RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Keytruda is a monoclonal antibody for the treatment of patients with advanced or unresectable melanoma, metastatic non-small cell lung cancer (NSCLC), metastatic nonsquamous non-small cell lung cancer (NSCLC), recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), refractory classical Hodgkin lymphoma (cHL), refractory mediastinal large B-cell lymphoma (PMBCL), recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma, microsatellite instability-high or mismatch repair deficient solid tumors that have progressed following prior treatments, and patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA approved test. Keytruda blocks a cellular pathway known as PD-1, human programmed death receptor-1, which restricts the body’s immune system from attacking cancer cells (1-3).

Regulatory Status
FDA-approved indication: Keytruda is a human programmed death receptor-1 (PD-1)-blocking antibody indicated for the treatment of:

1. Patients with unresectable or metastatic melanoma
2. Patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [(Tumor Proportion Score (TPS) ≥50%)] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC
3. Patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 as determined by an FDA-approved test and who have disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda
4. In combination with pemetrexed and carboplatin, as first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations
5. Patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy
6. Adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after 3 or more prior lines of therapy
7. Adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after 2 or more prior lines of therapy
8. Patients with locally advanced or metastatic urothelial carcinoma:
   a. who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combines Positive Score (CPS) ≥ 10] as determined by an FDA-approved test, or
   b. who are not eligible for any platinum containing chemotherapy regardless of PD-L1 status, or
   c. who have disease progression during or following platinum-containing chemotherapy, or
   d. within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
9. Adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan
10. Patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy
11. Patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA approved test

Limitations of Use:
Keytruda is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy (3).
The safety and effectiveness of Keytruda in pediatric patients with MSI-H central nervous system cancers have not been established (3).

This indication is approved under accelerated approval based on tumor response rate and progression-free survival. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials (3).

This indication is approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials (3).

Clinically significant immune-mediated adverse reactions may occur with Keytruda therapy including pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, and hypothyroidism. Based on the severity of the adverse reaction, Keytruda should be withheld or discontinued and corticosteroids administered. Patients should be monitored for signs and symptoms of pneumonitis, colitis, hypophysitis, thyroid disorders, and changes in liver and renal function. Keytruda may cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised of the potential hazard to a fetus (3).

Safety and effectiveness of Keytruda have been established in pediatric patients (3).

Summary
Keytruda is a monoclonal antibody indicated for the treatment of patients with advanced or unresectable melanoma, metastatic non-small cell lung cancer (NSCLC), metastatic nonsquamous non-small cell lung cancer (NSCLC), recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), refractory classical Hodgkin lymphoma (cHL) who are no longer responding to other drugs, refractory primary mediastinal large B-cell lymphoma (PMBCL), locally advanced or metastatic urothelial carcinoma, recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma, microsatellite instability-high or mismatch repair deficient solid tumors that have progressed following prior treatments, and recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. Clinically significant immune-
mediated adverse reactions may occur with Keytruda therapy including pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hyperthyroidism, and hypothyroidism. Based on the severity of the adverse reaction, Keytruda should be withheld or discontinued and corticosteroids administered. Keytruda may cause fetal harm when administered to a pregnant woman. Safety and effectiveness of Keytruda have been established in pediatric patients (1-4).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Keytruda while maintaining optimal therapeutic outcomes.

References