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

Dosing and administration guide

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 10-11 for related and other risks.

Patient selection for PEMAZYRE (pemigatinib)

Confirm the presence of an FGFR2 fusion or rearrangement prior to initiation of treatment[1]

- Select patients for the treatment of locally advanced or metastatic cholangiocarcinoma (CCA) with PEMAZYRE 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 CCA is available at fda.gov/CcompanionDiagnostics

FoundationOne® CDx is the FDA-approved companion diagnostic for PEMAZYRE

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.

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.

Please see Important Safety Information on pages 10-11 for related and other risks.

Recommended dosage and schedule of PEMAZYRE

Dosage with PEMAZYRE[1]

The recommended dose of PEMAZYRE is: **13.5 mg**

PEMAZYRE is taken orally, once daily, on a 21-day cycle

14 days of once-daily therapy

7 days of no therapy

Continue treatment until disease progression or unacceptable toxicity occurs.

How to take PEMAZYRE[1]

PEMAZYRE can be taken with or without food

- Instruct patients to take their dose of PEMAZYRE at approximately the same time every day
- Swallow tablets whole. Do not crush, chew, split, or dissolve tablets
- If the patient misses a dose by 4 or more hours, or if vomiting occurs, they should resume dosing with the next scheduled dose

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

Dosing strengths of PEMAZYRE (pemigatinib)

PEMAZYRE is available in 3 strengths[1]

DOSE	MARKINGS	NDC CODE
13.5-mg tablet in bottles of 14 with child-resistant closure	Round, white to off-white tablet debossed on one side with "I" and "13.5" on the other side	50881-028-01
9-mg tablet in bottles of 14 with child-resistant closure	Oval, white to off-white tablet debossed on one side with "I" and "9" on the other side	50881-027-01
4.5-mg tablet in bottles of 14 with child-resistant closure	Round, white to off-white tablet debossed on one side with "I" and "4.5" on the other side	50881-026-01

Tablets shown not actual size.

IMPORTANT SAFETY INFORMATION

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.

Dosing modifications for PEMAZYRE

Dose modifications should be considered for the management of toxicities or tolerability[1]

13.5 mg ▶ **9 mg** ▶ **4.5 mg**

Starting dose | **First dose reduction** | **Second dose reduction**

- All doses are taken for 14 days followed by 7 days off therapy, in 21-day cycles
- Permanently discontinue treatment if patient is unable to tolerate PEMAZYRE 4.5 mg once daily
- Dose modifications may be required for RPED, hyperphosphatemia, and other adverse reactions ≥ Grade 3
- Avoid concomitant use of strong and moderate CYP3A inhibitors 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

Follow the dose modification guidelines outlined on pages 6–9 in this guide and in the Full Prescribing Information for PEMAZYRE.

IMPORTANT SAFETY INFORMATION

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%).

Please see Important Safety Information on pages 10–11 for related and other risks.

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

Dose modifications for RPED[1]

- If asymptomatic and stable on serial examination, continue PEMAZYRE (pemigatinib)
- 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

Important considerations for elevated serum phosphate levels

Monitor for hyperphosphatemia[1]

- 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
- See dose modifications for hyperphosphatemia on page 7

Dose modifications for hyperphosphatemia[1]

Serum phosphate

>7 – ≤10 mg/dL

Initiate phosphate lowering therapy

▼

Monitor serum phosphate weekly

▼

Withhold PEMAZYRE if levels are not <7 mg/dL within 2 weeks of starting a 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

▼

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 10–11 for related and other risks.

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

Dosage modifications for other adverse reactions

For Grade 3

- Withhold PEMAZYRE (pemigatinib) 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

IMPORTANT SAFETY INFORMATION

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 Important Safety Information on pages 10-11 for related and other risks.

Dosage modification for concomitant use with strong or moderate CYP3A inhibitor[1]

- Avoid concomitant use of strong or moderate CYP3A inhibitors with PEMAZYRE
- If concomitant use with a strong or moderate CYP3A inhibitor cannot be avoided, adjust the dosage of PEMAZYRE as follows:

If the patient is taking this dose...		Reduce the dose to:
PEMAZYRE 13.5 mg	▶	PEMAZYRE 9 mg
PEMAZYRE 9 mg	▶	PEMAZYRE 4.5 mg

- If concomitant use of a strong or moderate CYP3A inhibitor is discontinued, increase the PEMAZYRE dose (after 3 plasma half-lives of the CYP3A inhibitor) to the dose that was used before starting the strong inhibitor

Avoid concomitant use of strong and moderate CYP3A inducers with PEMAZYRE.

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

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.

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 for PEMAZYRE.

Reference: 1. PEMAZYRE Prescribing Information. Incyte Corporation.

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

Dosing and administration guide for PEMAZYRE (pemigatinib)[1]

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).

- **Select patients based on the presence of an FGFR2 fusion or rearrangement** as detected by an FDA-approved test
- **PEMAZYRE is available in 3 dosage strengths** to facilitate dose reductions due to adverse reactions
- **The recommended dosage of PEMAZYRE is 13.5 mg**
- **PEMAZYRE is taken orally once daily for 14 days,** followed by 7 days off therapy, in 21-day cycles
- Instruct patients to **take PEMAZYRE at approximately the same time every day**
- **PEMAZYRE can be taken with or without food**
- **Continue treatment with PEMAZYRE** until disease progression or unacceptable toxicity occurs

Refer to Full Prescribing Information for more information on dose modifications.

Please see full Important Safety Information on pages 10-11, and click here for Full Prescribing Information for PEMAZYRE.

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

Incyte