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NCCN Guidelines™ Panel: Prostate Cancer

Dear NCCN,

On behalf of Centocor Ortho Biotech, I respectfully request the NCCN Guidelines™ - Prostate Cancer Panel to review the enclosed data for inclusion of ZYTIGA™ (abiraterone acetate) Tablets for the treatment of castration recurrent prostate cancer.

Specific Change: Recommend ZYTIGA™ as an additional systemic therapy for patients with castration recurrent prostate cancer.

FDA Clearance: FDA has approved ZYTIGA™ in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC) who have received prior chemotherapy containing docetaxel.

Rationale: Approval was based on a Phase 3, international, randomized, double-blind, placebo-controlled, multicenter study in patients with metastatic castration-resistant prostate cancer (mCRPC) whose disease had progressed after receiving docetaxel-based chemotherapy (N = 1195). At the protocol pre-specified interim analysis, treatment with ZYTIGA in combination with prednisone showed a statistically significant improvement in median overall survival compared to the placebo plus prednisone arm and resulted in a 35 percent reduction in the risk of death (14.8 months vs. 10.9 months; hazard ratio [HR] = 0.646; 95 percent confidence interval [CI]: 0.543, 0.768;  $p < 0.0001$ ). In an updated survival analysis, results were consistent with those from the interim analysis (median 15.8 months vs. 11.2 months; HR = 0.74; 95 % CI: 0.638, 0.859). The most common adverse reactions ( $\geq 5\%$ ) are joint swelling or discomfort, hypokalemia, edema, muscle discomfort, hot flush, diarrhea, urinary tract infection, cough, hypertension, arrhythmia, urinary frequency, nocturia, dyspepsia and upper respiratory tract infection.

The following publications are submitted with the Full Prescribing Information in support of this proposed addition. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

1. ZYTIGA™ (abiraterone acetate) Tablets PRESCRIBING INFORMATION, Distributed by Centocor Ortho Biotech Inc., Horsham, PA. April 2011.

2. de Bono JS, Logothetis CJ, Fizazi K, et al. Abiraterone acetate (AA) plus low dose prednisone (P) improves overall survival (OS) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) who have progressed after docetaxel-based chemotherapy (chemo): results of COU-AA-301, a randomized double-blind placebo-controlled phase III study [abstract]. *Ann Oncol*. 2010;21 (Suppl 8): viii3. Abstract LBA5.
3. Fizazi K, de Bono JS, Logothetis C, et al. Abiraterone acetate plus low-dose prednisone has a favourable safety profile in metastatic castration-resistant prostate cancer progressing after docetaxel-based chemotherapy: results from COU-AA-301, a randomised, double-blind, placebo-controlled phase 3 study [poster]. Presented at the European Association of Urology Annual Meeting; Vienna, Austria; March 18 - 23, 2011.
4. Scher HI, Logothetis C, Molina A, et al. Improved survival outcomes in clinically relevant patient subgroups from COU-AA-301, a phase III study of abiraterone acetate plus prednisone in patients with metastatic castration-resistant prostate cancer progressing after docetaxel-based chemotherapy [poster]. Presented at the American Society of Clinical Oncology 2011 Genitourinary Cancers Symposium; Orlando, Florida; February 17 - 19, 2011.

Sincerely,

Lisa Meadows RPh, PharmD-c, BCOP  
Manager, Medical Information