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

The first and only FDA-approved treatment for previously treated, unresectable locally advanced or metastatic cholangiocarcinoma (CCA) with an FGFR2 fusion or rearrangement[1]

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 466 patients who received PEMAZYRE across clinical trials, RPED occurred in 6% of patients, including Grade 3-4 RPED in 0.6%. The median time to first onset of RPED was 62 days. RPED led to dose interruption of PEMAZYRE in 1.7% of patients, and dose reduction and permanent discontinuation in 0.4% and in 0.4% of patients, respectively. RPED resolved or improved to Grade 1 levels in 87.5% 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 466 patients who received PEMAZYRE across clinical trials, dry eye occurred in 27% of patients, including Grade 3-4 in 0.6% of patients. Treat patients with ocular demulcents as needed.

Please see Important Safety Information on pages 14-15 for related and other risks.

Molecular profiling and biomarker-targeted therapy are transforming patient care in intrahepatic cholangiocarcinoma (iCCA)[2]

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

FGFR2 fusions are among the most common actionable genomic alterations in iCCA[5,7,8]

10%–16% of patients with iCCA have FGFR2 fusions[5,7,8]

- FGFR2 fusions are detectable early in disease progression and 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 consideration of 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 should be considered."[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.

Testing for FGFR2 fusions or rearrangements can inform treatment in iCCA[3,12-14]

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

- Specifically detects FGFR2 fusions (distinct from FGFR2 mutations)
- Detects fusions with a wide range of fusion partners (whether known or unknown)
- A high-sensitivity NGS-based assay, such as **FoundationOne® CDx**, can detect FGFR2 fusions, including those with known or unknown fusion partners

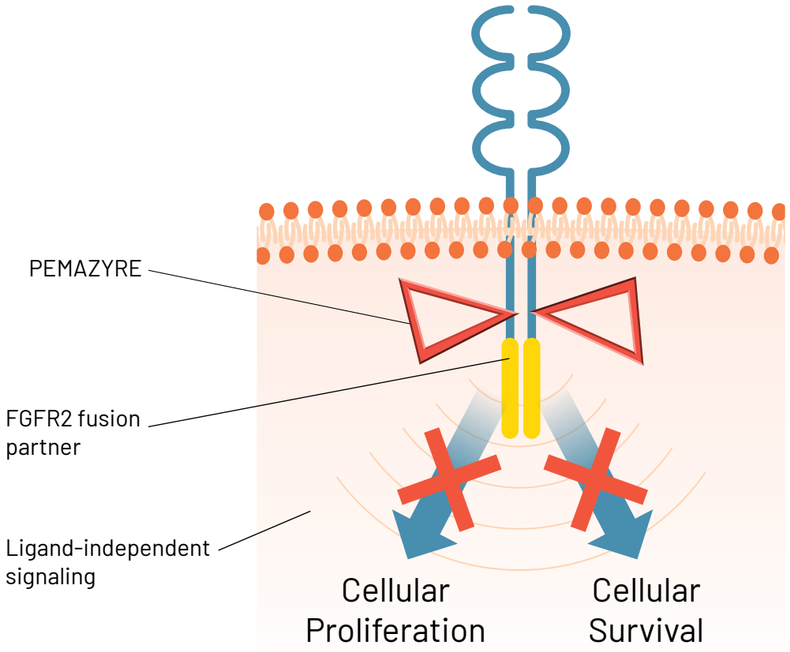
The first and only FDA-approved FGFR2-fusion-targeted therapy for CCA

PEMAZYRE (pemigatinib) is the first and only FDA-approved treatment for patients with previously treated, unresectable locally advanced or metastatic CCA with an FGFR2 fusion or rearrangement.[1]

Pemigatinib is a small-molecule kinase inhibitor of FGFR1, 2 and 3 with IC_{50} values of <2 nM.[1]

Constitutive FGFR signaling can support the proliferation and survival of malignant cells.[1]

Pemigatinib inhibits FGFR1–3 phosphorylation and signaling[1]



PEMAZYRE inhibits FGFR2 kinase activity, which may decrease tumor cell proliferation and survival in FGFR-driven tumors.[1]

Please see Important Safety Information on pages 14–15 for related and other risks.

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

PEMAZYRE (pemigatinib) provided durable responses[1]

PEMAZYRE was studied in the FIGHT-202 trial[1]

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 treatment 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

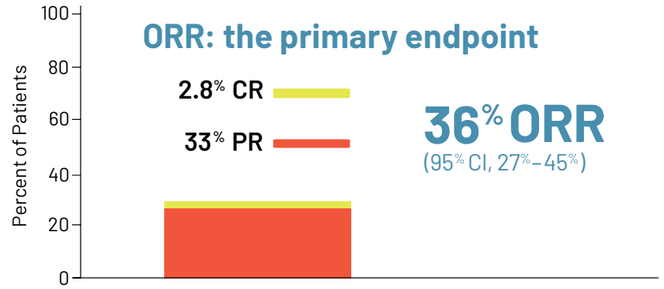
Hyperphosphatemia

Increases in phosphate levels are a pharmacodynamic effect of PEMAZYRE. Among 466 patients who received PEMAZYRE across clinical trials, hyperphosphatemia was reported in 92% 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 29% 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 14-15 for related and other risks.

