denominator used to calculate the rate varied from 142-146 based on the number of patients with a baseline value and at least one post-treatment value.

[b]Graded per NCI CTCAE 4.03.

[c]Based on CTCAE 5.0 grading.

[d]Graded based on comparison to upper limit of normal.

Increased creatinine[2]

Within the first 21-day cycle of PEMAZYRE dosing, serum creatinine increased (mean increase of 0.2 mg/dL) and reached steady state by Day 8, and then decreased during the 7 days off therapy. Consider alternative markers of renal function if persistent elevations in serum creatinine are observed.

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Safety considerations

Advise patients to inform you of any vision changes while taking PEMAZYRE (pemigatinib)[2]

PEMAZYRE can cause retinal pigment epithelial detachment (RPED), which may cause symptoms such as blurred vision, visual floaters, or photopsia. Clinical trials of PEMAZYRE did not conduct routine monitoring including optical coherence tomography (OCT) to detect asymptomatic RPED; therefore, the incidence of asymptomatic RPED with PEMAZYRE is unknown.[2]

- Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, RPED occurred in 11% of patients, including Grade 3-4 RPED in 1.3%
  - The median time to first onset of RPED was 56 days
  - RPED led to dose interruption of PEMAZYRE in 3.1% of patients
  - 1.3% of patients required dose reduction for RPED
  - 0.2% of patients discontinued treatment due to RPED
  - RPED resolved or improved to Grade 1 levels in 76% of patients who required dosage modification for RPED

Perform a comprehensive ophthalmological examination including OCT prior to initiation of PEMAZYRE and every 2 months for the first 6 months and every 3 months thereafter during treatment. For onset of visual symptoms, refer patients for ophthalmologic evaluation urgently, with follow-up every 3 weeks until resolution or discontinuation of PEMAZYRE.

Modify the dose or permanently discontinue PEMAZYRE as recommended.

Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, dry eye occurred in 31% of patients, including Grade 3-4 in 1.6% of patients. Treat patients with ocular demulcents as needed.

When to perform a comprehensive ophthalmological examination, including OCT[2]

Prior to initiation of therapy → **then** → **Every 2 months** for the first 6 months of treatment → **then** → **Every 3 months** thereafter during treatment

For onset of visual symptoms, refer patients for ophthalmologic evaluation urgently, with follow-up every 3 weeks until resolution or discontinuation of PEMAZYRE

Dosage modifications for RPED[2]

- If asymptomatic and stable on serial examination, continue PEMAZYRE
- If symptomatic or worsening on serial examination, withhold PEMAZYRE
  - If asymptomatic and improved on subsequent examination, resume PEMAZYRE at a lower dose
  - If symptoms persist or examination does not improve, consider permanent discontinuation of PEMAZYRE, based on clinical status

Hyperphosphatemia was observed in patients treated with PEMAZYRE[2]

- PEMAZYRE can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcification, calcinosis, and non-uremic calciphylaxis. Increases in phosphate levels are a pharmacodynamic effect of PEMAZYRE
- Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, hyperphosphatemia was reported in 93% of patients based on laboratory values above the upper limit of normal
- The median time to onset of hyperphosphatemia was 8 days (range 1–169)[2]
- Phosphate lowering therapy was required in 33% of patients receiving PEMAZYRE

Recommendations for management of hyperphosphatemia[2]

Monitor for hyperphosphatemia.

- Initiate a low phosphate diet when serum phosphate level is >5.5 mg/dL
- For serum phosphate levels >7 mg/dL, initiate phosphate lowering therapy and withhold, reduce the dose, or permanently discontinue PEMAZYRE based on duration and severity of hyperphosphatemia

Dosage Modifications for Hyperphosphatemia[2]

Severity	PEMAZYRE Dosage Modification
Serum phosphate >7 mg/dL – ≤10 mg/dL	• Initiate phosphate lowering therapy and monitor serum phosphate weekly • Withhold PEMAZYRE if levels are not <7 mg/dL within 2 weeks of starting phosphate lowering therapy • Resume PEMAZYRE at the same dose when phosphate levels are < 7 mg/dL for first occurrence; resume at a lower dose level for subsequent recurrences
Serum phosphate >10 mg/dL	• Initiate phosphate lowering therapy and monitor serum phosphate weekly • Withhold PEMAZYRE if levels are not ≤ 10 mg/dL within 1 week after starting phosphate lowering therapy • Resume PEMAZYRE at the next lower dose level when phosphate levels are <7 mg/dL • Permanently discontinue PEMAZYRE for recurrence of serum phosphate > 10 mg/dL following 2 dose reductions

Please see Important Safety Information on pages 18–19 for related and other risks.

