Generic Name: Pembrolizumab

Therapeutic Class or Brand Name: Keytruda®

Applicable Drugs (if Therapeutic Class): N/A

GPI Code: 2135305300

Preferred: N/A

Non-preferred: N/A

Date of Origin: 4/19/2017

Date Last Reviewed / Revised: 2/9/2020

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through III are met)

I. Documented diagnosis of one of the following conditions A through H AND must meet criteria listed under applicable diagnosis:

A. Unresectable or metastatic melanoma OR as adjuvant treatment after surgery for resectable disease with lymph node involvement and criterion 1 is met:

1. Keytruda® will be used as a single agent.

B. Non-small cell lung cancer (NSCLC):

1. Combination therapy with either a or "b" and criteria under each is met:

a) Metastatic nonsquamous NSCLC undergoing first-line treatment and criteria 1 and 2 are met:

(1) EGFR or ALK genomic tumor aberrations are not present.

(2) Keytruda® will be used in combination with pemetrexed and platinum chemotherapy.

b) Metastatic squamous NSCLC undergoing first-line treatment and criteria 1 is met:

(1) Keytruda® will be used in combination with carboplatin and either paclitaxel or paclitaxel protein-bound.

2. Monotherapy either "a" or "b" and the criteria under each is met:

a) NSCLC tumor expresses PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test and the following criteria 1 through 3 are met:

(1) EGFR or ALK genomic tumor aberrations are not present.

(2) Disease is stage III and patient is not a candidate for surgical resection or definitive chemoradiation OR is disease is metastatic

(3) Keytruda® will be used as a single agent

b) Metastatic NSCLC tumor expresses PD-L1 (TPS ≥1%) as determined by an FDA-approved test the following criteria 1 through 3 are met:

(a) Has disease progression on or after platinum-containing chemotherapy.
(b) Patient has received FDA approved trEGFR or ALK genomic tumor aberrations are present and patient has received FDA approved treatment aberrations.
(c) Keytruda® will be used as a single agent

C. Small Cell Lung Cancer (SCLC) and the following criteria is met:
    1. Documentation of metastatic disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.
D. Metastatic head and neck squamous cell carcinoma (HNSCC) and ONE of the following criteria are met:
    1. Metastatic, unresectable, or recurrent HNSCC
        a) Keytruda® will be used in combination with platinum and fluorouracil.
    2. Metastatic, unresectable, or recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test
        a) Keytruda® will be used as a single agent.
    3. Documentation of disease progression on or after platinum-containing chemotherapy.
        a) Keytruda® will be used as a single agent.
E. Refractory classical Hodgkin lymphoma (cHL) and criteria 1 and 2 are met:
    1. Documentation that disease has relapsed after 3 or more prior lines of therapy.
    2. Keytruda® will be used as a single agent.
F. Primary Mediastinal Large B-Cell Lymphoma (PMBCL) with refractory disease in adult and pediatric patients and criteria 1 through 3 are met:
    1. Documentation of relapse after 2 or more prior lines of therapy
    2. Documentation patient did not receive urgent cytoreductive therapy.
    3. Keytruda® will be used as a single agent.
G. Urothelial carcinoma, locally advanced or metastatic disease and one of the following criteria are met:
    1. For initial therapy when criteria a through c are met:
        a) Patient is not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA-approved test.

b) Patients is not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.
c) Keytruda® will be used as a single agent.

2. Patient has disease progression and criteria a and b are met:
   a) During or following platinum-containing chemotherapy or has had treatment within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.
   b) Keytruda® will be used as a single agent
3. Patients with Bacillus Calmette-Guerin (BCG)- unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.
   a) Keytruda® will be used as a single agent

H. Unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumors or colorectal cancer and criteria 1 and 2 are met:
   1. One of the following a or b is met:
      a) If the patient has solid tumors, documentation of disease progression following prior treatment and that patient has no satisfactory alternative treatment options.
      b) If the patient has colorectal cancer, documentation of disease progression following prior treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.
   2. Keytruda® will be used as a single agent.

I. Locally Advanced or metastatic gastric or gastroesophageal junction adenocarcinoma when one of the following criteria are met:
   1. Documentation that tumor has expression of PD-L1[Combined Positive Score (CPS) ≥ 1]
      a) Keytruda® will be used as a single agent.
   2. 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.
      a) Keytruda® will be used as a single agent.

J. Recurrent, locally advanced or metastatic squamous cell carcinoma of the esophagus when the following criteria 1 through 3 are met:
   1. Documentation the tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA-approved test.

2. Documentation of disease progression after one or more lines of systemic therapy.
3. Keytruda® will be used as a single agent.

K. Recurrent or metastatic cervical cancer and the following criteria 1 through 2 are met:
1. Documentation of disease progression on or after chemotherapy whose tumors express PD-L1[Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test.
2. Keytruda® will be used as a single agent.

L. Hepatocellular Carcinoma (HCC)and the following criteria 1 through 2 are met:
1. Documentation of previous treatment with sorafenib.
2. Keytruda® will be used as a single agent.

