

Name: Suzana Giffin, AVP
Company/Organization: Merck & Co., Inc.
Address: 2000 Galloping Hill Rd, Kenilworth, NJ 07033
Phone: 908-740-6708
Email: suzana.giffin@merck.com
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NCCN Guidelines Panel: Pediatric Hodgkin Lymphoma

NCCN Pediatric Hodgkin Lymphoma Panel: On behalf of Merck & Co., Inc., I respectfully request the NCCN Pediatric Hodgkin Lymphoma Panel to review the enclosed information for KEYTRUDA® (pembrolizumab), in reference to classical Hodgkin lymphoma.

Specific Changes: We respectfully request the inclusion of the updated indication for KEYTRUDA for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy in the appropriate sections of the NCCN Hodgkin Lymphoma Guidelines v1.2021 (page PHL-E 2 of 3).

FDA Clearance:

- KEYTRUDA is indicated for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL).
- KEYTRUDA is indicated for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

Please refer to the KEYTRUDA (pembrolizumab) prescribing information for other FDA-approved indications.¹

Rationale: KEYTRUDA has received FDA approval for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy. This approval is supported by evidence from clinical trials in adults with additional pharmacokinetic, efficacy and safety data in pediatric patients. KEYNOTE-204 was a randomized, open-label, active-controlled trial comparing pembrolizumab 200 mg administered intravenously (IV) every 3 weeks (Q3W) (n=151) versus brentuximab vedotin (BV) 1.8 mg/kg IV Q3W (n=153) in adult patients with relapsed or refractory cHL. The main efficacy outcome measure was progression-free survival (PFS) as assessed by blinded independent central review. The PFS analysis included 81 events (54%) in the pembrolizumab arm and 88 events (58%) in the BV arm with a hazard ratio of 0.65 (95% Confidence Interval [CI], 0.48, 0.88 and p=0.0027). Kaplan-Meier estimated median PFS was 13.2 months (95% CI 10.9, 19.4) in the pembrolizumab arm, compared to 8.3 months (95% CI 5.7, 8.8) in the BV arm. Additionally, the objective response rate (ORR) was 66% (95% CI 57, 73) in the pembrolizumab arm, versus 54% (95% CI 46, 62) in the BV arm, with a complete response observed in 25% and 24% of patients, respectively; partial responses were observed in 41% and 30% of patients, respectively. Serious adverse reactions occurred in 30% of patients receiving pembrolizumab. Serious adverse reactions occurring in ≥1% of patients included pneumonitis, pneumonia, pyrexia, myocarditis, acute kidney injury, febrile neutropenia, and sepsis. Three patients (2%) died from causes other than disease progression.¹ Additional safety information for pediatric use based on KEYNOTE-051 is included in the KEYTRUDA prescribing information. In KEYNOTE-051, pediatric patients with advanced melanoma, lymphoma, or PD-L1 positive solid tumors received pembrolizumab 2 mg/kg Q3W. Out of 161 pediatric patients, pyrexia (33%), vomiting (30%), upper respiratory tract infection (29%), and headache (25%) occurred at a ≥10% higher rate in pediatric patients when compared to adults.¹

Georger B et al. published interim analysis results from KEYNOTE-051, a phase 1/2, open-label, single-arm trial investigating the safety and antitumor activity of pembrolizumab 2 mg/kg administered IV Q3W in 154 pediatric patients with multiple tumor types, including 15 patients with Hodgkin lymphoma (HL). The primary endpoints of the phase 2 part of this study included safety and tolerability, as well as the objective response rate within each tumor type according to Response Evaluation Criteria in Solid Tumors version 1.1. The ORR in the 15 HL pediatric patients was 60% (95% CI 32.3, 83.7) with 2 patients achieving a CR and 7 patients achieving a PR. Of the 154 patients treated, 69 (45%) experienced grade 3–5 adverse events, 13 (8%) experienced grade 3–5 treatment related adverse events (TRAEs), 14 (9%) experienced serious TRAEs including 2 (1%) deaths. The most frequent TRAEs of any grade included anemia (8%), fatigue (8%), decreased lymphocyte count (7%), pyrexia (7%), increased serum aspartate aminotransferase (6%), diarrhea, hypothyroidism, nausea, and maculopapular rash (8% each).²

The above results from adult patients with relapsed or refractory cHL (KEYNOTE-204) in combination with pharmacokinetic and safety data in pediatric patients with multiple tumors, including HL (KEYNOTE-051), support the antitumor activity of pembrolizumab as a treatment option in pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

The following resources are submitted to assist the committee with their review.

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Georger B, Kang HJ, Yalon-Oren M, et al. Pembrolizumab in paediatric patients with advanced melanoma or a PD-L1-positive, advanced, relapsed, or refractory solid tumour or lymphoma (KEYNOTE-051): interim analysis of an open-label, single-arm, phase 1–2 trial. *Lancet Oncol.* 2020;21:121–33.

Thank you for considering this request. Below is my contact information should you need to contact me for additional information.

Sincerely,



Suzana Giffin, AVP
Global Medical Affairs
Merck & Co., Inc.
2000 Galloping Hill Rd
Kenilworth, NJ 07033
908-740-6708
suzana.giffin@merck.com