pemigatinib (Pemazyre™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO191

Description

Pemigatinib (Pemazyre) is an orally administered fibroblast growth factor receptor (FGFR) inhibitor, with activity against FGFR1 and FGFR2 fusions or rearrangements.

Length of Authorization

- N/A

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
pemigatinib (Pemazyre)	13.5 mg tablet	Previously treated, unresectable, locally advanced or metastatic cholangiocarcinoma in adults with FGFR2 fusions or rearrangements	14 tablets/21 days
	9 mg tablet		
	4.5 mg tablet	Relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with FGFR1 rearrangement.	30 tablets/30 days

Initial Evaluation

I. **Pemigatinib (Pemazyre)** is considered investigational when used for all conditions, including but not limited to cholangiocarcinoma and relapsed or refractory myeloid/lymphoid neoplasms (MLNs).

Renewal Evaluation

I. N/A

Supporting Evidence

Treatment of Cholangiocarcinoma

I. Pemigatinib (Pemazyre) is the first targeted therapy for cholangiocarcinoma that harbors FGFR2 fusions or rearrangements. Pemigatinib (Pemazyre) is a second-line chemotherapy option.

Guideline preferred first line chemotherapy is gemcitabine and cisplatin, while second-line options include mFOLFOX, FOLFIRI, and regorafenib (Stivarga).

II. Pemigatinib (Pemazyre) was evaluated in FIGHT-202, an open-label, single-arm, multi-cohort Phase 2 trial. Patients (N=146) with locally advanced or metastatic CCA, previously treated with at least 1 chemotherapy were included. FDA approval was based on the overall response rate (ORR) in patients with FGFR2 gene fusion or rearrangements.

III. The primary efficacy endpoint was objective response rate (ORR). Secondary endpoints were progression-free survival (PFS), overall survival (OS), and duration of response (DOR). Based on analysis of this clinical trial data, quality of the evidence is considered low given the lack of comparator and open-label trial design, as well as, the lack of clinically meaningful outcomes in morbidity, mortality, and quality of life – medication efficacy has not yet been confirmed.

IV. Pemigatinib (Pemazyre) received accelerated approval from the FDA based on ORR and DOR. Continued approval for this drug may be contingent upon verification of clinical benefit in confirmatory trials. There is a Phase 3 trial underway to assess pemigatinib (Pemazyre) monotherapy versus gemcitabine + cisplatin in the first-line treatment of CCA with FGFR2 alterations.

V. The safety profile of pemigatinib (Pemazyre) was based on adverse reactions observed in all cohorts during CT (N=146). The most common adverse events (≥20% incidence) included hyperphosphatemia, alopecia, nausea, diarrhea, nail toxicity, back pain, fatigue, dysgeusia, dry eyes, and serous retinal detachment. There are no specific contraindications to pemigatinib (Pemazyre); however, warnings and precautions include: ocular toxicity, hyperphosphatemia, GI toxicity and renal function. Pemigatinib (Pemazyre) showed 9% treatment discontinuation rate, 14% dose reductions rate, and 42% dose interruption rate due to adverse events.

VI. As of January 2023, The National Comprehensive Cancer Network (NCCN) treatment guideline for hepatobiliary cancer has included pemigatinib (Pemazyre) as second-line treatment with a Category 2A recommendation. Pemigatinib (Pemazyre) is useful in treatment of tumor with confirmed FGFR2 fusions or rearrangements, and which are refractory to first line chemotherapy.

<u>Treatment of Myeloid/Lymphoid Neoplasms</u>

VII. Myeloid/lymphoid neoplasms (MLNs) with FGFR1 rearrangement are rare hematologic malignancies included in the World Health Organization (WHO) major category “MLNs with eosinophilia and rearrangements of PDGFRA, PDGFRB, FGFR1, or with PCM1-JAK2.” In this group of neoplasms the formation of a fusion gene, or (rarely) from a mutation, results in the expression of an aberrant tyrosine kinase. MLNs with FGFR1 rearrangement are an extremely rare and aggressive that impacts less than 1 in 100,000 people in the United States per year with less than 100 patients reported worldwide as of 2010.

