LONG-TERM DATA

4-YEAR FOLLOW-UP ANALYSIS

SEE PAGES 9-10

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

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).

PEMAZYRE was granted accelerated approval based on the 15.4-month primary analysis of the FIGHT-202 study. The 4-year follow-up data from FIGHT-202 have not been submitted to or reviewed by the FDA, and potential inclusion of these data in the final FDA-approved labeling has yet to be determined.

TARGET CCA WITH AN ESTABLISHED TREATMENT[1]

Primary analysis[1]

36%
overall response rate
(95% CI, 27–45)*

9.1 months
median duration of response
(95% CI, 6.0–14.5)†

1 pill
taken once a day, 14 days on, 7 days off, on a 21-day cycle[1]

CCA, cholangiocarcinoma; CI, confidence interval; CR, complete response; FDA, Food and Drug Administration; IRC, independent review committee; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.
*All evaluable patients (n=107). Note: Data are from IRC per RECIST v1.1, and CR and PR are confirmed.[1]
†The 95% CI was calculated using the Brookmeyer and Crowley's method.[1]

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.

Please see Important Safety Information on pages 20-21 for related and other risks.

PEMAZYRE IS THE FIRST TARGETED THERAPY TO BE APPROVED BY THE FDA FOR ADULTS WHO HAVE CCA WITH *FGFR2* FUSIONS[1]

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).

<<5+>> YEARS of experience since FDA approval

with <<1,500+>> PATIENTS treated after FDA approval[2*]

NCCN RECOMMENDS

National Comprehensive Cancer Network® (NCCN®) recommends pemigatinib (PEMAZYRE) as a subsequent-line systemic therapy option for unresectable or metastatic CCA with *FGFR2* fusions or rearrangements following disease progression[3†‡§]

CCA, cholangiocarcinoma; FDA, Food and Drug Administration; FGFR, fibroblast growth factor receptor; NGS, next-generation sequencing.

*Commercially available in the US since 2020.

†See the NCCN Clinical Practice Guidelines in Oncology (NCCN 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.

§NCCN Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus (≥85% of the Panel) that the intervention is appropriate.[3]

IMPORTANT SAFETY INFORMATION (cont'd)

Ocular Toxicity (cont'd)

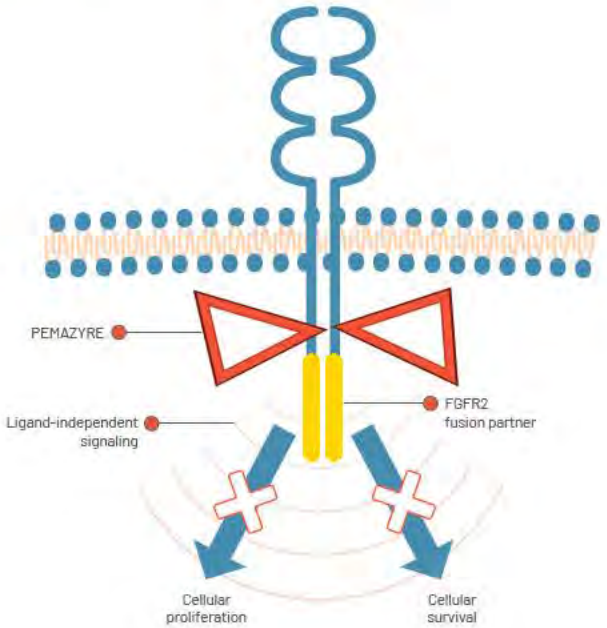
Perform a comprehensive ophthalmological examination including OCT prior to initiation of PEMAZYRE and every 2 months for the first 6 months and every 3 months thereafter during treatment. For onset of visual symptoms, refer patients for ophthalmologic evaluation urgently, with follow-up every 3 weeks 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 20-21 for related and other risks.

PEMAZYRE INHIBITS FGFR1, 2, AND 3 PHOSPHORYLATION AND SIGNALING[1]

PEMAZYRE is a small-molecule kinase inhibitor of FGFR1, 2, and 3



Constitutive FGFR signaling can support the proliferation and survival of malignant cells. PEMAZYRE inhibits FGFR kinase activity, which may decrease tumor cell proliferation and survival in *FGFR*-driven tumors.