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Safety considerations *(continued)*

Embryo-fetal toxicity[2]

- Based on findings in an animal study and its mechanism of action, PEMAZYRE (pemigatinib) can cause fetal harm when administered to a pregnant woman
- Oral administration of pemigatinib to pregnant rats during the period of organogenesis caused malformations, fetal growth retardation, and embryo-fetal death at maternal exposures lower than the human exposure based on area under the curve at the clinical dose of 13.5 mg

Advise patients of potential risks[2]	
Pregnant women	Advise pregnant women of the potential risk to the fetus.
Female patients	Advise female patients of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the last dose. Advise females to inform their healthcare provider if they are pregnant or become pregnant. Inform female patients of the risk to a fetus and potential loss of pregnancy. Advise patients not to breastfeed during treatment with PEMAZYRE and for 1 week after the last dose.
Male patients	Advise males with female partners of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the last dose.

One pill, once daily that can be taken at home with or without food[2]

The recommended dosage of PEMAZYRE is 13.5 mg taken orally once daily on a 21-day treatment cycle.[2]

Continue treatment until disease progression or unacceptable toxicity occurs.[2]

Instructions for patients[2]

PEMAZYRE can be taken with or without food

Instruct patients to take their dose of PEMAZYRE at approximately the same time every day

Do not crush, chew, split, or dissolve tablets

If the patient misses a dose by 4 or more hours or if vomiting occurs, resume dosing with the next scheduled dose

Please see Important Safety Information on pages 18–19 for related and other risks.

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Dosage modifications[2]

- PEMAZYRE (pemigatinib) is available in 3 strengths to enable dose modifications as needed—13.5 mg, 9 mg, and 4.5 mg

13.5 mg ▶ **9 mg** ▶ **4.5 mg**

Starting dose | **First dose reduction** | **Second dose reduction**

  - Permanently discontinue PEMAZYRE if unable to tolerate 4.5 mg once daily for 14 days of each 21-day cycle. 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 occurs.

- Reduce the dose of PEMAZYRE for adverse reactions
  - **RPED:** If asymptomatic and stable on serial examination, continue PEMAZYRE. If symptomatic or worsening on serial examination, withhold PEMAZYRE. If asymptomatic and improved on subsequent examination, resume PEMAZYRE at a lower dose. If symptoms persist or examination does not improve, consider permanent discontinuation of PEMAZYRE, based on clinical status.
  - **Hyperphosphatemia:** If serum phosphate >7 mg/dL to ≤10 mg/dL, initiate phosphate lowering therapy and monitor serum phosphate weekly. Withhold PEMAZYRE if levels are not <7 mg/dL within 2 weeks of starting phosphate lowering therapy, and resume PEMAZYRE at the same dose when phosphate levels are <7 mg/dL for first occurrence. Resume at a lower dose level for subsequent recurrences. If serum phosphate >10 mg/dL, initiate phosphate lowering therapy and monitor serum phosphate weekly, withhold PEMAZYRE if levels are not ≤10 mg/dL within 1 week after starting phosphate lowering therapy, and resume PEMAZYRE at the next lower dose level when phosphate levels are <7 mg/dL. Permanently discontinue PEMAZYRE for recurrence of serum phosphate >10 mg/dL following 2 dose reductions.
  - **Other adverse reactions.** For Grade 3, withhold PEMAZYRE until resolves to Grade 1 or baseline. Resume PEMAZYRE at next lower dose if resolves within 2 weeks, and permanently discontinue PEMAZYRE if does not resolve within 2 weeks. Permanently discontinue PEMAZYRE for recurrent Grade 3 after 2 dose reductions. For Grade 4, permanently discontinue PEMAZYRE.
- Avoid concomitant use of strong and moderate CYP3A inhibitors during treatment with PEMAZYRE
  - If concomitant use with a strong or moderate CYP3A inhibitor cannot be avoided, reduce the dose of PEMAZYRE
- Avoid concomitant use of strong and moderate CYP3A inducers with PEMAZYRE
- The recommended dosage of PEMAZYRE for patients with severe renal impairment (eGFR estimated by Modification of Diet in Renal Disease [MDRD] 15 to 29 mL/min/1.73 m^2) is 9 mg with the schedule (intermittent or continuous) designated for the indication
- The recommended dosage of PEMAZYRE for patients with severe hepatic impairment (total bilirubin >3 × upper limit of normal [ULN] with any AST) is 9 mg with the schedule (intermittent or continuous) designated for the indication

Refer to Full Prescribing Information for more information on dose modifications.
Your representative can provide more information regarding dosing modifications.

