

FDA NEWS RELEASE

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FDA Approves New Indication for Tasigna
Approval expands use in treatment of rare type of leukemia

The U.S. Food and Drug Administration today approved a new indication for Tasigna (nilotinib) for the treatment of a rare blood cancer when it is first diagnosed. The cancer, called Philadelphia chromosome positive chronic phase chronic myeloid leukemia (Ph+ CP-CML), is a slowly progressing blood and bone marrow disease linked to a genetic abnormality.

Tasigna is believed to work by blocking a signal that leads to leukemic cell development. The new indication expands the use of Tasigna to adult patients in earlier stages of the disease. The FDA originally approved Tasigna in October 2007 for the treatment of Ph+CP-CML in adult patients whose disease had progressed or who could not tolerate other therapies, including Gleevec (imatinib).

When Tasigna was originally approved in October 2007, the FDA identified that the therapy placed patients at risk of an abnormal heart rhythm called QT prolongation. In March 2010, the FDA approved a Risk Evaluation and Mitigation Strategy (REMS) for Tasigna to help patients and health care professionals to better understand this risk. The REMS includes an updated Medication Guide and a communication plan to help reduce medication errors involving drug-food interactions and incorrect dosing intervals.

"It's important for companies to continue developing oncology drugs for earlier stages of the disease once they have demonstrated clinical effectiveness in resistant forms of cancer," said Richard Pazdur, M.D., director of the Office of Oncology Drug Products, part of the FDA's Center for Drug Evaluation and Research. "This approach has the potential to increase the availability of an effective treatment to more patients."

In CML, too many blood stem cells develop into a type of white blood cell called granulocytes. These granulocytes are abnormal and do not become healthy white blood cells. These cells can build up in the blood and bone marrow so there is less room for healthy white blood cells, red blood cells, and platelets. When this happens, infection, anemia, or unexpected bleeding may occur.

The FDA granted Tasigna a priority review for Ph+ CP-CML. The agency completed the review in six months. The new indication for Tasigna was approved under the FDA's accelerated approval program, which allows FDA to approve a drug to treat serious diseases with an unmet medical need based on an endpoint thought to reasonably predict clinical benefit. The company is required to collect additional long term efficacy and safety information data confirming the drug's benefit. The accelerated approval program provides earlier patient access to promising new drugs while the confirmatory clinical trials are being conducted.

The safety and effectiveness of Tasigna were evaluated in a single clinical trial enrolling 846

patients with newly diagnosed Ph+ CP-CML. Patients received either Tasigna or Gleevec until the disease worsened, or until unacceptable side effects developed. The study was designed to measure a significant reduction in the surrogate endpoint of the number of CML cancer cells in the blood stream (i.e., major molecular response) at 12 months. About 44 percent of patients who received Tasigna experienced a major molecular response, compared with 22 percent of patients receiving Gleevec.

In patients with newly diagnosed CP-CML, the most commonly reported non-blood-related adverse drug reactions were rash, itching (pruritus), headache, nausea, fatigue, and muscle pain (myalgia). Serious blood-related drug reactions included decrease in bone marrow activity (myelosuppression), low level of platelets in the blood (thrombocytopenia), decrease in infection-fighting white blood cells (neutropenia), and anemia.

Other FDA-approved drugs to treat CML include Gleevec in May 2001 and Sprycel (dasatinib) in June 2006. Tasigna and Gleevec are marketed by East Hanover, N.J.-based Novartis Pharmaceuticals. Sprycel is marketed by New York City-based Bristol-Myers Squibb.