***FGFR* fusions in CCA can be detected through NGS testing[4]**

Please see Important Safety Information on pages 20-21 for related and other risks.

TRANSFORM YOUR PATIENT CARE IN CCA WITH EARLY NGS TESTING[5,6]

Molecular profiling at the time of diagnosis can help identify the best treatment options from the start[6,7]

***FGFR2* fusions are among the most common actionable genomic alterations in iCCA[5,8-10]**

~50%
of patients with iCCA have actionable genomic alterations[5,8-10]

10%-16%
of patients with iCCA have *FGFR2* fusions[5,10,11]

- *FGFR2* fusions may be detectable early in disease progression and are key drivers of tumor growth[7,12]

NCCN RECOMMENDS

NCCN recommends comprehensive molecular testing for patients with unresectable or metastatic CCA[3*†‡]

"Given emerging evidence regarding actionable targets for treating BTCs, comprehensive molecular profiling is recommended for patients with unresectable or metastatic BTC who are candidates for systemic therapy."

BTC, biliary tract cancer; CCA, cholangiocarcinoma; FDA, Food and Drug Administration; FGFR, fibroblast growth factor receptor; iCCA, intrahepatic CCA; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing.
*See the NCCN 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 (≥85% of the Panel) that the intervention is appropriate.[3]

IMPORTANT SAFETY INFORMATION (cont'd)

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 20-21 for related and other risks.

TEST EARLY, TEST RIGHT

Ensure
patients receive molecular profiling at the time of diagnosis[6,7]

Select
an appropriate NGS test that[8,13]:

- Specifically detects *FGFR2* fusions (distinct from *FGFR2* mutations)
- Detects fusions with a wide range of fusion partners, both known and unknown

Consider
PEMAZYRE for your adult patients with previously treated, unresectable locally advanced or metastatic CCA with an *FGFR2* fusion or other rearrangement as detected by an FDA-approved test[1]

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

Test for *FGFR2* fusions at diagnosis of CCA

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Please see Important Safety Information on pages 20-21 for related and other risks.

STUDIED IN THE LARGEST CLINICAL TRIAL TO DATE FOR AN APPROVED SECOND-LINE TREATMENT FOR *FGFR2* FUSION-POSITIVE CCA[1]

FIGHT-202 was a Phase 2, multicenter, open-label, single-arm study in previously treated patients with locally advanced or metastatic cholangiocarcinoma (N=146)[1,14]

N=146 → n=107

Key inclusion criteria

- Adults with unresectable locally advanced or metastatic CCA
- Documented FGF/FGFR status*
- Progression after ≥1 prior therapy (including patients with ≥3 prior LoT)
- ECOG PS of 0 to 2
- No prior treatment with a selective FGFRi

Efficacy evaluable population

Patients with *FGFR2* gene fusions or non-fusion rearrangements*

PEMAZYRE 13.5 mg once daily†

21-day cycle:
14 days on/7 days off

Primary Endpoint‡:

- ORR

Secondary Endpoints‡:

- DoR
- DCR
- PFS
- OS
- Safety

CCA, cholangiocarcinoma; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance score; FGF, fibroblast growth factor; FGFR, FGF receptor; FGFRi, FGFR inhibitor; IRC, independent review committee; LoT, lines of therapy; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.

*FGFR2 fusion or non-fusion rearrangement status determined by a clinical trial assay performed at a central laboratory.[1]

†PEMAZYRE was administered until disease progression or unacceptable toxicity.[1]

‡For select endpoints, as determined by an IRC according to RECIST v1.1.[14]

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: Cholangiocarcinoma (cont'd)

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.