Please see Important Safety Information on pages 18–19 for related and other risks.

Pemazyre (pemigatinib) tablets 13.5 mg · 9 mg · 4.5 mg

Access and Support

PEMAZYRE is available through Biologics by McKesson specialty pharmacy who also provides support to help patients with their prescribed treatments. To request PEMAZYRE for your patients through Biologics, please call 1-800-850-4306 or complete and fax a PEMAZYRE Enrollment Form.

Specialty Pharmacy and Distribution

Specialty Distributors (SDs)

PEMAZYRE is available for purchase from these authorized Specialty Distributors:

- ASD Healthcare
- Cardinal Specialty
- McKesson Specialty
- Oncology Supply

IncyteCARES for PEMAZYRE

We're Here to Support Your Eligible Patients During Treatment

Our mission is to help your patients start and stay on therapy by assisting with access and ongoing support.

Information and resources available through IncyteCARES include:

- Benefits verification and as-needed prior authorization or appeal support
- Pharmacy outreach call to help patients get started on treatment
- Flexibly scheduled calls from a pharmacy care team specialist
- Treatment history and medication monitoring
- Text message refill reminders
- Education and support resources
- Information about financial assistance options*
- Practice resources and forms

*Terms and conditions apply.

Our Team Is Here To Help!

Call us at
1-855-452-5234

Monday through Friday, 8 AM–8 PM ET

Or contact Biologics directly at
1-800-850-4306

IncyteCARES

IMPORTANT SAFETY INFORMATION

Ocular Toxicity

Retinal Pigment Epithelial Detachment (RPED): PEMAZYRE can cause RPED, which may cause symptoms such as blurred vision, visual floaters, or photopsia. Clinical trials of PEMAZYRE did not conduct routine monitoring including optical coherence tomography (OCT) to detect asymptomatic RPED; therefore, the incidence of asymptomatic RPED with PEMAZYRE is unknown.

Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, RPED occurred in 11% of patients, including Grade 3-4 RPED in 1.3%. The median time to first onset of RPED was 56 days. RPED led to dose interruption of PEMAZYRE in 3.1% of patients, and dose reduction and permanent discontinuation in 1.3% and in 0.2% of patients, respectively. RPED resolved or improved to Grade 1 levels in 76% of patients who required dosage modification of PEMAZYRE for RPED.

Perform a comprehensive ophthalmological examination including OCT prior to initiation of PEMAZYRE and every 2 months for the first 6 months and every 3 months thereafter during treatment. For onset of visual symptoms, refer patients for ophthalmologic evaluation urgently, with follow-up every 3 weeks until resolution or discontinuation of PEMAZYRE. Modify the dose or permanently discontinue PEMAZYRE as recommended in the prescribing information for PEMAZYRE.

Dry Eye: Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, dry eye occurred in 31% of patients, including Grade 3-4 in 1.6% of patients. Treat patients with ocular demulcents as needed.

Hyperphosphatemia and Soft Tissue Mineralization

PEMAZYRE can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcification, calcinosis, and non-uremic calciphylaxis. Increases in phosphate levels are a pharmacodynamic effect of PEMAZYRE. Among 635 patients who received a starting dose of PEMAZYRE 13.5 mg across clinical trials, hyperphosphatemia was reported in 93% of patients based on laboratory values above the upper limit of normal. The median time to onset of hyperphosphatemia was 8 days (range 1-169). Phosphate lowering therapy was required in 33% of patients receiving PEMAZYRE.

Monitor for hyperphosphatemia and initiate a low phosphate diet when serum phosphate level is > 5.5 mg/dL. For serum phosphate levels > 7 mg/dL, initiate phosphate lowering therapy and withhold, reduce the dose, or permanently discontinue PEMAZYRE based on duration and severity of hyperphosphatemia as recommended in the prescribing information.

Embryo-Fetal Toxicity

Based on findings in an animal study and its mechanism of action, PEMAZYRE can cause fetal harm when administered to a pregnant woman. Oral administration of pemigatinib to pregnant rats during the period of organogenesis caused fetal malformations, fetal growth retardation, and embryo-fetal death at maternal exposures lower than the human exposure based on area under the curve (AUC) at the clinical dose of 13.5 mg.

Advise pregnant women of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the last dose.

