The Medical Letter®

on Drugs and Therapeutics

Volume 60 January 1, 2018

ISSUE No. 1537

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The Medical Letter®
on Drugs and Therapeutics

Volume 60 (Issue 1537) January 1, 2018

IN BRIEF

Pembrolizumab *(Keytruda)* for Cancers with Biomarkers

The immune checkpoint inhibitor pembrolizumab (*Keytruda* – Merck), a programmed death receptor-1 (PD-1) inhibitor, has been granted accelerated approval by the FDA for use in adults and children who have unresectable or metastatic microsatellite-instability-high (MSI-H) or mismatch-repair-deficient (dMMR) solid tumors that have progressed following treatment, and do not have any satisfactory alternative treatment options. For metastatic colorectal cancer, the indication is limited to tumors that have progressed following combination treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. This is the first approval of a cancer drug based solely on the presence of certain biomarkers, regardless of the organ in which the cancer originated or the histology of the tumor.

MSI-H and dMMR are markers for abnormalities in cancer cells that prevent DNA replication and postreplicative DNA repair.[1] These biomarkers are found most commonly in cancers of the endometrium, stomach, and colon. The incidence of MSI-H or dMMR in these tumors appears to be lower in advanced disease than in early-stage disease; about 5% of patients with metastatic colorectal cancer have MSI-H or dMMR tumors.[2]

FDA approval was based on data from five unpublished, single-arm trials of pembrolizumab (summarized in the package insert) that included a total of 149 previously treated adults with various MSI-H or dMMR metastatic or unresectable tumors (90 patients had colorectal cancer). The overall objective response rate was 39.6% and the complete response rate was 7.4%. The median duration of response had not been reached by the end of the study; 78.0% of patients had a response duration of ≥6 months. Adverse reactions, including immune-mediated effects, were similar to those reported previously with pembrolizumab.

The recommended adult dosage of pembrolizumab for this indication is 200 mg IV (2 mg/kg up to a maximum of 200 mg for children) every 3 weeks for a maximum of 24 months. The cost for one adult dose is about $9162.[3]

Pembrolizumab was previously approved for treatment of unresectable or metastatic melanoma,[4] metastatic non-small cell lung cancer (NSCLC), including nonsquamous NSCLC in combination with pemetrexed and carboplatin,[5] recurrent or metastatic head and neck squamous cell carcinoma, refractory classical Hodgkin lymphoma, locally advanced or metastatic urothelial carcinoma,[6] and recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma.

1. A Copija et al. Clinical significance and prognostic relevance of microsatellite instability in sporadic colorectal cancer patients. Int J Mol Sci 2017 Jan 6 (epub).
2. S Lemery et al. First FDA approval agnostic of cancer site - when a biomarker defines the indication. N Engl J Med 2017; 377:1409.
3. Approximate WAC. WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. December 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy.
4. Pembrolizumab (Keytruda) for metastatic melanoma. Med Lett Drugs Ther 2014; 56: e114.
5. Pembrolizumab (Keytruda) for first-line treatment of metastatic NSCLC. Med Lett Drugs Ther 2017; 59:22.
6. Three more immune checkpoint inhibitors for advanced bladder cancer. Med Lett Drugs Ther 2017; 59:e202.

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