P&T Committee Meeting Minutes
Commercial/Marketplace/GHP Kids E-vote
June 17, 2020

DRUG REVIEWS

PEMAZYRE (pemigatinib)

Review: Pemazyre is a kinase inhibitor targeting fibroblast growth factor receptor 1 (FGFR1), FGFR2, and FGFR3 indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma (CCA) with a FGFR2 fusion or other rearrangement. It is the first targeted drug therapy indicated for the treatment of cholangiocarcinoma and is recommended as a second line treatment option in patients with FGFR2 fusions or rearrangements.

The efficacy of Pemazyre was shown in the FIGHT-202 trial, an open-label, single-arm, multicohort phase 2 study in adult patients with locally advanced or metastatic CCA with documented disease progression following at least one previous systemic cancer treatment. Of the 146 patients with CCA enrolled in the trial, 107 had FGFR2 fusions or rearrangements, 20 had other FGF/FGFR alterations, and 18 had no FGF/FGFR alterations. Patients receive Pemazyre 13.5 mg tablets by mouth once daily for 21-day cycles (14 days on, 7 days off) until disease progression, unacceptable toxicity, or discontinuation by the patient or physician. The primary efficacy endpoint measuring the proportion of patients with FGFR2 fusions achieving an objective response showed a 35.5% response rate with a majority of patients having a partial response (35 out of 107). The median duration or response was 7.5 months for patients with FGFR2 fusions. No patients with other FGF/FGFR alterations or no FGF/FGFR alterations achieved a response and progression free survival and overall survival remained poor in these cohorts.

Pemazyre has warnings for ocular toxicity which included dry eye (27%) and retinal pigment epithelial detachment (RPED) (6%). Patients should be monitored through comprehensive ophthalmological examinations and RPED should be managed with dose modification or permanent discontinuation depending on severity. Increases in phosphate levels were also reported in 92% of patients. Patients with elevated phosphate levels can be treated with low phosphate diet, dose interruption or modification, or permanent discontinuation depending on the severity.

During clinical trials, serious adverse events were reported in 45% of patients and led to discontinuation, dose interruptions, and dose reductions in 9%, 43%, and 14% of patients, respectively. Permanent discontinuation due to adverse reaction occurred in 9% of patients, including intestinal obstruction and acute kidney injury. Dosage interruptions and reductions were reported in 43% and 14% of patients, respectively, and included stomatitis, arthralgia, palmar-plantar erythrodysesthesia syndrome, asthenia, and onychomadesis.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Pemazyre is a pharmacy benefit that will be added to the formulary on the OralOncBrandNP tier. The following prior authorization criteria will apply:

- Medical record documentation that prescription is written by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**

- Medical record documentation of locally advanced or metastatic cholangiocarcinoma **AND**
- Medical record documentation of a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as verified by an FDA-approved test* **AND**
- Medical record documentation of one prior line of therapy

***NOTE:** The FDA approved test is FoundationOne CDx.

AUTHORIZATION DURATION: Initial approval will be for **12 months**. Subsequent approvals will be for an additional 12 months and will require medical record documentation of continued disease improvement or lack of disease progression.

QUANTITY LIMIT: 14 tablets per 21 days

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

XCOPRI (cenobamate)

Review: Xcopri is a novel tetrazole alkyl carbamate derivative indicated for the treatment of partial-onset seizures in adult patients. The exact mechanism by which Xcopri exerts its anticonvulsant effects is unknown but it is thought to reduce neuronal excitability through its effect on sodium channels and modulation of $GABA_A$ ion channels.

The efficacy of Xcopri was evaluated in two double-blind placebo-controlled parallel group studies in adult patients with uncontrolled focal epilepsy despite current anti-epileptic regimens. Patients were required to be taking one to three antiepileptic drugs (with certain exclusions) and have recorded seizure activity during the 8 week baseline assessment period according to protocol.

In Study 013, 222 patients were randomized 1:1 to receive placebo (n=109) or Xcopri (n=113) titrated to a targeted dose of 200 mg once daily during a 6-week titration phase then maximum tolerated dose during a 6-week maintenance phase. The primary efficacy endpoint evaluating percentage change from baseline in 28-day focal seizure frequency showed a 55.6% decrease (7.8 to 3.8 seizures) in the Xcopri treatment group compared to 21.5% decrease (5.5 to 5.0) in the placebo group. There were also a greater proportion of patients treated with Xcopri who achieved a secondary endpoint measuring proportion of patients with a $\geq$ 50% reduction in seizure frequency. Reductions in seizure frequency were consistent across all seizure types.

