

**IND SAFETY REPORT: INITIAL WRITTEN REPORT**

To: *Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA*

FAX: 301-796-9845

1. IND NUMBER 58443 46211	2. AGENT NAME PS-341 (bortezomib; Velcade) Alvocidib (flavopiridol)	3. DATE September 3, 2010
4. SPONSOR Division of Cancer Treatment and Diagnosis, National Cancer Institute		
5. REPORTER'S NAME, TITLE, AND INSTITUTION John Wright, MD, PhD-Associate Branch Chief for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI L. Austin Doyle, M.D., Senior Investigator for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196
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8a. PROTOCOL NUMBER (AE #) 6413 (AE# 1358314)	8b. AE GRADE: AE Grade 3: Colitis	
9. PATIENT IDENTIFICATION 046	10. AGE 65 yrs	11. SEX Male
12. DESCRIPTION OF ADVERSE EVENT The patient is a 65-year-old male with multiple myeloma who experienced grade 3 colitis while on a phase 1 study utilizing the investigational agents bortezomib and flavopiridol. He began the investigational therapy on May 17, 2010, and received his last doses of bortezomib and flavopiridol on July 2, 2010 (Cycle 3, Day 4). On July 6, 2010 (Cycle 3, Day 8), the patient presented to the clinic with persistent nausea and vomiting since the start of Cycle 3 therapy. He also reported at least 1 loose bowel movement per day. An acute abdominal series was suggestive of ileus versus early small bowel obstruction. A CT scan of the abdomen was consistent with enterocolitis. The patient was admitted, made NPO, and started on IV fluids. On July 11, 2010 (Cycle 3, Day 13), the stool cultures were negative. Additional information has been requested from the investigational site. <b>There is a reasonable possibility that the experience may have been caused by the drug.</b>		
13. DOSE, ROUTE, AND SCHEDULE: Cycle = 21 Days Bortezomib: 1.3 mg/m <sup>2</sup> IVP over 3-5 seconds on Days 1, 4, 8, and 11 Flavopiridol: 75 mg/m <sup>2</sup> IV over 1 hour on Days 1, 4, 8, and 11		
14. DATES OF TREATMENT The patient began the investigational therapy on May 17, 2010, and received his last doses of bortezomib and flavopiridol on July 2, 2010 (Cycle 3, Day 4).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bortezomib = 3,231 and flavopiridol = 2145. There have been 7 other cases of colitis reported to the NCI through AdEERS as serious adverse events for bortezomib and 6 other cases of colitis reported to the NCI through AdEERS as serious adverse events for flavopiridol.		
16. COMMENTS: AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOW-UP REPORT WILL BE SUBMITTED IN ACCORDANCE WITH 21CFR 312.32(d)(2). <b>DISCLAIMER per 21 CFR 312.32(e): THIS SAFETY REPORT DOES NOT NECESSARILY REFLECT A CONCLUSION OR ADMISSION BY THE CTEP IDB SENIOR INVESTIGATOR/SPONSOR THAT THE INVESTIGATIONAL AGENT/THERAPY CAUSED OR CONTRIBUTED TO THE ADVERSE EXPERIENCE BEING REPORTED.</b>		

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