Adverse Reactions: Cholangiocarcinoma

Serious adverse reactions occurred in 45% of patients receiving PEMAZYRE (n=146). Serious adverse reactions in ≥2% of patients who received PEMAZYRE included abdominal pain, pyrexia, cholangitis, pleural effusion, acute kidney injury, cholangitis infective, failure to thrive, hypercalcemia, hyponatremia, small intestinal obstruction, and urinary tract infection. Fatal adverse reactions occurred in 4.1% of patients, including failure to thrive, bile duct obstruction, cholangitis, sepsis, and pleural effusion.

Permanent discontinuation due to an adverse reaction occurred in 9% of patients who received PEMAZYRE. Adverse reactions requiring permanent discontinuation in ≥1% of patients included intestinal obstruction and acute kidney injury.

Dosage interruptions due to an adverse reaction occurred in 43% of patients who received PEMAZYRE. Adverse reactions requiring dosage interruption in ≥1% of patients included stomatitis, palmar-plantar erythrodysesthesia syndrome, arthralgia, fatigue, abdominal pain, AST increased, asthenia, pyrexia, ALT increased, cholangitis, small intestinal obstruction, alkaline phosphatase increased, diarrhea, hyperbilirubinemia, electrocardiogram QT prolonged, decreased appetite, dehydration, hypercalcemia, hyperphosphatemia, hypophosphatemia, back pain, pain in extremity, syncope, acute kidney injury, onychomadesis, and hypotension.

Dose reductions due to an adverse reaction occurred in 14% of patients who received PEMAZYRE. Adverse reactions requiring dosage reductions in ≥1% of patients who received PEMAZYRE included stomatitis, arthralgia, palmar-plantar erythrodysesthesia syndrome, asthenia, and onychomadesis.

Clinically relevant adverse reactions occurring in ≤10% of patients included fractures (2.1%). In all patients treated with pemigatinib, 0.5% experienced pathologic fractures (which included patients with and without cholangiocarcinoma [N = 635]). Soft tissue mineralization, including cutaneous calcification, calcinosis, and non-uremic calciphylaxis associated with hyperphosphatemia were observed with PEMAZYRE treatment.

Within the first 21-day cycle of PEMAZYRE dosing, serum creatinine increased (mean increase of 0.2 mg/dL) and reached steady state by Day 8, and then decreased during the 7 days off therapy. Consider alternative markers of renal function if persistent elevations in serum creatinine are observed.

In cholangiocarcinoma (n=146) the most common adverse reactions (incidence ≥20%) were hyperphosphatemia (60%), alopecia (49%), diarrhea (47%), nail toxicity (43%), fatigue (42%), dysgeusia (40%), nausea (40%), constipation (35%), stomatitis (35%), dry eye (35%), dry mouth (34%), decreased appetite (33%), vomiting (27%), arthralgia (25%), abdominal pain (23%), hypophosphatemia (23%), back pain (20%), and dry skin (20%).

Drug Interactions

Avoid concomitant use of strong and moderate CYP3A inhibitors with PEMAZYRE. Reduce the dose of PEMAZYRE if concomitant use with a strong or moderate CYP3A inhibitor cannot be avoided. Avoid concomitant use of strong and moderate CYP3A inducers with PEMAZYRE.

Special Populations

Advise lactating women not to breastfeed during treatment with PEMAZYRE and for 1 week after the last dose.

Reduce the recommended dose of PEMAZYRE for patients with severe renal impairment as described in the prescribing information.

Reduce the recommended dose of PEMAZYRE for patients with severe hepatic impairment as described in the prescribing information.

