Keytruda

The U.S. Food and Drug Administration on September 4, 2014 granted accelerated approval to Keytruda (pembrolizumab) for treatment of patients with advanced or unresectable melanoma who are no longer responding to other drugs.

Melanoma, which accounts for approximately 5 percent of all new cancers in the United States, occurs when cancer cells form in skin cells that make the pigment responsible for color in the skin. According to the National Cancer Institute, an estimated 76,100 Americans will be diagnosed with melanoma and 9,710 will die from the disease this year.

Keytruda is the first approved drug that blocks a cellular pathway known as PD-1, which restricts the body's immune system from attacking melanoma cells. Keytruda is intended for use following treatment with ipilimumab, a type of immunotherapy. For melanoma patients whose tumors express a gene mutation called BRAF V600, Keytruda is intended for use after treatment with ipilimumab and a BRAF inhibitor, a therapy that blocks activity of BRAF gene mutations.

"Keytruda is the sixth new melanoma treatment approved since 2011, a result of promising advances in melanoma research," said Richard Pazdur, M.D., director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "Many of these treatments have different mechanisms of action and bring new options to patients with melanoma."

The five prior FDA approvals for melanoma include: ipilimumab (2011), peginterferon alfa-2b (2011), vemurafenib (2011), dabrafenib (2013), and trametinib (2013).

The FDA granted Keytruda breakthrough therapy designation because the sponsor demonstrated through preliminary clinical evidence that the drug may offer a substantial improvement over available therapies. It also received priority review and orphan product designation. Priority review is granted to drugs that have the potential, at the time the application was submitted, to be a significant improvement in safety or effectiveness in the treatment of a serious condition. Orphan product designation is given to drugs intended to treat rare diseases.

The FDA action was taken under the agency's accelerated approval program, which allows approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients. This program provides earlier patient access to promising new drugs while the company conducts confirmatory clinical trials. An improvement in survival or disease-related symptoms has not yet been established.

Keytruda's efficacy was established in 173 clinical trial participants with advanced melanoma whose disease progressed after prior treatment. All participants were treated with Keytruda, either at the recommended dose of 2 milligrams per kilogram (mg/kg) or at a higher dose of 10 mg/kg. In the half of the participants who received Keytruda at the recommended dose of 2 mg/kg, approximately 24 percent had their tumors shrink. This effect lasted at least 1.4 to 8.5 months and continued beyond this period in most patients. A similar percentage of patients had their tumor shrink at the 10 mg/kg dose.

Keytruda's safety was established in the trial population of 411 participants with advanced melanoma. The most common side effects of Keytruda were fatigue, cough, nausea, itchy skin (pruritus), rash, decreased appetite, constipation, joint pain (arthralgia) and diarrhea. Keytruda also has the potential for severe immune-mediated side effects. In the 411 participants with advanced melanoma, severe immune-mediated side effects involving healthy organs, including the lung, colon, hormone-producing glands and liver, occurred uncommonly.

Keytruda is marketed by Merck & Co., based in Whitehouse Station, New Jersey.