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

The first 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.

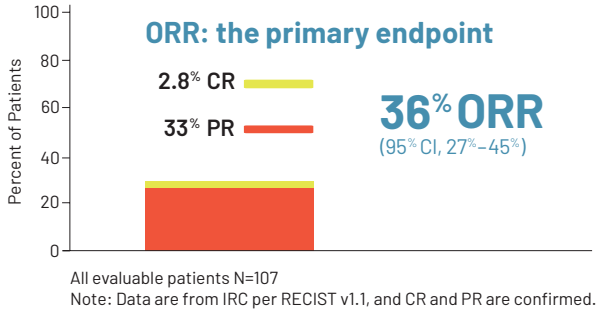
This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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 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

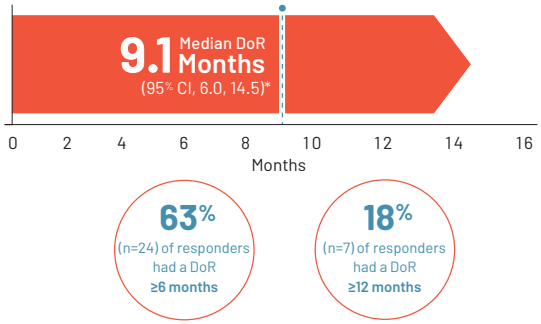
PEMAZYRE demonstrated a 36% ORR[1]



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]



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.

Molecular profiling is necessary to detect FGFR2 fusions or rearrangements

A next-generation sequencing assay, such as FoundationOne® CDx, meets the following criteria to detect FGFR2 fusions[2-5]:

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

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend pemigatinib (PEMAZYRE) as a subsequent-line treatment option for unresectable or metastatic cholangiocarcinoma with FGFR2 fusions or rearrangements following disease progression[6†‡§]

†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

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.

Please see additional Important Safety Information on the back for related and other risks.

IMPORTANT SAFETY INFORMATION (CONTINUED)

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 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 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]). 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.

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.

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 click here for Full Prescribing Information.

References: 1. PEMAZYRE Prescribing Information. Incyte Corporation. **2.** Lowery MA, Ptashkin R, Jordan E, et al. *Clin Cancer Res*. 2018;24(17):4154-4161. **3.** Javle MM, Murugesan K, Shroff RT, et al. *J Clin Oncol*. 2019;37(15 suppl):4087. **4.** Hollebecque A, de Bono JS, Plummer R, et al. *Ann Oncol*. 2019;30(suppl 1):mdz029. **5.** Frampton GM, Fichtenholtz A, Otto GA, et al. *Nat Biotechnol*. 2013;31(11):1023-1031. **6.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers V.5.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed October 7, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org.

Learn more about testing and treating your appropriate patients. Visit hcp.PEMAZYRE.com

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

Incyte