mobocertinib (Exkivity™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO242

Description

mobocertinib (Exkivity) is an orally administered EGFR tyrosine kinase inhibitor.

Length of Authorization

- N/A

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
mobocertinib (Exkivity)	40 mg capsules	Metastatic non-small-cell lung cancer with exon 20 insertion mutation after progression on platinum-based chemotherapy	120 capsules/30 days

Initial Evaluation

I. Mobocertinib (Exkivity) is considered not medically necessary when used for all other conditions, including but not limited to non-small cell lung cancer (NSCLC).

Renewal Evaluation

I. N/A

Supporting Evidence

I. Mobocertinib (Exkivity) is an oral EGFR tyrosine kinase inhibitor (TKI) that is being evaluated for exon 20 insertion mutant-positive NSCLC (EGFRex20ins-NSCLC) in those that have had disease progression on platinum-based chemotherapy. This specific type of NSCLC is thought to account for 2-3% of NSCLC cases annually, and is more commonly seen in those that do not have a smoking history.

II. Mobocertinib (Exkivity) is the second therapy specifically FDA-approved for EGFRex20ins-NSCLC. Amivantamab-vmjw (Rybrevant), an IV human antibody, was FDA-approved in May 2021. Approval was based off of the Phase 1 CHYRSALIS trial, a single-arm, open-label trial in 81 patients that previously progressed on platinum chemotherapy.

III. Platinum-based chemotherapy is utilized first-line for this condition, and is considered standard of care. Mobocertinib (Exkivity) is the first TKI specifically FDA-approved for this mutation. Other EGFR TKIs (e.g., osimertinib [Tagrisso]) have been used in this setting off-label; however, most cases of EGFRex20ins-NSCLC are resistant to those therapies.

IV. Interim results of the Phase 1/2 trial are being used to support accelerated FDA-approval. Mobocertinib (Exkivity) was granted Priority Review, as well as Breakthrough Therapy, Fast Track and Orphan Drug designations. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials. Continued Phase 2, as well as Phase 3 trials are underway to assess safety and efficacy. Both of these therapies are expected to be utilized in the second-line treatment setting; however, given expected preference for the targeted indication – use in the first-line setting may appeal to patients and providers. Mobocertinib (Exkivity) is being evaluated in a Phase 3, open-label trial versus platinum-based chemotherapy in patients with advanced or metastatic EGFRex20ins-NSCLC. Per ClinicalTrials.gov, the study is recruiting; however, there have been potential pauses in recruitment due to futility analyses.

V. Mobocertinib (Exkivity) is being evaluated in a Phase 1/2, single-arm, open-label trial in 114 patients with metastatic EGFRex20ins-NSCLC that were previously treated with platinum chemotherapy. Interim results showed an overall response rate (ORR). Other trial outcomes include duration of response (DoR), and progression-free survival (PFS). The quality of the evidence is low given the open-label and single-arm trial design, and small sample size. True medication efficacy is unknown due to the observational nature of the data. Additionally, the endpoints evaluated have not been correlated with meaningful outcomes such as improved survival or quality of life. The results are similar to those seen for amivantamab-vmjw (Rybrevant). Use of this therapy in any treatment setting is considered experimental and investigational at this time given the unknown clinical benefit and ongoing clinical trials to evaluate safety and efficacy.

VI. The safety profile is based on the 114 patients that have received therapy to date. Treatment related adverse events (AE) occurred in 99% of patients. Common AE: diarrhea 91%, rash (45%), paronychia (38%), decreased appetite (35%), nausea (34%), dry skin (31%), vomiting (30%), increased creatinine (25%), stomatitis (24%), pruritus (21%). Grade 3-4 AE occurred in 47% and 49% of patients were documented to have serious AE. Dose reduction due to AE occurred in 25% of patients, and AE leading to treatment discontinued occurred in 17% of patients. One patient experienced cardiac failure, a TRAE leading to death. Given the observational nature of the data in a small population, the severity and extent of AE that are due to the drug versus the disease are unknown at this time.

VII. NCCN guidelines for advanced or metastatic EGFRex20ins-NSCLC recommend platinum-based combination chemotherapy for first-line treatment, this is a Category 1 recommendation. Mobocertinib (Exkivity) and amivantamab-vmjw (Rybrevant) have been added as subsequent therapy options (Category 2A recommendation). The recommendations are specific to patients with an ECOG score 0-2, and for those with PS 3-4, best supportive care is recommended (Category 2A recommendation). Clinical trials are highly encouraged for all settings. ASCO provides similar recommendations for platinum-based combination chemotherapy in the first-line setting; however, have not been updated to include the targeted therapies. Guidelines do not recommend conventional EGFR TKIs for this mutation, and ASCO recommends platinum chemotherapy after progression on a conventional EGFR TKI if one was utilized.

VIII. Due to lack of conclusive clinical data to direct a path to curative therapies, NCCN guidelines for NSCLC notes that the best management for any patient with cancer is in a clinical trial setting, and participation in trial is especially encouraged. Patients participating in clinical trials receive regular care, often at leading health care facilities with experts in the field while participating in important medical research and further advancements in treatment, with close safety monitoring and follow-up. Participation in a clinical trial remains the most favorable treatment option for patients with advanced NSCLC.

Investigational or Not Medically Necessary Uses

I. Mobocertinib (Exkivity) is being withdrawn from the market based on the outcome of the Phase 3 EXCLAIM-2 confirmatory trial in the setting of metastatic non-small-cell lung cancer with exon 20 insertion mutation after progression on platinum-based chemotherapy which did not meet its primary endpoint and thus did not fulfill the confirmatory data requirements of the Accelerated Approval granted by the U.S. FDA nor the conditional marketing approvals granted in other countries. Takeda is working with the FDA towards the withdrawal of Exkivity from the U.S. market and will also withdrawal Exkivity globally where approved.

References

1. Riely GJ, Neal JW, Camidge DR, et al. Activity and safety of mobocertinib (TAK-788) in previously treated non-small cell lung cancer with egfr exon 20 insertion mutations from a phase I/II trial. Cancer Discov. 2021;11(7):1688-1699.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology, Non-Small Cell Lung cancer. V6.2021. Updated September 30,2021. Accessed October 6, 2021. Available at: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1450
3. Hanna NH, Robinson AG, Temin S, et al. Therapy for stage iv non-small-cell lung cancer with driver alterations: ASCO and OH (CCO) joint guideline update. J Clin Oncol. 2021;39(9):1040-1091.
4. Rybrevant [Prescribing Information]. Janssen Pharmaceuticals. Horsham, PA. May 2021.
5. American Cancer Society. Treatment non-small cell lung cancer. Accessed August 23, 2021. https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell.html.

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated from E/I to not medically necessary following withdrawal from U.S. market	02/2024
Policy created	11/2021