



# MASSACHUSETTS

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## Medical Policy

### Melanoma Vaccines

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#### Policy Number: 453

BCBSA Reference Number: 2.03.04A (For Plan internal use only)

NCD/LCD: N/A

#### Related Policies

Adoptive Immunotherapy, #[455](#)

#### Policy

### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue<sup>SM</sup> and Medicare PPO Blue<sup>SM</sup> Members

Melanoma vaccines are considered [INVESTIGATIONAL](#).

#### Prior Authorization Information

##### Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

##### Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is <b>not</b> a covered service.
Commercial PPO and Indemnity	This is <b>not</b> a covered service.
Medicare HMO Blue <sup>SM</sup>	This is <b>not</b> a covered service.
Medicare PPO Blue <sup>SM</sup>	This is <b>not</b> a covered service.

#### CPT Codes / HCPCS Codes / ICD Codes

*Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.*

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

## CPT Codes

There is no specific CPT code for this service.

## Description

Tumor vaccines are a type of active immunotherapy that attempts to stimulate the patient's own immune system to respond to tumor antigens. Melanoma has been viewed as a particularly promising tumor for this type of treatment because of its immunologic features, which include the prognostic importance of lymphocytic infiltrate at the primary tumor site, the expression of a wide variety of antigens, and the occasional occurrence of spontaneous remissions. Melanoma vaccines can be generally categorized or prepared in a variety of ways.

## Summary

Despite considerable interest and numerous studies over the past 20 years, to date no melanoma vaccine has been shown to demonstrate safety and efficacy in a well-controlled published Phase III clinical trial and no vaccine treatment for this cancer has been approved by FDA. A wide range of vaccine choices are available including use of autologous tumor cells, allogeneic tumor cells, and tumor-specific moieties including peptides, gangliosides, and DNA plasmids. A variety of mechanisms appear to exist as possible obstacles to successful active immunotherapy using vaccines. Current studies are focused on the use of new and different vaccine preparations, as well as on various forms of immune-modulation as potential techniques for enhancing vaccine effectiveness.

## Policy History

Date	Action
2/2020	Policy updated with literature review through February 1, 2020, no references added. Policy statements unchanged.
7/2015	Annual policy review. New references added.
6/2013	Annual policy review. New references added.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
1/17/2012	Annual policy review. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
9/2010	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
4/2010	Annual policy review. No changes to policy statements.
9/2009	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
10/2008	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
9/2008	Annual policy review. No changes to policy statements.
11/2007	Annual policy review. No changes to policy statements.

## Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

- [Medical Policy Terms of Use](#)
- [Managed Care Guidelines](#)
- [Indemnity/PPO Guidelines](#)
- [Clinical Exception Process](#)
- [Medical Technology Assessment Guidelines](#)

