

*The following is a message from the FDA's Office of Oncology Drug Products Director, Dr. Richard Pazdur:*

On November 8, 2007, the U. S. Food and Drug Administration (FDA) granted accelerated approval of a new dosing regimen of dasatinib (SPRYCEL™, Bristol-Myers Squibb) for the treatment of adults with chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to prior therapy, including imatinib mesylate.

The new dosing regimen is 100 mg taken orally once daily. FDA had previously granted accelerated approval to dasatinib in June, 2006 for the treatment of adults with CP, accelerated phase, or myeloid or lymphoid blast phases of CML with resistance to or intolerance to prior therapy, including imatinib mesylate. In June 2006, the FDA also granted regular approval for the treatment of patients with Philadelphia positive acute lymphoblastic leukemia. The recommended dosing regimen in the 2006 approval was 70 mg twice daily.

A randomized, 2x2, open-label study evaluated the safety and efficacy of four dosing regimens of dasatinib in patients with CP CML. Dasatinib was administered at a dose of 100 mg once daily, 140 mg once daily, 50 mg twice daily or 70 mg twice daily. Patients with significant cardiac disease were excluded from the study. A total of 670 patients were randomized. The primary endpoint was major cytogenetic response (MCyR), defined as elimination or substantial diminution (by at least 65%) of Ph+ hematopoietic cells. The primary analysis showed comparable efficacy for the 100 mg once daily schedule (MCyR=53%, 95% CI: 44%-62%) and the 70 mg twice daily schedule (MCyR=51%, 95% CI: 42%-60%).

Safety analyses revealed a reduction in adverse reactions with the 100 mg once daily dose regimen compared with the previously approved 70 mg twice daily regimen. These adverse events included fluid retention all grades (24% vs. 32%), pleural effusion all grades (10% vs. 18%), and grade 3/4 hematologic toxicities, including neutropenia (34% vs. 43%), thrombocytopenia (22% vs. 38%), and anemia (10% vs. 17%).

Submission of further follow-up data from ongoing studies will convert this accelerated approval to regular approval. Full prescribing information, including clinical trial information, safety, dosing, drug-drug interactions and contraindications is available at <http://www.fda.gov/cder/foi/label/2007/021986s001lbl.pdf>.