Drug Policy:

Opdivo™ (nivolumab)

POLICY NUMBER UM ONC_1274	**SUBJECT** Opdivo™ (nivolumab)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 4**
DATES COMMITTEE REVIEWED 03/27/15, 10/14/15, 04/13/16, 06/22/16, 12/21/16, 03/08/17, 03/14/18, 03/13/19, 12/11/19, 03/11/20, 04/08/20, 06/10/20, 07/08/20, 10/14/20	**APPROVAL DATE** October 14, 2020	**EFFECTIVE DATE** October 30, 2020	**COMMITTEE APPROVAL DATES** (latest version listed last) 03/27/15, 10/14/15, 04/13/16, 06/22/16, 12/21/16, 03/08/17, 03/14/18, 03/13/19, 12/11/19, 03/11/20, 04/08/20, 06/10/20, 07/08/20, 10/14/20	
PRIMARY BUSINESS OWNER: UM **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1	**NCQA STANDARDS** UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Opdivo (nivolumab) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR

2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR
3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision AND
5. When available, generic alternatives are preferred over brand-name drugs.

B. Melanoma

1. Opdivo (nivolumab) is being used as a single agent for ONE of the following:
   a. As a single agent for adjuvant therapy of high-risk Stage III melanoma following complete resection of the primary tumor and a complete regional lymph node dissection. NOTE: In the above clinical setting nivolumab can be dosed at 240 mg every 2 weeks x 24 cycles or 480 mg every 4 weeks x 12 cycles (1year maximum duration of therapy).

      NOTE: Either Keytruda(pembrolizumab) or Opdivo(nivolumab) may be used in the above setting per NCH Policy

   b. As a single agent or in combination with Yervoy (ipilimumab) for recurrent/metastatic melanoma, as initial therapy, or as subsequent therapy(if the combination was not used previously).

      NOTE: When Opdivo (nivolumab) is used in combination with Yervoy (ipilimumab), the recommended dose of Yervoy (ipilimumab) should not exceed 1 mg/kg every 3 weeks for a maximum of 4 cycles with Opdivo (nivolumab) dosed at 3 mg/kg every 3 weeks followed by maintenance Opdivo (nivolumab) 240 mg every 2 weeks or 480 mg every 4 weeks.

C. Non-Small Cell Lung Cancer (NSCLC)

NOTE: Per NCH Policy & NCH Pathway, the combination of Opdivo (nivolumab) + Yervoy (ipilimumab), with or without chemotherapy, for first line therapy of metastatic Non-Small Cell Lung Cancer is a Non-Preferred regimen. Please refer to the NCH Pathway document for the recommended regimens in the above setting.

1. Opdivo (nivolumab) may be used as a single agent for subsequent/second line or beyond therapy:
   a. For members with recurrent/metastatic NSCLC that is negative for EGFR, ALK, ROS-1 genomic alterations, who have experienced disease progression on platinum-based chemotherapy OR
   b. For members whose cancer is positive for EGFR/ALK/ROS1 genomic alterations, and who have experienced progression on targeted therapy, and platinum-based therapy.

D. Renal Cell Carcinoma

1. The member has recurrent/metastatic/surgically unresectable stage IV disease and Opdivo (nivolumab) is being used for ONE of the following:
   a. As first line therapy in combination with Yervoy (ipilimumab), ipilimumab is dosed at 1 mg/kg x 4 cycles only, followed by single agent Opdivo (nivolumab) for intermediate or poor risk disease as defined by the IMDC (International Metastatic Renal Cell Carcinoma Database Consortium)
   b. IMDC criteria: Please see table below

CRITERIA= Assign 1 point for each	RISK CATEGORIES= RISK SCORE
Time to systemic treatment less than 1 year from diagnosis	Favorable Risk = 0
Performance Status < 80% Karnofsy Scale	Intermediate Risk = 1-2
Hemoglobin < LLN; <12 g/dL	Poor Risk= 3-6
Calcium > ULN; > 12 mg/dL	
Neutrophils > ULN	
Platelets > ULN	

OR

c. As subsequent therapy as a single agent and the member has disease progression on prior therapy with tyrosine kinase inhibitors [e.g. Nexavar (sorafenib), Sutent (sunitinib), Cabometyx (cabozantinib), or Votrient (pazopanib)].

E. Hodgkin's Lymphoma

1. The member has classical Hodgkin' Lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) AND post-transplantation +/- Adcetris (brentuximab vedotin) OR has progressed after 3 or more prior lines of systemic therapy AND
2. NOTE: Opdivo (nivolumab) given in combination with Adcetris (brentuximab vedotin) is a Non-Preferred regimen per NCH Policy.

F. Head and Neck Cancer

1. The member has recurrent/metastatic NON-nasopharyngeal, squamous cell carcinoma of the head and neck cancer and Opdivo (nivolumab) is being used as a single agent following disease progression during or after platinum-based chemotherapy.

G. Urothelial Carcinoma including Upper Tract and Urethral carcinomas

1. NOTE: Unless contraindicated or not tolerated, Keytruda (pembrolizumab) is the preferred Checkpoint Inhibitor/Immunotherapy agent over Opdivo (nivolumab) for use in recurrent/metastatic urothelial cancer.
2. The member has locally advanced or metastatic urothelial carcinoma and has disease progression during or after platinum-based chemotherapy.

H. Colorectal Cancer

1. The member has unresectable/metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer that has progressed following prior treatment with a fluoropyrimidine, oxaliplatin, and irinotecan AND
2. Opdivo (nivolumab) is being used as a single agent AND
3. Member has not had disease progression on prior therapy with another checkpoint inhibitor, e.g. Keytruda (pembrolizumab).

I. Small Cell Lung Cancer (SCLC)

1. The member has recurrent/relapsed SCLC and Opdivo (nivolumab) is being used as a single agent or in combination with Yervoy (ipilimumab) as subsequent therapy AND
2. The member had no prior progression on a PD-L1/PD-1 inhibitor.

J. Hepatocellular Carcinoma (HCC)

1. Member has recurrent/metastatic/inoperable HCC, AND
2. Opdivo (nivolumab) is being used as a single agent AND

3. Member has experienced disease progression on or after therapy with sorafenib/ lenvatinib/regorafenib/cabozantinib OR
4. Opdivo (nivolumab) is being used in combination with Yervoy (ipilimumab) followed by single agent Opdivo AND
5. Member has experienced disease progression on or after therapy with Nexavar (sorafenib)/ Lenvima (Lenvatinib)/Stivarga (regorafenib)/Cabometyx (cabozantinib) AND single agent Opdivo (nivolumab).

K. Esophageal Squamous Cell Carcinoma

1. The member has advanced, recurrent, or metastatic esophageal squamous cell carcinoma AND
2. Has experienced disease progression on or after prior fluoropyrimidine based chemotherapy (e.g. fluorouracil or capecitabine) and platinum-based chemotherapy (e.g. cisplatin, carboplatin, or oxaliplatin) AND
3. Opdivo (nivolumab) will be used as a single agent as third line therapy, regardless of PD-L1 status.

III. EXCLUSION CRITERIA

A. Disease progression while taking Opdivo (nivolumab) or other PD-1/PDL-1 therapy, except when member is being switched to combination Opdivo (nivolumab) + Yervoy (ipilimumab) for melanoma.

B. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Opdivo prescribing information. Bristol-Myers Squibb Company. Princeton, NJ 2020.

B. Clinical Pharmacology Elsevier Gold Standard. 2020.

C. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2020.

D. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2020.

E. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2020.