References: 1. Data on file. Incyte Corporation. Wilmington, DE. **2.** PEMAZYRE Prescribing Information, Incyte Corporation. **3.** Ross JS, Wang K, Gay L, et al. *Oncologist*. 2014;19(3):235-242. **4.** Farshidfar F, Zheng S, Gingras MC, et al. *Cell Rep*. 2017;18(11):2780-2794. **5.** Graham RP, Barr Fritcher EG, Pestova E, et al. *Human Pathol*. 2014;45(8):1630-1638. **6.** Lowery MA, Ptashkin R, Jordan E, et al. *Clin Cancer Res*. 2018;24(17):4154-4161. **7.** Sia D, Losic B, Moeini A, et al. *Nat Commun*. 2015;6:6087. **8.** Chun SY, Javle M. *Cancer Contr*. 2017;24(3):1-7. **9.** Arai Y, Totoki Y, Hosoda F, et al. *Hepatology*. 2014;59(4):1427-1434. **10.** Borad MJ, Gores GJ, Roberts LR. *Curr Opin Gastroenterol*. 2015;31(3):264-268. **11.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed May 13, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. **12.** Silverman IM, Hollebecque A, Friboulet L, et al. Clinicogenomic analysis of FGFR2-rearranged cholangiocarcinoma identifies correlates of response and mechanisms of resistance to pemigatinib. *Cancer Discov*. 2021;11:326-339. **13.** Abou-Alfa GK, Sahai V, Hollebecque H, 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. **14.** Javle MM, Murugesan K, Shroff RT, et al. *J Clin Oncol*. 2019;37(15 suppl):4087. **15.** Hollebecque A, de Bono JS, Plummer R, et al. *Ann Oncol*. 2019;30(suppl 1):mdz029. **16.** Frampton GM, Fichtenholtz A, Otto GA, et al. *Nat Biotechnol*. 2013;31(11):1023-1031.

Please click here for Full Prescribing Information.

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Target Patients in Second-Line Treatment

3+ YEARS

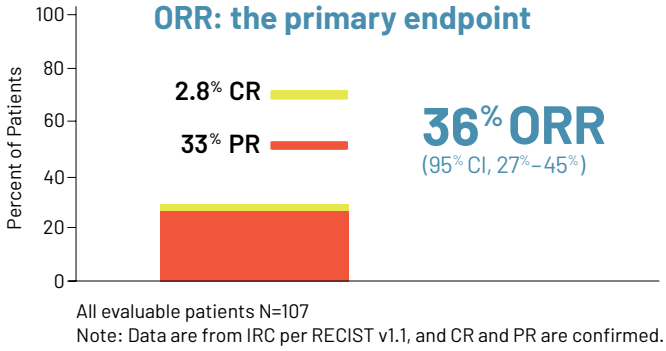
OF **CLINICAL EXPERIENCE** SINCE FDA APPROVAL WITH **1,000+ PATIENTS** TREATED[1,*]

*Commercially available in the US since 2020.

- 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 as detected by an FDA-approved test
  - This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)

- **Use an NGS test such as FoundationOne® CDx that can detect both known (frequently occurring) and unknown (rare or patient-specific) FGFR2 fusion partners[6,14-16]**
- **In the Phase 2 FIGHT-202 study:[2]**

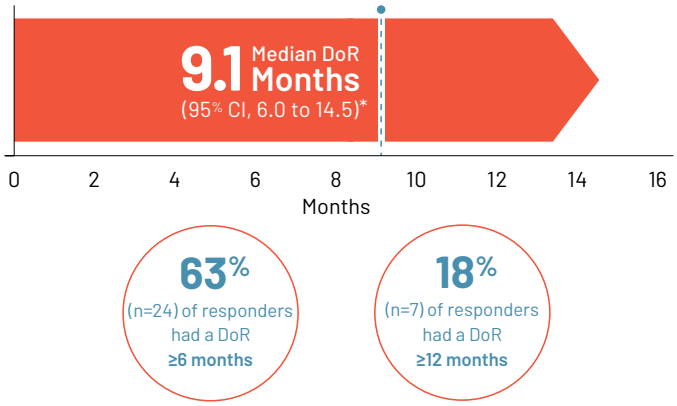
PEMAZYRE demonstrated a 36% ORR[2]



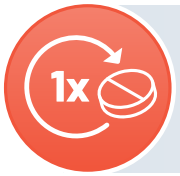
All evaluable patients N=107
Note: Data are from IRC per RECIST v1.1, and CR and PR are confirmed.

Median time to response was 2.7 months (range, 0.7–6.9 months)

Duration of response (DoR)[2]



CI, confidence interval; CR, complete response; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.
*The 95% CI was calculated using the Brookmeyer and Crowley's method.



One pill, once daily that can be taken at home with or without food regardless of dose[2]

PEMAZYRE can cause ocular toxicity, hyperphosphatemia and soft tissue mineralization, and embryo-fetal toxicity. These are not all of the risks. Please see Important Safety Information on pages 18–19.

In cholangiocarcinoma, the most common adverse reactions (incidence ≥ 20%) are hyperphosphatemia, alopecia, diarrhea, nail toxicity, fatigue, dysgeusia, nausea, constipation, stomatitis, dry eye, dry mouth, decreased appetite, vomiting, arthralgia, abdominal pain, hypophosphatemia, back pain, and dry skin.[2]

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