## References

1. Ray S, Chhabra A, Mehrotra S et al. Obstacles to and opportunities for more effective peptide-based therapeutic immunization in human melanoma. *Clin Dermatol* 2009; 27(6):603-13.
2. Cunningham TJ, Olson KB, Laffin R et al. Treatment of advanced cancer with active immunization. *Cancer* 1969; 24(5):932-7.
3. Eggermont AM. Therapeutic vaccines in solid tumours: can they be harmful? *Eur J Cancer* 2009; 45(12):2087-90.
4. Lens M. The role of vaccine therapy in the treatment of melanoma. *Expert Opin Biol Ther* 2008; 8(3):315-23.
5. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Special Report: Vaccines for the Treatment of Malignant Melanoma. 2001 TEC Assessments: Volume 16, Tab 4.
6. Rosenberg SA, Yang JC, Restifo NP. Cancer immunotherapy: moving beyond current vaccines. *Nat Med* 2004; 10(9):909-15.
7. Livingston PO, Adluri S, Helling F et al. Phase 1 trial of immunological adjuvant QS-21 with a GM2 ganglioside-keyhole limpet haemocyanin conjugate vaccine in patients with malignant melanoma. *Vaccine* 1994; 12(14):1275-80.
8. Wallack MK, Sivanandham M, Balch CM et al. Surgical adjuvant active specific immunotherapy for patients with stage III melanoma: the final analysis of data from a phase III, randomized, double-blind, multicenter vaccinia melanoma oncolysate trial. *J Am Coll Surg* 1998; 187(1):69-77; discussion 77-9.
9. Kirkwood JM, Ibrahim JG, Sosman JA et al. High-dose interferon alfa-2b significantly prolongs relapse-free and overall survival compared with the GM2-KLH/QS-21 vaccine in patients with resected stage IIB-III melanoma: results of intergroup trial E1694/S9512/C509801. *J Clin Oncol* 2001; 19(9):2370-80.
10. Sondak VK, Liu PY, Tuthill RJ et al. Adjuvant immunotherapy of resected, intermediate-thickness, node-negative melanoma with an allogeneic tumor vaccine: overall results of a randomized trial of the Southwest Oncology Group. *J Clin Oncol* 2002; 20(8):2058-66.
11. Hersey P, Coates AS, McCarthy WH et al. Adjuvant immunotherapy of patients with high-risk melanoma using vaccinia viral lysates of melanoma: results of a randomized trial. *J Clin Oncol* 2002; 20(20):4181-90.
12. Morton DI, Mozzillo N, Thompson JF et al. An international, randomized phase III trial of bacillus Calmette-Guerin (BCG) plus allogeneic melanoma vaccine (MCV) or placebo after complete resection of melanoma metastatic to regional or distant sites. *J Clin Oncol* 2007; 25(18S):8508.
13. Mitchell MS, Abrams J, Thompson JA et al. Randomized trial of an allogeneic melanoma lysate vaccine with low-dose interferon Alfa-2b compared with high-dose interferon Alfa-2b for Resected stage III cutaneous melanoma. *J Clin Oncol* 2007; 25(15):2078-85.
14. Testori A, Richards J, Whitman E et al. Phase III comparison of vitespen, an autologous tumor-derived heat shock protein gp96 peptide complex vaccine, with physician's choice of treatment for stage IV melanoma: the C-100-21 Study Group. *J Clin Oncol* 2008; 26(6):955-62.
15. Schwartzenuber DJ, Lawson D, Richards J et al. A Phase III multi-institutions randomized study of immunization with the gp100.209-217 (210M) peptide followed by high-dose IL-2 compared with high-dose IL-2 alone in patients with metastatic melanoma. 2009 ASCO Annual Meeting 2009.
16. Schadendorf D, Ugurel S, Schuler-Thurner B et al. Dacarbazine (DTIC) versus vaccination with autologous peptide-pulsed dendritic cells (DC) in first-line treatment of patients with metastatic melanoma: a randomized phase III trial of the DC study group of the DeCOG. *Ann Oncol* 2006; 17(4):563-70.
17. Hodi FS, O'Day SJ, McDermott DF et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med* 2010; 363(8):711-23.
18. Schwartzenuber DJ, Lawson DH, Richards JM et al. gp100 peptide vaccine and interleukin-2 in patients with advanced melanoma. *N Engl J Med* 2011; 364(22):2119-27.
19. Chi M, Dudek AZ. Vaccine therapy for metastatic melanoma: systematic review and meta-analysis of clinical trials. *Melanoma Res* 2011; 21(3):165-74.
20. Garbe C, Eigentler TK, Keilholz U et al. Systematic review of medical treatment in melanoma: current status and future prospects. *Oncologist* 2011; 16(1):5-24.
21. Chapman PB. Melanoma vaccines. *Semin Oncol* 2007; 34(6):516-23.

22. Gajewski TF. Molecular profiling of melanoma and the evolution of patient-specific therapy. *Semin Oncol* 2011; 38(2):236-42.
23. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology, Melanoma (v2.2013). Available online at: [http://www.nccn.org/professionals/physician\\_gls/pdf/melanoma.pdf](http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf).
24. Gibney GT, Kudchadkar RR, DeConti RC, et al. Safety, correlative markers, and clinical results of adjuvant nivolumab in combination with vaccine in resected high-risk metastatic melanoma. *Clin Cancer Res*. Feb 15 2015;21(4):712-720. PMID 25524312
25. Riker AI, Rossi GR, Masih P, et al. Combination immunotherapy for high-risk resected and metastatic melanoma patients. *Ochsner J*. Summer 2014;14(2):164-174. PMID 24940124
26. Weber JS, Kudchadkar RR, Yu B, et al. Safety, efficacy, and biomarkers of nivolumab with vaccine in ipilimumab-refractory or -naive melanoma. *J Clin Oncol*. 2013;31(34):4311-4318.
27. Jha G, Miller JS, Curtsinger JM, et al. Randomized phase II study of IL-2 with or without an allogeneic large multivalent immunogen vaccine for the treatment of stage IV melanoma. *Am J Clin Oncol*. Jun 2014;37(3):261-265. PMID 23241505