M. Recurrent locally advanced or metastatic Merkel Cell Carcinoma (MCC) in adults and pediatric patients and the following criteria is met:
1. Keytruda® will be used as a single agent.

N. Renal Cell Carcinoma (RCC) and the following criteria is met:
1. Keytruda® will be used as first line treatment with Inlyta® (axitinib).

O. Advanced endometrial carcinoma that is not MSI-H or dMMR and the following criteria 1 through 3 are met:
1. Documentation of disease progression following prior systemic therapy.
2. Patient is not a candidate for curative surgery or radiation
3. Keytruda® will be used in combination with Lenvima™(lenvatinib).

II. Minimum age requirement: 2 years old.

III. Prescribing physician is an oncologist or a hematologist.

EXCLUSION CRITERIA

- Prior treatment with a programmed death receptor-1 (PD-1)-blocking antibody or a programmed death-ligand 1 (PD-L1) blocking antibody (i.e. Bavencio®, Imfinzi™, Keytruda®, Opdivo®, or Tecentriq®).

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

Adult dosing

- Melanoma unresectable or metastatic
  - 200 mg every 3 weeks until disease progression or unacceptable toxicity
- Melanoma adjuvant treatment
  - 200 mg every 3 weeks up to 12 months
- NSCLC, SCLC, HNSCC, cHL, PMBCL, Urothelial carcinoma, MSI-H cancer, Gastric Cancer
  - 200 mg every 3 weeks up 24 months.

Pediatric dosing:

- cHL, PMBCL, MSI-H cancer, MCC
  - Pediatrics: 2mg/kg (up to 200 mg) every 3 weeks x 24 months.

APPROVAL LENGTH

- **Authorization:** 6 months
- **Re-Authorization:** An updated letter of medical necessity or progress notes showing that current medical necessity criteria are met and that the medication is effective. *Please note:* For all diagnoses except for melanoma as noted above, Keytruda® is only indicated to be given for up to a total of 24 months

APPENDIX

N/A

REFERENCES

1. http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf.
2. Medi-Span.

HISTORICAL TRACKING OF CHANGES MADE TO POLICY

Date	Notes/Changes
2/9/2020	1. **Added**. A.Non-small cell lung cancer (NSCLC): 1.Combination therapy with either "a" or "b" and criteria under each is met: a.Metastatic nonsquamous NSCLC undergoing first-line treatment and criteria 1 and 2 are met:1.EGFR or ALK genomic tumor aberrations are not present.2.Keytruda® will be used in combination with pemetrexed and platinum chemotherapy. b.Metastatic squamous NSCLC undergoing first-line treatment and criteria 1 is

	met:1.Keytruda® will be used in combination with carboplatin and either paclitaxel or paclitaxel protein-bound.2.Monotherapy either "a" or "b" and the criteria under each is met: a.NSCLC tumor expresses PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test and criteria 1 through 3 are met::1.EGFR or ALK genomic tumor aberrations are not present.2.Disease is stage III and patient is not a candidate for surgical resection or definitive chemoradiation OR is disease is metastatic3.Keytruda® will be used as a single agent b.Metastatic NSCLC tumor expresses PD-L1 (TPS ≥1%) as determined by an FDA-approved test and the criteria 1 through 3 are met:1.Has disease progression on or after platinum-containing chemotherapy. 2.Patient has received FDA approved trEGFR or ALK genomic tumor aberrations are present and patient has received FDA approved treatment aberrations.3.Keytruda® will be used as a single agent B.Small Cell Lung Cancer (SCLC) and the following criteria is met:1.Documentation of metastatic disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.C.Metastatic head and neck squamous cell carcinoma (HNSCC) and ONE of the following criteria are met:1.Metastatic, unresectable, or recurrent HNSCC a.Keytruda® will be used in combination with platinum and fluorouracil.2.Metastatic, unresectable, or recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test a.Keytruda® will be used as a single agent.E.Primary Mediastinal Large B-Cell Lymphoma (PMBCL) with refractory disease in adult and pediatric patients and criteria 1 through 3 are met: 1.Documentation of relapse after 2 or more prior lines of therapy 2.Documentation patient did not receive urgent cytoreductive therapy.3.Keytruda® will be used as a single agent. F.Urothelial carcinoma, locally advanced or metastatic disease and one of the following criteria are met:1.For initial therapy when criteria a through c are met:a.Patient is not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA-approved test.b.Patients is not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.c.Keytruda® will be used as a single agent.2.Patient has disease progression and criteria a and b are met:a.During or following platinum-containing chemotherapy or has had treatment within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.b.Keytruda® will be used as a single agent 3.Patients with Bacillus Calmette-Guerin (BCG)- unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.a.Keytruda® will be used as a single agent G.Recurrent, locally advanced or metastatic squamous cell carcinoma of the esophagus when the following criteria are met:1.Documentation the tumors express PD-L1 [Combined Positive Score (CPS) ≥10] as determined by an FDA-approved test.2.Documentation of disease progression after one or more lines of systemic therapy.3.Keytruda® will be used as a single agent. H.Recurrent or metastatic cervical cancer and the following criteria 1 though 2 are met:1.Documentation of disease progression on or after chemotherapy whose tumors express PD-L1[Combined Positive Score (CPS) ≥ 1] as determined by an FDA approved test. 2.Keytruda® will be used as a single agent.I.Hepatocellular Carcinoma (HCC)and the following criteria 1 through 3 are met:1.Documentation of previous treatment with sorafenib.2.Keytruda®

