



Submitted by:  
Lorraine Dethlefsen, PharmD  
Celgene Corporation  
86 Morris Avenue  
Summit NJ 07901  
Ph: 908-673-1651  
Email: ldethlefsen@celgene.com  
Date of Request: December 21, 2012

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 chemonaive 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-naive 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,



Lorraine Dethlefsen, PharmD  
Senior Manager, Medical Information – Solid Tumors



Victoria Manax, MD  
Senior Director, Medical Affairs Disease Lead – Solid Tumors