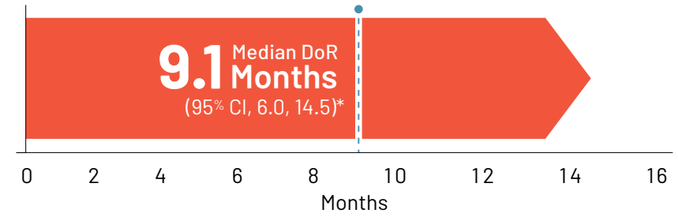
PEMAZYRE (pemigatinib) demonstrated a 36% ORR[1]



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)[1]



63% (n=24) of responders had a DoR **≥6 months**

18% (n=7) of responders had a DoR **≥12 months**

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 final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the final dose.

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The safety of PEMAZYRE (pemigatinib) was evaluated in FIGHT 202[1]

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. 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[1]

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

Adverse Reaction	PEMAZYRE N=146 All Grades[a] (%)	PEMAZYRE N=146 Grades ≥3* (%)
Metabolism and nutrition disorders		
Hyperphosphatemia[b]	60	0
Decreased appetite	33	1.4
Hypophosphatemia[c]	23	12
Dehydration	15	3.4
Skin and subcutaneous tissue disorders		
Alopecia	49	0
Nail toxicity[d]	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

Adverse Reaction	PEMAZYRE N=146 All Grades[a] (%)	PEMAZYRE N=146 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[e]	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

*Only Grades 3–4 were identified.

[a]Graded per NCI CTCAE 4.03.

[b]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.

[c]Includes hypophosphatemia and blood phosphorous decreased.

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

[e]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, 1.3% experienced pathologic fractures (which included patients with and without cholangiocarcinoma [N=466]).

Please see Important Safety Information on pages 14-15 for related and other risks.

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

Select laboratory abnormalities (≥10%) worsening from baseline in patients receiving PEMAZYRE (pemigatinib) in FIGHT-202[1]

Laboratory Abnormality	PEMAZYRE[a] N=146 All Grades[b] (%)	Grades ≥3 (%)
Hematology		
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[1]

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.

Hyperphosphatemia was observed in patients treated with PEMAZYRE (pemigatinib)[1]

- Among 466 patients who received PEMAZYRE across clinical trials, hyperphosphatemia was reported in **92%** of patients based on laboratory values above the upper limit of normal[1]
- The median time to onset of hyperphosphatemia was 8 days (range 1–169)[1]
- Phosphate lowering therapy was used by **29%** of patients during treatment with PEMAZYRE[1]
- No patients discontinued treatment due to hyperphosphatemia[15]

Recommendations for management of hyperphosphatemia

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[1]

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 14-15 for related and other risks.

Pemazyre (pemigatinib) tablets 13.5mg 9mg 4.5mg

Safety considerations

Advise patients to inform you of any vision changes while taking PEMAZYRE (pemigatinib)[1]

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.

- Among 466 patients who received PEMAZYRE across clinical trials, **RPED** occurred in 6% of patients, including Grade 3–4 RPED in 0.6%[1]
  - The median time to first onset of RPED was 62 days
  - RPED led to dose interruption of PEMAZYRE in 1.7% of patients
  - 0.4% of patients required dose reduction for RPED
  - 0.4% of patients discontinued treatment due to RPED
  - RPED resolved or improved to Grade 1 levels in 87.5% 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 466 patients who received PEMAZYRE across clinical trials, **dry eye** occurred in 27% of patients[1]
  - Grade 3-4 dry eye occurred in 0.6% of patients
  - Treat patients with ocular demulcents as needed

When to perform a comprehensive ophthalmological examination, including OCT[1]

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[1]

- 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

Embryo-fetal toxicity[1]

- 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 malformations, fetal growth retardation, and embryo-fetal death at maternal exposures than the human exposure based on area under the curve at the clinical dose of 13.5 mg

Advise patients of potential risks[1]	
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 final 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 final 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 final dose.

PEMAZYRE (pemigatinib) is a once-daily oral therapy[1]

The recommended dosage of PEMAZYRE is 13.5 mg taken orally once daily on a 21-day treatment cycle.[1]

Continue treatment until disease progression or unacceptable toxicity occurs.[1]

Please see Important Safety Information on pages 14-15 for related and other risks.

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

PEMAZYRE (pemigatinib) can be taken with or without food[1]

- 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

Dosage modifications[1]

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

13.5 mg (Starting dose) ▶ **9 mg** (First dose reduction) ▶ **4.5 mg** (Second dose reduction)

  - Permanently discontinue PEMAZYRE if unable to tolerate 4.5 mg once daily
- 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.

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 14-15 for related and other risks.

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

Access and Support

PEMAZYRE (pemigatinib) is dispensed exclusively by Biologics by McKesson specialty pharmacy. Biologics will work with you and your patient to provide their therapeutic expertise and individualized support.

