PDL DRUG REVIEW

Proprietary Name: Pemazyre®
Common Name: pemigatinib
PDL Category: Antineoplastics

Summary

Pharmacology/Usage: Pemigatinib, the active ingredient of Pemazyre®, is a kinase inhibitor. It is a small molecule kinase inhibitor that targets fibroblast growth factor receptor (FGFR) 1, 2, and 3.

Indication: 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).

There is no pregnancy category for this medication; however, the risk summary indicates that based on findings in an animal study and its mechanism of action, Pemazyre® can cause fetal harm or loss of pregnancy when given to a pregnant woman. There are no available data on use in pregnant women. Advise pregnant women of the potential risk to a fetus. In addition, verify pregnancy status of females of reproductive potential prior to starting treatment and advise this population as well as males with female partners of reproductive potential to use effective contraception during treatment and for 1 week after the final dose. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Tablets: 4.5mg, 9mg, 13.5mg. Swallow tablets whole; do not crush, chew, spit, or dissolve.

Recommended Dosage: Select patients for the treatment of locally advanced or metastatic cholangiocarcinoma based on the presence of an FGFR2 fusion or rearrangement as detected by an FDA approved test. Information on FDA-approved test(s) for the detection of an FGFR2 fusion or rearrangement in cholangiocarcinoma is available at http://www.fda.gov/CompanionDiagnostics.

Take 13.5mg PO QD for 14 consecutive days followed by 7 days off therapy, in 21-day cycles. Continue treatment until disease progression or unacceptable toxicity occurs. Take with or without food at about the same time every day.

Dose modifications may be required for adverse reactions, such as retinal pigment epithelial detachment, hyperphosphatemia, or other adverse reactions. Refer to the prescribing information for additional information.

Dose adjustments are not required with mild or moderate renal impairment, or with mild or moderate hepatic impairment. The recommended dose has not been established for patients with severe renal or severe hepatic impairment.

Drug Interactions: Concomitant use of Pemazyre® with a strong or moderate CYP3A inducer decreases pemigatinib plasma levels, which may reduce the efficacy of Pemazyre®. Avoid concomitant use of strong and moderate CYP3A inducers with Pemazyre®.

Concomitant use of a strong or moderate CYP3A inhibitor with Pemazyre® increases pemigatinib plasma levels, which may increase the incidence and severity of adverse reactions. Avoid concomitant use of strong and moderate CYP3A inhibitors with Pemazyre®. If concomitant use cannot be avoided, reduce the Pemazyre® dose (from 13.5mg to 9mg or from 9mg to 4.5mg).

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Pemazyre®) for all grades. Please note that there was no placebo data to compare with listed in the prescribing information.* The most frequently reported adverse events included hyperphosphatemia (60%), decreased appetite (33%), hypophosphatemia (23%), dehydration (15%), alopecia (49%), nail toxicity (43%), dry skin (20%), palmar-plantar erythrodysesthesia syndrome (15%), diarrhea (47%), nausea (40%), constipation (35%), stomatitis (35%), dry mouth (34%), vomiting (27%), abdominal pain (23%), fatigue (42%), edema peripheral (18%), dysgeusia (40%), headache (16%), dry eye (35%), arthralgia (25%), back pain (20%), pain in extremity (19%), urinary tract infection (16%), and weight loss (16%).

Laboratory abnormalities included decreased hemoglobin (43%), decreased lymphocytes (36%), decreased platelets (28%), increased leukocytes (27%), decreased leukocytes (18%), increased phosphate (94%), decreased phosphate (68%), increased alanine aminotransferase (43%), increased aspartate aminotransferase (43%), increased calcium (43%), increased alkaline phosphatase (41%), increased creatinine (41%), decreased sodium (39%), increased glucose (36%), decreased albumin (34%), increased urate (30%), increased bilirubin (26%), decreased potassium (26%), decreased calcium (17%), increased potassium (12%), and decreased glucose (11%).

Pemazyre® can cause retinal pigment epithelial detachment (RPED), which may cause symptoms such as blurred vision, visual floaters, or photopsia. Perform a comprehensive ophthalmological exam, including optical coherence tomography (OCT) prior to the start of treatment 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.

Increases in phosphate levels are an effect of Pemazyre®. The median time to onset of hyperphosphatemia was 8 days. Monitor for hyperphosphatemia and initiate a low phosphate diet when serum phosphate level is >5.5mg/dL. For serum phosphate levels >7mg/dL, initiate phosphate lowering therapy and withhold, reduce the dose, or permanently discontinue Pemazyre® based on duration and severity of hyperphosphatemia.

Contraindications: There are no contraindications listed with this product.

Manufacturer: Incyte Corp.

Analysis: The efficacy of Pemazyre® was assessed in a multicenter, open-label, single arm study that included patients (N=107) with locally advanced unresectable or metastatic cholangiocarcinoma whose disease had progressed on or after at least 1 prior therapy and who had an FGFR2 gene fusion or non-fusion rearrangement. The median age of included patients was 56 years, while 61% were female, 74% were white, 95% had a baseline Eastern Cooperative Oncology Group (ECOG) performance status of 0 (42%) or 1 (53%), and 98% had intrahepatic cholangiocarcinoma. All patients had at least 1 prior line of systemic therapy, while 27% had 2 prior lines of therapy and 12% had 3 or more prior lines of therapy.

The primary efficacy outcome measures were overall response rate (ORR) and duration of response (DoR) as determined by an independent review committee (IRC) per RECIST v1.1. Efficacy results can be seen in the table below, which was adapted from the prescribing information.

Efficacy	Pemazyre (N=107)
ORR	36%
Complete Response	2.8%
Partial Response	33%
Median DoR (months)	9.1
Patients with DoR ≥6 months, n (%)	24 (63%)
Patients with DoR ≥12 months, n (%)	7 (18%)

Place in Therapy: Pemazyre®, an oral kinase inhibitor, 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). In a single arm, open-label study (N=107), 36% had an overall response rate, with 33% having a partial response.

It is recommended that Pemazyre® should be non-recommended with conditions in order to confirm the appropriate diagnosis and clinical parameters for use, as well as prior trials.

PDL Placement: ☐ **Recommended**
☒ **Non-Recommended with Conditions**

References

[1] Pemazyre [package insert]. Wilmington, DE: Incyte Corporation; 2020.