In Study 017, 437 patients were randomized 1:1:1:1 to receive Xcopri 100 mg/day (n=108), 200 mg/day (n=110), 400 mg/day (n=111) or placebo (n=108). Patients were titrated up to the target (dose or maximally tolerated dose) over a 6 week titration period followed by a 12 week maintenance period. The primary efficacy endpoint evaluating percentage change from baseline in seizure frequency averaged over 28 days in the 18-week treatment period showed reduction of 35.5% in Xcopri 100 mg group and 55% in Xcopri 200 mg group and 400 mg group compared to 24% in the placebo group. During the 12-week maintenance phase, a $\geq$ 50% reduction from baseline in seizure frequency was shown in 40% in the Xcopri 100 mg group, 56% in the Xcopri 200 mg group, and 64% in the Xcopri 400 mg group compared to 25% of patients in the placebo group. Secondary endpoint results were consistent with the primary endpoint results, with increasing percentages of responders corresponding with increased dose.

Xcopri has warning for Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) which occurred during trials of Xcopri and appears to correlate with rapid titration. It also contains warning for shortening of the QT interval and should be avoided in patients with Familial Short QT. During study 1 and 2, adverse events occurred in

77% of patients treated with Xcopri and 68% treated with placebo. The most common adverse events that occurred in Xcopri treated patients with an incidence of at least 10% greater than placebo were somnolence, dizziness, fatigue, diplopia, and headache.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Xcopri is a pharmacy benefit that will be added to the formulary on the brand non-preferred tier. The following prior authorization criteria will apply:

- Medical record documentation that Xcopri is being prescribed by or in consultation with a neurologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of partial onset seizures
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives

QUANTITY LIMIT: Pharmacist note to CSR: *Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).*

50 mg, 100 mg, 150 mg , 200 mg : 1 tablet per day
Maintenance Pack: 2 tablets per day
Titration Pack: 28 tablets per 180 days

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

FAST FACTS

DIFICID (fidamoxacin)

Updated Indication: Dificid is a macrolide antibacterial indicated in adult and pediatric patients 6 months of age and older for the treatment of *C. difficile*-associated diarrhea.

Previously Dificid was only indicated in adult patients.

Updated Dosing for New Indication: There is no change to the recommended dosage for adult patients (200 mg twice daily for 10 days).

Dosage for Pediatric Patients (6 months to less than 18 years of age):
For patients weighing at least 12.5 kg and able to swallow tablets, the recommended dosage is 200 mg twice daily for 10 days. For patients unable to swallow tablets, pediatric patients may be dosed with Dificid oral suspension according to body weight (Table 1).

Table 1. Recommended dosage of Dificid oral suspension in pediatric patients, based on weight[1]

Body Weight	Dose Administered Twice Daily	Volume of 40 mg/mL Suspension to be Administered Orally Twice Daily
4 kg to less than 7 kg	80 mg	2 mL
7 kg to less than 9 kg	120 mg	3 mL
9 kg to less than 12.5 kg	160 mg	4 mL
12.5 kg and above	200 mg	5 mL

Currently, Dificid is available as 200 mg tablets. Although currently unavailable, a new formulation of granules for oral suspension will be manufactured for pediatric patients with the new indication. Dificid will be available in 150 mL bottle of granules for oral suspension with a concentration of 40 mg / mL (200 mg per 5 mL) after reconstitution. The unused remainder of the reconstituted suspension should be discarded after 12 days.

Current formulary status: Brand non-preferred tier requiring a prior authorization (Dificid Tablets)

Recommendation: For Dificid tablets, no changes are recommended to the formulary placement, the current quantity limits, and the current prior authorization duration. It is recommended to make the following changes to the prior authorization criteria based on the new age approval:

- Medical record documentation of a diagnosis of Clostridium difficile associated diarrhea in members greater than or equal to ~~18 years of age~~ 6 months of age **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to vancomycin capsules. Must try at least two courses of treatment, one course must be a taper or pulsed regimen

OR

- Initiation of therapy with Dificid in the hospital

AUTHORIZATION DURATION: 10 days, RX count 1

When Dificid granules for oral suspension become available it should be added to the Brand Non-Preferred tier of the Commercial, Marketplace, and CHIP formularies and will be reviewed with Commercial Policy 239.0. The following quantity limits and authorization duration should be added to Commercial Policy 239.0 for Dificid oral suspension:

QUANTITY LIMIT: Dificid Oral Suspension: 150 mL per fill

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

Future Scheduled Meetings

The next bi-monthly scheduled meeting will be held on Tuesday, July 21, 2020 at 1:00 HCN3A & 3B Conference room

All of these meetings are scheduled to be held at Geisinger Health Plan, Hughes Center North and South Buildings; 108 Woodbine Lane; Danville, PA 17821.