	will be used as a single agent.J.Recurrent locally advanced or metastatic Merkel Cell Carcinoma (MCC) in adults and pediatric patients and the following criteria is met:Keytruda® will be used as a single agent.O.Advanced endometrial carcinoma that is not MSI-H or dMMR and the following criteria 1 through 3 are met:1.Documentation of disease progression following prior systemic therapy.2.Patient is not a candidate for curative surgery or radiation3.Keytruda® will be used in combination with Lenvima™(lenvatinib) **Under Prior Authorization Criteria** 2. **Added** Keytruda® will be used as first line treatment with Inlyta® (axitinib) for Renal Cell Carcinoma **Under Prior Authorization Criteria.** 3. **Updated and Added dosing for all indications.** 4. **Removed** "https://regence.myprime.com/content/dam/prime/memberportal/forms/AuthorForms/Cambia/Program_Summaries/dru367reg.pdf" and "http://www.bcbsnc.com/assets/services/public/pdfs/medicalpolicy/pd_1_inhibitors.pdf" **under References**.
4/17/2018	1. **Added** "Locally Advanced or metastatic gastric or gastroesophageal junction adenocarcinoma and one of the following criteria are met 1. Documentation that tumor has expression of PD-L1[Combined Positive Score (CPS) ≥ 1] 2. 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. 2. **Added** "Bavencio®" under "Prior treatment" list **under Exclusion Criteria** 3. **Combined Quantity/Days Supply for** "Melanoma, NSCLC, HNSCC, Urothelial carcinoma, Gastric Cancer: 200 mg every 3 weeks x 24 days 4. **Deleted** http://blue.regence.com/trgmedpol/drugs/dru367.pdf. And **Added/Updated** https://regence.myprime.com/content/dam/prime/memberportal/forms/AuthorForms/Cambia/Program_Summaries/dru367reg.pdf
5/25/2017	1. **Changed** "I. Documented diagnosis of one of the following conditions A through E…" **to** "I. Documented diagnosis of one of the following conditions A through H…"**, and added** "D. Metastatic nonsquamous nonsmall cell lung cancer (NSCLC) and criterion 1 is met: 1. Keytruda® will be used in combination with Alimta® (pemetrexed) and carboplatin…G. Locally advanced or metastatic urothelial carcinoma and criteria 1 and 2 are met: 1. Documentation of one of the following a or b: a. Patient is not eligible for cisplatin-containing chemotherapy; b. Disease progression during or following any platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; 2. Keytruda® will be used as a single agent; H. Unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient solid tumors or colorectal cancer and criteria 1 and 2 are met: 1. One of the following a or b is met: a. If the patient has solid tumors, documentation of disease progression following prior treatment and that patient has no satisfactory alternative treatment options; b. If the patient has colorectal cancer, documentation of disease progression following prior treatment with a fluoropyrimidine, oxaliplatin, and irinotecan; 2. Keytruda® will be used as a single agent…" **under Prior Authorization Criteria**.

	2. **Changed** "Unresectable or metastatic melanoma: 2 mg/kg every 3 weeks; Metastatic non-small cell lung cancer (NSCLC) & Recurrent or metastatic head and neck squamous cell carcinoma (HNSCC): 200 mg every 3 weeks x 24 months; Refractory classical Hodgkin lymphoma (cHL): Adults: 200mg every 3 weeks x 24 months; Pediatrics: 2mg/kg (up to 200 mg) every 3 weeks x 24 months" **to** "Melanoma: 2 mg/kg every 3 weeks; NSCLC, HNSCC, & Urothelial carcinoma: 200 mg every 3 weeks x 24 months; cHL & MSI-H cancer: Adults: 200mg every 3 weeks x 24 months; Pediatrics: 2mg/kg (up to 200 mg) every 3 weeks x 24 months" **under Quantity/Days Supply Restrictions**. 3. **Changed** "…Please note: For all diagnoses except for melanoma (NSCLC, HNSCC, & cHL), Keytruda® is only indicated to be given for up to a total of 24 months" **to** "…Please note: For all diagnoses except for melanoma (NSCLC, HNSCC, cHL, Urothelial carcinoma, & MSI-H cancer), Keytruda® is only indicated to be given for up to a total of 24 months" **following Re-Authorization under Approval Length**.
5/18/2017	1. **Added** "Imfinzi™" **to** "Prior treatment…" list **under Exclusion Criteria**.