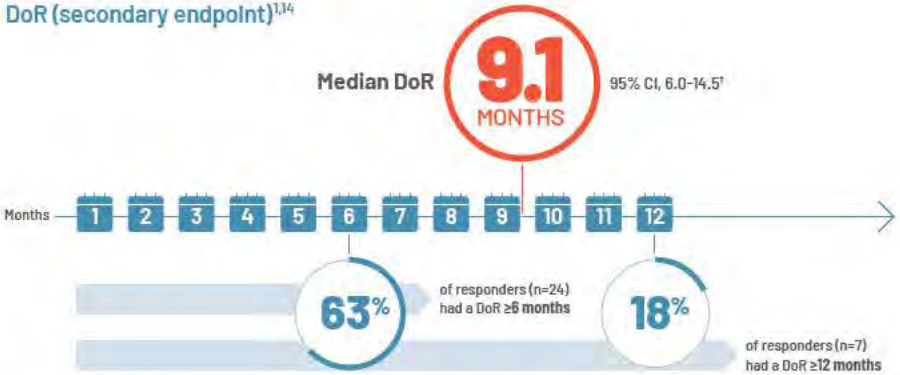
Dosage interruptions due to an adverse reaction occurred in 43% of patients who received PEMAZYRE. Adverse reactions requiring dosage interruption in ≥1% of patients included stomatitis, palmar-plantar erythrodysesthesia syndrome, arthralgia, fatigue, abdominal pain, AST increased, asthenia, pyrexia, 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.

Please see Important Safety Information on pages 20-21 for related and other risks.

ROBUST, DURABLE RESPONSES

In the FIGHT-202 primary analysis PEMAZYRE demonstrated a 36% ORR (primary endpoint)[1,14]*

DoR (secondary endpoint)[1,14]



*All evaluable patients (n=107). Note: Data are from IRC per RECIST v1.1, and CR and PR are confirmed.[1]

†The 95% CI was calculated using the Brookmeyer and Crowley's method.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: Cholangiocarcinoma (cont'd)

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.

Please see Important Safety Information on pages 20-21 for related and other risks.

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[1]

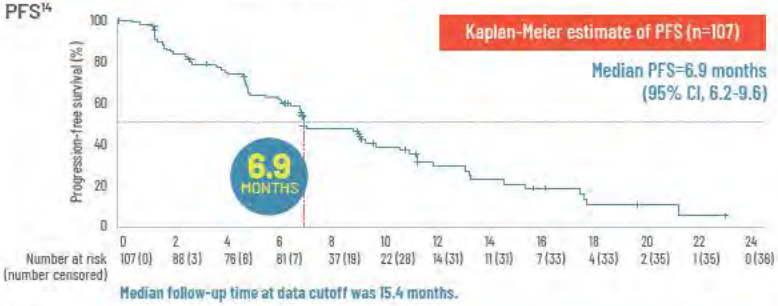
- DCR, PFS, and OS were secondary endpoints studied in FIGHT-202 that are not reflected in the full Prescribing Information[1,14]
- Due to the potential variability in the natural history of the disease, a single-arm study may not adequately characterize these time-to-event endpoints
- For this reason, a confirmatory Phase 3 study in cholangiocarcinoma is underway

In the FIGHT-202 primary analysis[14]

DCR was defined as CR+PR+SD

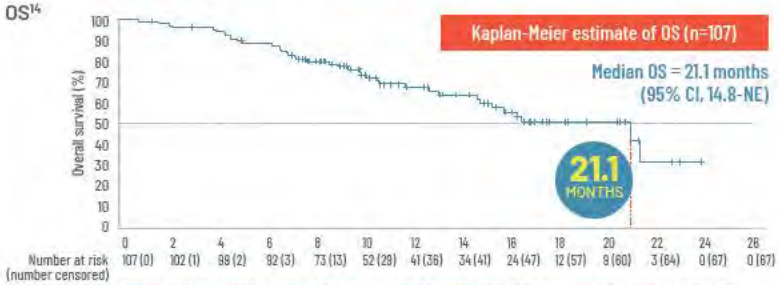
- CR in 2.8% of patients (n=3); PR in 32.7% of patients (n=35); SD in 46.7% of patients (n=50)
- FIGHT-202 was a single-arm study
  - In this setting, the DCR results may reflect the natural history of cholangiocarcinoma in an individual patient rather than the direct effect of the treatment

PFS[14]



Median follow-up time at data cutoff was 15.4 months.

OS[14]



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.

CCA, cholangiocarcinoma; CI, confidence interval; CR, complete response; DCR, disease control rate; FDA, Food and Drug Administration; OS, overall survival; NE, not evaluable; PFS, progression-free survival; PR, partial response; SD, stable disease.

