FDA Approves Lorbrena for Metastatic ALK-Positive Lung Cancer

The targeted therapy delayed disease progression in people with advance non-small-cell lung cancer, including those with brain metastasis.

March 5, 2021 By Food and Drug Administration (FDA)

FDA approves lorlatinib for metastatic ALK-positive NSCLC

On March 3, 2021, the Food and Drug Administration granted regular approval to lorlatinib (Lorbrena, Pfizer Inc.) for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive, detected by an FDA-approved test.

The FDA also approved the Ventana ALK (D5F3) CDx Assay (Ventana Medical Systems, Inc.) as a companion diagnostic for lorlatinib.

Lorlatinib received accelerated approval in November 2018 for the second- or third-line treatment of ALK-positive metastatic NSCLC.

This current approval is based on data from Study B7461006 (NCT03052608), a randomized, multicenter, open-label, active-controlled trial conducted in 296 patients with ALK-positive metastatic NSCLC who had not received prior systemic therapy for metastatic disease. Patients were required to have ALK-positive tumors detected by the VENTANA ALK (D5F3) CDx assay. Patients were randomized 1:1 to receive lorlatinib 100 mg orally once daily (n=149) or crizotinib 250 mg orally twice daily (n=147).

Study B7461006 demonstrated an improvement in progression-free survival (PFS) as assessed by blinded independent central review (BICR), with a hazard ratio of 0.28 (95% CI: 0.19, 0.41; $p<0.0001$). Median PFS was not estimable in the lorlatinib arm and was 9.3 months (95% CI: 7.6, 11.1) for those treated with crizotinib. Overall survival data were immature at the PFS analysis.

Central nervous system (CNS) involvement was assessed in all patients. There were 17 patients in the lorlatinib arm and 13 in the crizotinib arm with measurable CNS lesions based on baseline brain imaging. Among these patients, the intracranial ORR, as assessed by the BICR, was 82% (95% CI: 57, 96) in the lorlatinib arm and 23% (95% CI: 5, 54) in the crizotinib arm. The duration of intracranial response was ≥ 12 months in 79% and 0% of patients in the lorlatinib and crizotinib arms, respectively.

The most common adverse reactions (incidence ≥20%), including Grade 3-4 laboratory abnormalities, in patients receiving lorlatinib, were edema, peripheral neuropathy, weight gain, cognitive effects, fatigue, dyspnea, arthralgia, diarrhea, mood effects, hypercholesterolemia, hypertriglyceridemia, and cough.

The recommended lorlatinib dose is 100 mg orally once daily.

View full prescribing information for Lorbrena.

This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, FDA collaborated with the Australian Therapeutic Goods Administration (TGA), the Brazilian Health Regulatory Agency (ANVISA), Health Canada, and United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA). The application reviews are ongoing at the other agencies.

This review used the Real-Time Oncology Review (RTOR) pilot program, which streamlined data submission prior to the filing of the entire clinical application, and the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment. The FDA approved this application 8 weeks ahead of the FDA goal date.

This application was granted priority review and orphan drug designation. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

This announcement was originally published on the Food and Drug Administration website on March 3, 2021.
