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NCCN Guidelines Panel: Prostate Cancer NCCN Evidence Blocks

On behalf of Astellas and Medivation, we are respectfully request that the NCCN Prostate Cancer NCCN Evidence Blocks Panel review and revise ratings and category classifications for enzalutamide in the setting of systemic therapy for M1 castration-recurrent prostate cancer (CRPC) for patients with and without visceral metastases.

Specific Changes: We are requesting that within the NCCN Prostate Cancer NCCN Evidence Block guidelines, the category 1 designation for enzalutamide be clearly depicted, specifically on page PROS-11A. Additionally we request that the “efficacy of regimen/agent” rating for patients with visceral metastases be reconsidered based on available data for patients receiving enzalutamide with M1 CRPC with visceral metastases.

FDA Clearance: Enzalutamide is currently approved for the treatment of patients with metastatic CRPC.<sup>1</sup>

Rationale: On page PROS-11A of the Prostate Cancer NCCN Evidence Blocks, a footnote at the bottom of the page states “All recommendations are category 2A unless otherwise indicated” for the drugs and regimens listed.<sup>2</sup> Enzalutamide is classified as a category 1 recommendation for M1 CRPC (PROS-11) in the NCCN Guidelines for Prostate Cancer (Version 2.2016), and this is not accurately represented within the rating chart on PROS-11A in the NCCN Evidence Blocks.<sup>3</sup> In addition to being classified as a category 1 recommendation for CRPC patients with and without visceral metastases in the NCCN Guidelines, enzalutamide data for patients with visceral metastases is available as part of the AFFIRM and PREVAIL trials, and subsequent subgroup analyses confirmed the benefit of enzalutamide in these patients.<sup>4-7</sup> AFFIRM was a phase 3, double-blind, placebo-controlled, randomized controlled trial that included 1199 men with metastatic CRPC after chemotherapy.<sup>4</sup> PREVAIL was a phase 3, multinational, double-blind, placebo-controlled, randomized controlled trial in 1717 men treated with enzalutamide or placebo with metastatic CRPC before chemotherapy.<sup>5</sup> The NCCN Evidence Blocks ratings on page PROS-11A do not appear to reflect these data under the “efficacy of regimen/agent” section, as enzalutamide in visceral metastases has a lower rating than another agent that does not have a category 1 recommendation.

In summary, we request the “efficacy of regimen/agent” rating to be reevaluated to reflect the randomized controlled study data of enzalutamide within patients with visceral metastases. Additionally, enzalutamide should be identified as a category 1 recommendation to be consistent with the NCCN Guidelines for Prostate Cancer (Version 2.2016).<sup>3</sup>

We kindly ask for reexamination and revision and thank you for your time and consideration.

Additional details of the trials can be accessed here:

AFFIRM: <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1207506>  
PREVAIL : <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1405095>  
AFFIRM subgroup analysis : <http://meetinglibrary.asco.org/content/113918-132>  
PREVAIL subgroup analysis:  
<http://www.aua2014.org/webcasts/index.cfm?ID=5947,5946,5944,5945,3810&title=6&LanguageID=0>

Respectfully submitted,

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**End:** Xtandi Prescribing Information

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