Pemazyre™
pemigatinib (tablets)

FDA APPROVED

PEMAZYRE is a kinase inhibitor 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).

Study Design[1]

The efficacy and safety of PEMAZYRE were evaluated in a multicenter, open-label, single-arm trial in previously treated patients with locally advanced unresectable or metastatic CCA.

- The efficacy population consists of 107 patients with disease that had progressed on or after at least 1 prior therapy and who had an FGFR2 fusion or rearrangement, as determined by a clinical trial assay performed at a central laboratory
- The major efficacy outcome measures were ORR and DoR, as determined by an independent review committee (IRC) according to RECIST v1.1

PEMAZYRE Clinical Response Rates[1]

PEMAZYRE demonstrated a

36% ORR

(95% CI, 27%-45%)

Note: Data are from IRC per RECIST v1.1, and CR and PR are confirmed. CR: 2.8%; PR: 33%

Median time to response:
2.7 months (range, 0.7-6.9 months)

	Efficacy Evaluable Population (N=107)
Median DoR (months) (95% CI)*	**9.1 (6.0, 14.5)**
Patients with DoR ≥6 months, % (n)	**63% (24)**
Patients with DoR ≥12 months, % (n)	**18% (7)**

Coverage policies, formularies, care plans, and order sets can be updated to include PEMAZYRE for appropriate patients with CCA

CCA, cholangiocarcinoma; CI, confidence interval; CR, complete response; DoR, duration of response; FDA, US Food and Drug Administration; ORR, overall response rate; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors.
* The 95% CI was calculated using the Brookmeyer and Crowley 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 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 4-5 for related and other risks.

Dosing[1]

- The recommended dosage of PEMAZYRE is 13.5 mg orally once daily for 14 consecutive days followed by 7 days off therapy, in 21-day cycles

- Continue treatment until disease progression or unacceptable toxicity occurs
- Dose modifications may be required for RPED, hyperphosphatemia and other adverse reactions ≥Grade 3. Avoid concomitant use of strong and moderate CYP3A inducers during treatment
- If concomitant use with a strong or moderate CYP3A inhibitor cannot be avoided, reduce the dose of PEMAZYRE

Companion Diagnostic

- Test for FGFR2 fusions using an FDA-approved companion diagnostic test that meets the following criteria for detection[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®)

Consider molecular testing in patients who present with unresectable or metastatic CCA[6]

Review medical records of patients with CCA for the presence of FGFR2 fusions or rearrangements to determine eligibility for PEMAZYRE

Information about an FDA-approved companion test can be found at www.fda.gov/CompanionDiagnostics.

Coverage policies, care plans, and order sets can be updated to include the FDA-approved companion diagnostic for appropriate patients with CCA

NCCN, National Comprehensive Cancer Network; RPED, retinal pigment epithelial detachment.

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.

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Pemazyre™ pemigatinib (tablets)

PEMAZYRE™ (pemigatinib) Product Specifications and Distribution

Cholangiocarcinoma ICD-10 Diagnosis Codes

- C22.1 (intrahepatic bile duct carcinoma)
- C24.0 (malignant neoplasm of extrahepatic bile duct)

How Supplied[1]

PEMAZYRE tablets are available as follows:

NDC Number	Strength	Description and Photo	Unit of Sale	Approximate Unit Weight	Approximate Unit Dimensions (L x W x H)
50881-026-01	4.5 mg	Round, white to off-white tablet with "I" on one side and "4.5" on the other side 	Bottles of 14 with child-resistant closure	26 g	$1\frac{5}{8}$" x $1\frac{5}{8}$" x 3"
50881-027-01	9 mg	Oval, white to off-white tablet with "I" on one side and "9" on the other side 	Bottles of 14 with child-resistant closure	27 g	
50881-028-01	13.5 mg	Round, white to off-white tablet with "I" on one side and "13.5" on the other side 	Bottles of 14 with child-resistant closure	28 g	

Tablets shown are not actual size.

Storage and Handling[1]

Store PEMAZYRE tablets at room temperature, 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F).

Specialty Pharmacy and Distribution

PEMAZYRE is dispensed by Biologics by McKesson specialty pharmacy. To request PEMAZYRE for your patients, please call 1-800-850-4306 or complete and fax a PEMAZYRE Enrollment Form. In addition, PEMAZYRE is available in specialty distribution through ASD Healthcare.

ICD-10, 10th revision of the International Statistical Classification of Diseases and Related Health Problems; NDC, National Drug Code.

References

1. PEMAZYRE Prescribing Information. Incyte Corporation. **2.** 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. **3.** Javle MM, Murugesan K, Shroff RT, et al. Profiling of 3,634 cholangiocarcinomas (CCA) to identify genomic alterations (GA), tumor mutational burden (TMB), and genomic loss of heterozygosity (gLOH). *J Clin Oncol*. 2019;37(15 suppl):4087. **4.** Hollebecque A, Silverman I, Owens S, et al. Comprehensive genomic profiling and clinical outcomes in patients (pts) with fibroblast growth factor receptor rearrangement-positive (FGFR2+) cholangiocarcinoma (CCA) treated with pemigatinib in the fight-202 trial. *Ann Oncol*. 2019;30(suppl 5):v276. **5.** Frampton GM, Fichtenholtz A, Otto GA, et al. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing. *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.1.2020. National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed April 1, 2020. 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.

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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.

Please see Important Safety Information on next page for related and other risks.

Important Safety Information (Continued)

Adverse Reactions (Continued)

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

Clinically relevant adverse reactions occurring in ≤10% of patients included fractures (2.1%). In all patients treated with pemigatinib, 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, 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.

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 see accompanying Full Prescribing Information for PEMAZYRE.

www.hcp.pemazyre.com

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Incyte