Please see Important Safety Information on pages 20-21 for related and other risks.

Pemazyre® (pemigatinib) tablets

LONG-TERM DATA

4-YEAR FOLLOW-UP ANALYSIS

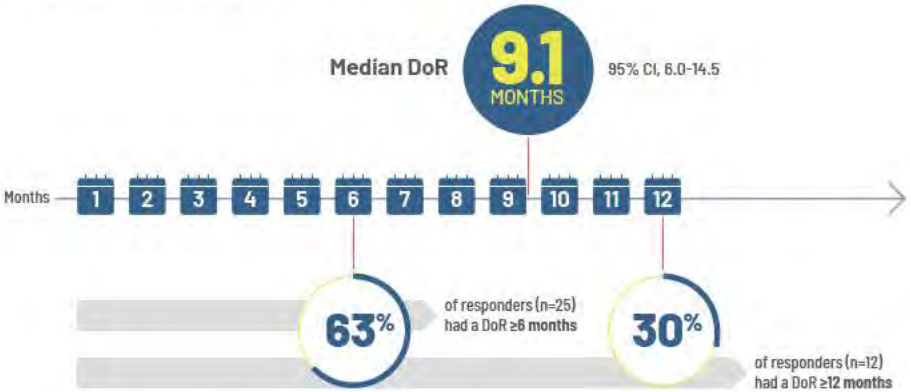
PEMAZYRE was granted accelerated approval based on the 15.4-month primary analysis of the FIGHT-202 study. The 4-year follow-up data from FIGHT-202 have not been submitted to or reviewed by the FDA, and potential inclusion of these data in the final FDA-approved labeling has yet to be determined.

In the 4-year follow-up analysis, the safety population consisted of 147 patients. The efficacy population consisted of 108 patients.[15]

4-year follow-up analysis: ORR (primary endpoint)[15]*

2.7 months median time to response
(range, 0.7-16.6 months)

4-year follow-up analysis: DoR (secondary endpoint)[15,16]



DoR, duration of response; IRC, independent review committee; ORR, overall response rate; RECIST, Response Evaluation Criteria in Solid Tumors.
*All evaluable patients (n=108). Note: Data are from IRC per RECIST v1.1.[15]

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: Cholangiocarcinoma (cont'd)

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%).

Please see Important Safety Information on pages 20-21 for related and other risks.

LONG-TERM DATA

4-YEAR FOLLOW-UP ANALYSIS—ADDITIONAL ENDPOINTS

PEMAZYRE was granted accelerated approval based on the 15.4-month primary analysis of the FIGHT-202 study. The 4-year follow-up data from FIGHT-202 have not been submitted to or reviewed by the FDA, and potential inclusion of these data in the final FDA-approved labeling has yet to be determined.

In the 4-year follow-up analysis, the safety population consisted of 147 patients. The efficacy population consisted of 108 patients.[15]

DCR[15]

DCR was defined as CR+PR+SD

- CR in 2.8% of patients (n=3)
- PR in 34.3% of patients (n=37)
- SD in 45.4% of patients (n=49)

PFS[15]

OS[15]

Median follow-up for PFS and OS was 42.9 months.[15]

Please see Important Safety Information on pages 20-21 for related and other risks.

Pemazyre® (pemigatinib) tablets

A TARGETED THERAPY WITH A WELL-ESTABLISHED SAFETY PROFILE[1]

The safety of PEMAZYRE was evaluated in 146 adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma. Patients were treated with PEMAZYRE 13.5 mg orally once daily for 14 days on followed by 7 days off therapy in 21-day cycles until disease progression or unacceptable toxicity. The median duration of treatment was 181 days (range: 7-730 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

To learn more about monitoring and managing adverse events, please visit hcp.pemazyre.com/adverse-reactions or scan this code.

Adverse reactions leading to permanent discontinuation occurred in 9% of patients[1]

CI, confidence interval; CR, complete response; DCR, disease control rate; FDA, Food and Drug Administration; OS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Please see Important Safety Information on pages 20-21 for related and other risks and the accompanying Full Prescribing Information for PEMAZYRE.

Adverse reactions (≥15%) in patients receiving PEMAZYRE[1]

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

AR, adverse reaction; CTCAE, Common Terminology Criteria for Adverse Events; NCI, National Cancer Institute.

