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NCCN Guidelines Panel: Prostate Cancer

On behalf of Astellas and Medivation, we are submitting this request for review of data for the NCCN Prostate Cancer Guideline Panel on Xtandi® (enzalutamide) from two multicenter, randomized, double-blind, double-dummy phase 2 clinical trials (TERRAIN and STRIVE) which compared enzalutamide to bicalutamide in men with castration-resistance prostate cancer (CRPC).<sup>1-3</sup> The TERRAIN trial enrolled 375 men with metastatic CRPC and the STRIVE trial enrolled 396 men with either metastatic or non-metastatic CRPC.

Specific Changes: We are providing data from the TERRAIN and STRIVE trials which evaluated the use of enzalutamide compared to bicalutamide in men with CRPC as described above; data from these trials were presented in plenary sessions at the 30<sup>th</sup> Annual Congress of the European Association of Urology in Madrid, Spain (TERRAIN), and the American Urological Association Annual 2015 Meeting in New Orleans, LA, respectively (STRIVE and TERRAIN).<sup>1-3</sup>

FDA Clearance: Enzalutamide is currently approved for the treatment of patients with mCRPC.<sup>4</sup>

Rationale: Two multicenter, randomized, double-blind, double-dummy phase 2 clinical trials, TERRAIN and STRIVE, demonstrated significant increases in progression-free survival (PFS) for enzalutamide 160 mg/day compared to bicalutamide 50 mg/day in men with CRPC: in TERRAIN, a significant increase in PFS was observed, with a hazard ratio (HR) of 0.44 (95% CI, 0.34-0.57;  $P < 0.0001$ ), while in STRIVE, the overall HR was 0.24 (95% CI, 0.18-0.32;  $P < 0.0001$ ) (HR for the subset of metastatic CRPC patients was 0.24 [95% CI, 0.17-0.34;  $P < 0.0001$ ], and 0.24 [95% CI, 0.14-0.42] for the non-metastatic subset) with the most common enzalutamide adverse events in these trials being fatigue, back pain, hot flush, and hypertension.<sup>1-3</sup>

Additional details of the TERRAIN and STRIVE trials can be accessed here:

TERRAIN:

[http://www.aua2015.org/webcasts/webcast\\_play.cfm?videoID=1851&agendaId=7271](http://www.aua2015.org/webcasts/webcast_play.cfm?videoID=1851&agendaId=7271)

STRIVE:

[http://www.aua2015.org/webcasts/webcast\\_play.cfm?videoID=1899&agendaId=9314](http://www.aua2015.org/webcasts/webcast_play.cfm?videoID=1899&agendaId=9314)

Respectfully submitted,



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Encl: Xtandi prescribing information.

### **Cited References**

1. Heidenreich A, Shore N, Villers A et al. A randomised, double-blind, phase 2, efficacy and safety study of enzalutamide versus bicalutamide in metastatic castration-resistant prostate cancer: TERRAIN trial. Proceedings of the 30th Annual Congress of the European Association of Urology, Madrid, Spain. [Slide Presentation]. 2015.
2. Shore N, Heidenreich A, Villers A et al. TERRAIN Trial: Prostate-specific Antigen Kinetics and Quality of Life Results of Enzalutamide versus Bicalutamide in Metastatic Castration-resistant Prostate Cancer. Proceedings of the 2015 American Urological Association (AUA) Annual Meeting, New Orleans, LA. [Oral Presentation - Abstract #P11-LBA4]. 2015.
3. Penson D, Armstrong A, Concepcion R et al. STRIVE: A multicenter phase 2 study of enzalutamide versus bicalutamide in men with nonmetastatic or metastatic castration-resistant prostate cancer. Proceedings of the 2015 American Urological Association (AUA) Annual Meeting, New Orleans, LA. [Oral Presentation - Abstract #P11-LBA10]. 2015.
4. XTANDI [package insert]. Northbrook, IL: Astellas, Inc. and San Francisco, CA: Medivation, Inc.