FOOD AND DRUG ADMINISTRATION

Center for Drug Evaluation and Research
Oncologic Drugs Advisory Committee
September 14, 2005

Questions to the Committee

Revlimid

Proposed Indication: "Treatment of patients with transfusion-dependent anemia due to low- or intermediate- 1- risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities"

Question #1

Randomized controlled trials allow for direct comparisons of treatment effects and safety between treatment arms. A single arm study has been submitted using an 8-week run-in period to serve as a baseline for each patient's transfusion requirements. A comparison is subsequently made to a follow-up 8-week period on Revlimid to compare transfusion requirements. Does this study design allow adequate characterization of Revlimid's treatment effect in the population described in the proposed indication?

Question #2

In this single arm trial, 80% of patients enrolled in MDS-003 had dose reductions and/or delays and 80% of patients experienced either grade 3 or 4 adverse events. Data do not exist on the efficacy and safety of lower Revlimid doses. Approval of a drug is contingent upon being able to write adequate product labeling, requiring a recommended dose and characterization of a safety profile. Do the data provided in this single-arm trial provide a basis for a recommended dose and adequate description of a safety profile?

Question #3

Please characterize the magnitude of Revlimid's benefit and risk in the indication being sought. After this characterization, does this risk/benefit analysis warrant approval?

Question #4

At this time, lenalidomide, a thalidomide analogue, does not have adequate nonclinical studies to assess reproductive/developmental safety. Should a risk/management program with a goal of no fetal exposures to Revlimid be instituted until the nonclinical reproductive/developmental safety assessments are addressed?