



Submitted by:
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Dear NCCN Melanoma Guidelines Panel:

On behalf of Celgene Corporation, we respectfully request that the NCCN Melanoma Guidelines Panel review and consider the enclosed data for Abraxane (albumin-bound paclitaxel) for the treatment of metastatic melanoma.

Specific changes:

Consider the recently presented data on the use of albumin-bound paclitaxel for the treatment of metastatic melanoma and include albumin-bound paclitaxel as a therapy option in the NCCN Clinical Practice Guidelines in Oncology for Melanoma.

FDA Clearance:

The FDA has not approved albumin-bound paclitaxel for the treatment of metastatic melanoma. Please refer to the enclosed prescribing information for the FDA-approved indications as well as safety information.

Rationale for recommended change: Results from the CA033 Phase III study were recently presented by Hersh et al. at the Society for Melanoma Research (SMR) Meeting on November 8-11, 2012. This multicenter, open-labeled study was conducted to compare the efficacy and safety of albumin-bound paclitaxel to dacarbazine in the treatment of chemo-naïve patients with metastatic melanoma. The primary efficacy endpoint was progression free survival (PFS). The results of this trial demonstrated significantly longer median PFS for albumin-bound paclitaxel (4.8 months) compared to dacarbazine (2.5 months) ($P=.044$; hazard ratio [HR] .792; 95.1% confidence interval [CI]: .631-.992).

The most common treatment-related adverse events (TRAEs) \geq Grade 3 reported in \geq 5% of patients in the albumin-bound paclitaxel arm were peripheral neuropathy (25%), neutropenia (20%), leukopenia (12%), lymphocytopenia (8%), fatigue (8%), and alopecia (5%). The most common \geq Grade 3 TRAEs reported in \geq 5% of patients in the dacarbazine arm were lymphocytopenia (11%), neutropenia (10%), and leukopenia (7%), thrombocytopenia (6%), and anemia (5%).

1. Hersh EM, Del Vecchio M, Brown MP, et al. Phase 3 study nab[®]-paclitaxel vs dacarbazine chemotherapy-naïve patients with metastatic malignant melanoma [oral]. *Oral presented at: Society for Melanoma Research Congress (SMR) 2012*; November 8-11; Hollywood, CA, USA.

Additionally, the following publications, posters and presentations demonstrating the efficacy and safety of albumin-bound paclitaxel either as single-agent or in combination are submitted in support of the proposed change:

2. Hersh EM, O'Day SJ, Ribas A, et al. A Phase 2 clinical trial of nab-paclitaxel in previously treated and chemotherapy-naïve patients with metastatic melanoma. *Cancer* 2010; 116(1): 155-63
3. Kottschade LA, Suman VJ, Amatruda T III, et al. A Phase II trial of nab-paclitaxel (ABI-007) and carboplatin in patients with unresectable stage IV melanoma: A north central cancer treatment group study, N057E1. *Cancer* 2011; 117(8): 1704-10.
4. Kottschade LA, Suman VJ, Perez DG, et al. A randomized Phase 2 study of temozolomide and bevacizumab or nab-paclitaxel, carboplatin, and bevacizumab in patients with unresectable stage IV melanoma: A North Central Cancer Treatment Group study, N0775 [published online ahead of print, August 22, 2012]. *Cancer* 2012; doi:10.1002/cncr.27760.
5. Lutzky J, Nunez Y, Deck R, et al. First-stage results of a Phase II study of carboplatin, nab-paclitaxel and sorafenib in patients with advanced melanoma [poster]. Poster presented at: Annual Meeting of the European Association of Dermato-Oncology 2009b; May 12-16; Vienna, Austria.
6. Lutzky J, Nunez Y, Deck R, et al. First-stage results of a Phase II study of carboplatin, nab-paclitaxel and sorafenib in patients with advanced melanoma [abstract]. Proceedings of the 7th World Melanoma Congress -5th Congress of the European Association of Dermato-Oncology 2009a; May 12-16; Vienna, Austria: Abstract #P38.
7. Boasberg PD, Weber RW, Cruickshank S, et al. Phase II trial of nab-paclitaxel and bevacizumab as first-line therapy in patients with unresectable melanoma [poster]. *Poster presented at: 47th Annual Meeting of the American Society of Clinical Oncology (ASCO) 2011*; June 3-7; Chicago, IL; USA.
8. Boasberg PD, Weber RW, Cruickshank S, et al. Phase II trial of nab-paclitaxel and bevacizumab as first-line therapy in patients with unresectable melanoma [abstract]. *Proceedings of the 47th Annual Meeting of the American Society of Clinical Oncology (ASCO) 2011*; June 3-7; Chicago, IL; USA: Abstract #8543.
9. Ott PA, Chang J, Madden K, et al. Oblimersen in combination with temozolomide and albumin-bound paclitaxel in patients with advanced melanoma: A Phase I trial [published online ahead of print, October 12, 2012]. *Cancer Chemotherapy and Pharmacology* 2012; doi:10.1007/s00280-012-1995-7.
10. Ott PA, Madden KM, Kannan R, et al. Oblimersen 1-hour IV infusion in combination with temozolomide and albumin-bound paclitaxel in patients with advanced melanoma [abstract]. *Journal of Clinical Oncology: ASCO Annual Meeting Proceedings 2010*; 28(15 Suppl): Abstract #8561.

Thank you for your consideration and we look forward to your reply concerning our request.

Sincerely,



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Senior Manager, Medical Information – Solid Tumors



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Senior Director, Medical Affairs Disease Lead – Solid Tumors