[a]Graded per NCI CTCAE v4.03.

[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.

Low rates of Grade 3 or 4 ARs with the exception of hypophosphatemia[1]

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 20-21 for related and other risks.

Selected laboratory abnormalities (≥10%) worsening from baseline in patients receiving PEMAZYRE[1]

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 to 146 based on the number of patients with a baseline value and at least one post-treatment value.

[b]Graded per NCI CTCAE v4.03.

[c]Based on CTCAE v5.0 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.

Please see Important Safety Information on pages 20-21 for related and other risks.

SAFETY CONSIDERATIONS[1]

Advise patients to inform you of any vision changes while taking PEMAZYRE

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 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, every 2 months for the first 6 months of treatment, 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[1]

Prior to initiation of therapy > Every 2 months for the first 6 months of treatment > 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 no improvement is observed upon examination, consider permanent discontinuation of PEMAZYRE based on clinical status

Please see Important Safety Information on pages 20-21 for related and other risks.

HYPERPHOSPHATEMIA WAS OBSERVED IN PATIENTS TREATED WITH PEMAZYRE[1]

- 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

Recommendations for management of hyperphosphatemia[1]

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 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 • 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 20-21 for related and other risks.

POTENTIAL FOR 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 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 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 last dose
- Advise female patients 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

Please see Important Safety Information on pages 20-21 for related and other risks.

ONE PILL, ONCE DAILY[1]

A single tablet, once a day, with or without food

The recommended dose of PEMAZYRE is 13.5 mg taken orally once daily on a 21-day cycle: 14 on, and 7 off

Continue treatment until disease progression or unacceptable toxicity occurs.

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 20-21 for related and other risks.

HOW TO MODIFY DOSAGE[1]

PEMAZYRE is available in three strengths to enable dose modifications as needed

13.5 MG Starting Dose > **9 MG** First Dose Reduction > **4.5 MG** Second Dose Reduction

Permanently discontinue PEMAZYRE if patient is unable to tolerate 4.5 mg once daily for 14 days of each 21-day cycle[1]

- 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 no improvement is observed upon examination, consider permanent discontinuation of PEMAZYRE based on clinical status
  - **Hyperphosphatemia:** If serum phosphate is >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 is >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 the adverse reaction resolves to Grade 1 or baseline. Resume PEMAZYRE at the next lower dose if the adverse reaction resolves within 2 weeks, and permanently discontinue PEMAZYRE if the adverse reaction 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 MDRD 15-29 mL/min/1.73 m²) is 9 mg with the schedule designated for cholangiocarcinoma
- 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 designated for cholangiocarcinoma

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

Pemazyre (pemigatinib) tablets

ACCESS AND SUPPORT FOR YOUR PEMAZYRE PATIENTS

Specialty pharmacy and distribution

Specialty distributors (SDs)
PEMAZYRE is available for purchase from these authorized SDs:
- ASD Healthcare
- Cardinal Specialty
- McKesson Specialty
- Oncology Supply

Specialty pharmacy providers (SPPs)
PEMAZYRE is available through Biologics by McKesson specialty pharmacy, which 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.

To request PEMAZYRE for your patients, please call 1-800-850-4306 or complete and fax a PEMAZYRE Enrollment Form

IncyteCARES—support for you and your patients

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

To learn more about IncyteCARES, visit incytecares.com/oncology-hematology/pemazyre/home.aspx or scan this code.

AST, aspartate aminotransferase; CYP, cytochrome P450; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; RPED, retinal pigment epithelial detachment.

IncyteCARES

The IncyteCARES for PEMAZYRE 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

IMPORTANT SAFETY INFORMATION

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.

Please see accompanying Full Prescribing Information for PEMAZYRE.

