RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Opdivo is a monoclonal antibody for the treatment of patients with unresectable (cannot be removed by surgery), metastatic (advanced) melanoma, adjuvant treatment of melanoma and metastatic non-small cell lung cancer, metastatic small cell lung cancer, renal cell carcinoma, hepatocellular carcinoma, relapsed or progressed classical Hodgkin lymphoma, recurrent or metastatic squamous cell carcinoma of the head and neck, locally advanced or metastatic urothelial carcinoma, or microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer who are no longer responding to other drugs. Opdivo works by inhibiting the PD-1 protein on cell surfaces, which blocks the immune system from attacking melanoma tumors. Opdivo is intended for patients who have been previously treated with ipilimumab and, for melanoma patients whose tumors express a gene mutation called BRAF V600, after treatment with ipilimumab and a BRAF inhibitor have lost effectiveness (1).

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

1. Unresectable or metastatic melanoma
   a. BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent
   b. BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent
   c. Unresectable or metastatic melanoma, in combination with ipilimumab

2. Adjuvant Treatment of Melanoma
   a. Melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting

3. Metastatic non-small cell lung cancer with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on a FDA-approved therapy for these aberrations prior to receiving Opdivo

4. Metastatic small cell lung cancer with progression after platinum-based chemotherapy and at least one other line of therapy
5. Advanced renal cell carcinoma in patients who have received prior anti-angiogenic therapy

6. Intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with ipilimumab

7. Classical Hodgkin lymphoma that has relapsed or progressed after:
   a. Autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin, OR
   b. 3 or more lines systemic therapy that includes autologous HSCT

8. Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy

9. Locally advanced or metastatic urothelial carcinoma who:
   a. Have disease progression during or following platinum-containing chemotherapy
   b. Have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

10. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, as a single agent or in combination with ipilimumab (Yervoy)

11. Hepatocellular carcinoma that has been previously treated with sorafenib (Nexavar)

**Off-Label Uses:** (2)

1. Malignant pleural mesothelioma
2. Small cell lung cancer
3. Metastatic anal cancer
4. Merkel cell carcinoma

Clinically significant immune-mediated adverse reactions may occur with Opdivo therapy including pneumonitis, colitis, hepatitis, nephritis, renal dysfunction, hyperthyroidism, and hypothyroidism. Patients should be monitored for signs and symptoms of adverse reactions and based on the severity, Opdivo should be withheld or discontinued and corticosteroids administered. Opdivo 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. Opdivo is administered every 2 weeks until disease progression or unacceptable toxicity (1).

The safety and effectiveness of Opdivo have been established in pediatric patients age 12 years and older (1).

**Summary**
Opdivo is a monoclonal antibody indicated for the treatment of various types of cancers. Opdivo works by inhibiting the PD-1 protein on cell surfaces, which blocks the immune system from attacking melanoma tumors. Opdivo may cause fetal harm when administered to a pregnant woman (1).

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

**References**