VIII. In August 2022, pemigatinib (Pemazyre) was approved for adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with fibroblast growth factor receptor 1 (FGFR1) rearrangement. Approval was based on interim results from the Phase 2 FIGHT-203 trial. FIGHT-203 was a multicenter, open-label, single-arm trial including patients with relapsed or refractory MLNs with FGFR1 rearrangement.

IX. Adult participants (N=28) who were not candidates for stem cell transplantation or other disease modifying therapy along with confirmed MLN with 8p11 rearrangement known to lead FGFR1 activation were included in the study population. The primary outcome measure was complete response (CR) rate and was reported per the morphologic disease type. Of the 18 patients with chronic phase in the marrow with or without extramedullary disease (EMD), 14 achieved CR (78%; 95% CI: 52, 94). The median time-to-CR was 104 days (range, 44 to 435). The median duration was not reached (range: 1+ to 988+ days). Of the 4 patients with blast phase in the marrow with or without EMD, 2 achieved CR (duration: 1+ and 94 days). Of 3 patients with EMD only, 1 achieved a CR (duration: 64+ days). Secondary endpoints reported in the interim results included complete cytogenic response (CCyR). In all 28 patients (including 3 patients without evidence of morphologic disease), the CCyR rate was 79% (22/28; 95% CI: 59, 92). Progression free survival and overall survival are to be reported at trial conclusion.

X. The safety profile of pemigatinib (Pemazyre) was based on 34 patients. All patients experienced ≥ 1 treatment-emergent adverse event (TEAE). The most common any-grade hematologic TEAEs were anemia (35%), thrombocytopenia (12%), and neutropenia (3%). The most common nonhematologic TEAEs (any grade) were hyperphosphatemia (68%), alopecia (59%), and diarrhea (50%). Grade 3 and 4 TEAEs occurred in 85% of patients. Reported TEAEs led to treatment interruption in 65% of patients, dose reduction in 59% of patients, and discontinuation in 12% of patients.

XI. Based on the interim results posted trial does not offer OS or PFS data. Overall survival and progression free survival data is to be reported as the conclusion of the phase 2 trial. Interim results without OS data limit the applicability of this treatment outside of a clinical trial space. Current NCCN guidelines prefer to clinical trial, and now pemigatinib (Pemazyre), as first line. However, there is a caveat in the guidelines that early referral to allogeneic HCT should be considered for eligible patients, since TKI therapy alone does not result in durable remissions. Given the lack of durability in TKI monotherapy, including pemigatinib (Pemazyre), the level of evidence is considered low.

XII. An FDA-approved test for detection of FGFR1 rearrangement in patients with relapsed or refractory myeloid/lymphoid neoplasm for selecting patients for treatment with pemigatinib (Pemazyre) is not available. However, FGFR 1 rearrangement can be detected with an 8p11 translocation on conventional cytogenetics and/or on break-apart fluorescence in situ hybridization testing (FISH).

Investigational or Not Medically Necessary Uses

I. Pemigatinib (Pemazyre) has not been sufficiently studied for safety and efficacy for conditions other than cholangiocarcinoma and myeloid/lymphoid neoplasms to date.

References

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Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy

Policy Name	Disease state
erdafitinib (Balversa™)	Advanced or metastatic urothelial carcinoma FGFR3 or FGFR2 genetic alteration, second-line after platinum therapy progression
infigratinib (Truseltiq™)	Previously treated adults with unresectable, locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or other rearrangement
Multi-Targeted Tyrosine Kinase Inhibitors (Multi-TKI)	Unresectable Hepatocellular Carcinoma
	Advanced Renal Cell Carcinoma
	Recurrent, High-risk or Metastatic Endometrial Carcinoma
	Locally Recurrent or Metastatic Progressive Thyroid Cancer
	Unresectable Liver Carcinoma

midostaurin (Rydapt®)	Acute myeloid leukemia, newly diagnosed, FLT3 mutation-positive, in combination with cytarabine/daunorubicin induction and cytarabine consolidation
ponatinib (Iclusig®)	CP-CML with resistance or intolerance to two prior kinase inhibitors
	AP-CML, BP-CML, and Ph+ ALL for whom no other kinase inhibitors are indicated
	T315I-positive CML (any phase) or T315I-positive Ph+ ALL

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated policy to include relapsed/refractory MLNs with supporting evidence. Updated references formatting, included related policies table.	01/2023
Policy created	06/2020