References: 1. PEMAZYRE Prescribing Information. Wilmington, DE: Incyte Corporation. **2.** Data on File. Incyte Corporation, Wilmington, DE. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Biliary Tract Cancers V.4.2024. ©National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed October 29, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **4.** Chun YS, Javle M. Systemic and adjuvant therapies for intrahepatic cholangiocarcinoma. *Cancer Control*. 2017;24(3):1073274817729241. **5.** Cho MT, Gholami S, Gui D, et al. Optimizing the diagnosis and biomarker testing for patients with intrahepatic cholangiocarcinoma: a multidisciplinary approach. *Cancers (Basel)*. 2022;14(2):392. **6.** Sohal DPS, Shrotriya S, Abazeed M, et al. Molecular characteristics of biliary tract cancer. *Crit Rev Oncol Hematol*. 2016;107:111-118. **7.** Borad MJ, Gores GJ, Roberts LR. Fibroblast growth factor receptor 2 fusions as a target for treating cholangiocarcinoma. *Curr Opin Gastroenterol*. 2015;31(3):264-268. **8.** Lowery MA, Ptashkin R, Jordan E, et al. Comprehensive molecular profiling of intrahepatic and extrahepatic cholangiocarcinomas: potential targets for intervention. *Clin Cancer Res*. 2018;24(17):4154-4161. **9.** Sia D, Losic B, Moeini A, et al. Massive parallel sequencing uncovers actionable *FGFR2-PPHLN1* fusion and *ARAF* mutations in intrahepatic cholangiocarcinoma. *Nat Commun*. 2015;6:6087. **10.** Ross JS, Wang K, Gay L, et al. New routes to targeted therapy of intrahepatic cholangiocarcinomas revealed by next-generation sequencing. *Oncologist*. 2014;19(3):235-242. **11.** Graham RP, Fritcher EGB, Pestova E, et al. Fibroblast growth factor receptor 2 translocations in intrahepatic cholangiocarcinoma. *Hum Pathol*. 2014;45(8):1630-1638. **12.** Arai Y, Totoki Y, Hosoda F, et al. Fibroblast growth factor receptor 2 tyrosine kinase fusions define a unique molecular subtype of cholangiocarcinoma. *Hepatology*. 2014;59(4):1427-1434. **13.** 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(2):326-339. **14.** Abou-Alfa GK, Sahai V, Hollebecque A, 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. **15.** Vogel A, Sahai V, Hollebecque A, et al. An open-label study of pemigatinib in cholangiocarcinoma: final results from FIGHT-202. *ESMO Open*. 2024;9(6):103488. **16.** Vogel A, Sahai V, Hollebecque A, et al. An open-label study of pemigatinib in cholangiocarcinoma: final results from FIGHT-202. Supplemental material. *ESMO Open*. 2024;9(6):103488. Accessed October 9, 2024. https://www.esmoopen.com/article/S2059-7029(24)01257-2/fulltext

CHOOSE PEMAZYRE TO TARGET CCA

LONG-TERM DATA

4-YEAR FOLLOW-UP ANALYSIS

SEE PAGES 9-10

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).
- PEMAZYRE was granted accelerated approval based on the 15.4-month primary analysis of the FIGHT-202 study. The 4-year follow-up data from FIGHT-202 have not been submitted to or reviewed by the FDA, and potential inclusion of these data in the final FDA-approved labeling has yet to be determined.

PEMAZYRE targets *FGFR2* fusions—a key driver of CCA[1,7,12,13]

An NGS test at the time of diagnosis can help identify the best treatment options from the start[6,7]

Robust, durable responses in the Phase 2 FIGHT-202 study[1,14]

Primary analysis

36% **ORR** (95% CI, 27-45)*

9.1 **months median DoR** (95% CI, 6.0-14.5)†

- 2.7 months median time to response

One pill, once daily[1]

- Taken with or without food on a 21-day cycle—14 days on, and 7 days off

A well-established safety profile[1]

- 9% discontinuation due to treatment-related ARs

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 20-21.

In cholangiocarcinoma, 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.

Learn more at hcp.pemazyre.com

AR, adverse reaction; CI, confidence interval; CR, complete response; DoR, duration of response; CCA, cholangiocarcinoma; FDA, Food and Drug Administration; IRC, independent review committee; NGS, next-generation sequencing; ORR, overall response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.

*All evaluable patients (n=107). Note: Data are from IRC per RECIST v1.1, and CR and PR are confirmed.[1]

†The 95% CI was calculated using the Brookmeyer and Crowley's method.[1]

Pemazyre® (pemigatinib) tablets

Incyte

MAT-PEM-00577-v2