IncyteCARES FOR PEMAZYRE

At IncyteCARES, our mission is to help eligible patients access their prescribed Incyte medication and to offer information and resources that promote adherence and provide extra support during treatment.

OUR TEAM PROVIDES SUPPORT FOR YOUR ELIGIBLE PATIENTS DURING TREATMENT THAT MAY 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 an oncology nurse specialist to support adherence
- Treatment history and medication monitoring
- Refill reminders
- Education and support resources
- Information about financial assistance options*

*Terms and conditions apply.

Our team is here to help!

Call us at:
1-866-708-8806
Monday through Friday,
8 AM–8 PM ET

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

IncyteCARES
Connecting to Access, Reimbursement, Education and Support

IMPORTANT SAFETY INFORMATION

Ocular Toxicity

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Among 466 patients who received PEMAZYRE across clinical trials, RPED occurred in 6% of patients, including Grade 3-4 RPED in 0.6%. The median time to first onset of RPED was 62 days. RPED led to dose interruption of PEMAZYRE in 1.7% of patients, and dose reduction and permanent discontinuation in 0.4% and in 0.4% of patients, respectively. RPED resolved or improved to Grade 1 levels in 87.5% 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 466 patients who received PEMAZYRE across clinical trials, dry eye occurred in 27% of patients, including Grade 3-4 in 0.6% of patients. Treat patients with ocular demulcents as needed.

Hyperphosphatemia

Increases in phosphate levels are a pharmacodynamic effect of PEMAZYRE. Among 466 patients who received PEMAZYRE across clinical trials, hyperphosphatemia was reported in 92% 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 29% 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 final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with PEMAZYRE and for 1 week after the final dose.

Adverse Reactions

Serious adverse reactions occurred in 45% of patients receiving PEMAZYRE. 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, 1.3% experienced pathologic fractures (which included patients with and without cholangiocarcinoma [N=466]).

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.

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 final dose.

Please click here for Full Prescribing Information.

References: 1. PEMAZYRE (pemigatinib) Prescribing Information. Incyte Corporation. **2.** Hallinan N, Finn S, Cuffe S, Rafee S, O'Byrne K, Gately K. *Cancer Treatment Rev*. 2016;46:51-62. **3.** Lowery MA, Ptashkin R, Jordan E, et al. *Clin Cancer Res*. 2018;24(17):4154-4161. **4.** Sia D, Losic B, Moeini A, et al. *Nat Commun*. 2015;6:6087. **5.** Ross JS, Wang K, Gay L, et al. *Oncologist*. 2014;19(3):235-242. **6.** Chun SY, Javle M. *Cancer Contr*. 2017;24(3):1-7. **7.** Farshidfar F, Zheng S, Gingras MC, et al. *Cell Rep*. 2017;18(11):2780-2794. **8.** Graham RP, Barr Fritcher EG, Pestova E, et al. *Human Pathol*. 2014;45(8):1630-1638. **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.4.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed June 19, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **12.** Javle MM, Murugesan K, Shroff RT, et al. *J Clin Oncol*. 2019;37(15 suppl):4087. **13.** Hollebecque A, de Bono JS, Plummer R, et al. *Ann Oncol*. 2019;30(suppl 1):mdz029. **14.** Frampton GM, Fichtenholtz A, Otto GA, et al. *Nat Biotechnol*. 2013;31(11):1023-1031. **15.** Data on file. Incyte Corporation. Wilmington, DE.

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

Target FGFR2-fusion-positive CCA with PEMAZYRE (pemigatinib)

The **first and only FDA-approved treatment** for previously treated, unresectable locally advanced or metastatic cholangiocarcinoma (CCA) with an FGFR2 fusion or rearrangement[1]

Test for FGFR2 fusions or rearrangements

- FGFR2 fusions are among the most common actionable genomic alterations in iCCA[5,7,8]
- **10%–16%** of patients with iCCA have FGFR2 fusions[5,7,8]
- An NGS-based assay, such as **FoundationOne® CDx**, can detect FGFR2 fusions, including those with known or unknown fusion partners[3,12–14]

Treat with PEMAZYRE

- PEMAZYRE demonstrated durable responses in previously treated patients[1]
  - **ORR** of 36% (95% CI: 27%, 45%)
  - **Median DoR** of 9.1 months (95% CI: 6.0, 14.5)

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 466 patients who received PEMAZYRE across clinical trials, RPED occurred in 6% of patients, including Grade 3-4 RPED in 0.6%. The median time to first onset of RPED was 62 days. RPED led to dose interruption of PEMAZYRE in 1.7% of patients, and dose reduction and permanent discontinuation in 0.4% and in 0.4% of patients, respectively. RPED resolved or improved to Grade 1 levels in 87.5% 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 466 patients who received PEMAZYRE across clinical trials, dry eye occurred in 27% of patients, including Grade 3-4 in 0.6% of patients. Treat patients with ocular demulcents as needed.

Please see Important Safety Information on pages 14–15 for related and other risks.

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