

# Drug Policy:

## Yervoy™ (ipilimumab)

<b>POLICY NUMBER</b> UM ONC_1201	<b>SUBJECT</b> Yervoy™ (ipilimumab)		<b>DEPT/PROGRAM</b> UM Dept	<b>PAGE 1 OF 4</b>
<b>DATES COMMITTEE REVIEWED</b> 01/04/12, 10/16/13, 10/14/15, 04/13/16, 02/08/17, 02/14/18, 02/13/19, 12/11/19, 02/12/20, 04/08/20, 06/10/20, 11/11/20, 02/10/21, 04/14/21	<b>APPROVAL DATE</b> April 14, 2021	<b>EFFECTIVE DATE</b> April 30, 2021	<b>COMMITTEE APPROVAL DATES</b> (latest version listed last) 01/04/12, 10/16/13, 10/14/15, 04/13/16, 02/08/17, 02/14/18, 02/13/19, 12/11/19, 02/12/20, 04/08/20, 06/10/20, 11/11/20, 02/10/21, 04/14/21	
<b>PRIMARY BUSINESS OWNER:</b> UM		<b>COMMITTEE/BOARD APPROVAL</b> Utilization Management Committee		
<b>URAC STANDARDS</b> HUM 1	<b>NCQA STANDARDS</b> UM 2		<b>ADDITIONAL AREAS OF IMPACT</b>	
<b>CMS REQUIREMENTS</b>	<b>STATE/FEDERAL REQUIREMENTS</b>		<b>APPLICABLE LINES OF BUSINESS</b> Commercial, Exchange, Medicaid	

### I. PURPOSE

To define and describe the accepted indications for Yervoy (ipilimumab) 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. NOTE: The PREFERRED dose of Yervoy (ipilimumab), whenever used in combination with Opdivo (nivolumab), is 1 mg/kg.**

**C. Melanoma**

NOTE: The preferred drugs, per NCH Policies & NCH Pathway, for the adjuvant therapy of completely resected stage III melanoma are Opdivo (nivolumab) OR Keytruda (pembrolizumab). Please refer to *UM ONC\_1274 Opdivo (nivolumab) policy* or *UM ONC\_1263 Keytruda (pembrolizumab) policy*. Adjuvant ipilimumab is not recommended in this setting. This recommendation is based on randomized data showing inferior outcomes with ipilimumab compared to nivolumab.

1. The member has cutaneous melanoma and Yervoy (ipilimumab) is being used as any of the following:
  - a. For unresectable or metastatic melanoma:
    - i. First line therapy in combination with Opdivo (nivolumab) OR
    - ii. Second line or subsequent therapy as a single agent or in combination with Opdivo (nivolumab) who have not received prior therapy with Yervoy (ipilimumab).

**D. Renal Cell Carcinoma**

1. The member has a relapsed/metastatic or surgically unresectable disease AND
2. Yervoy (ipilimumab) is being used in combination with Opdivo (nivolumab) for 4 cycles followed by single agent nivolumab for Intermediate or Poor risk disease (as defined by the IMDC criteria). The recommended dose of Yervoy (ipilimumab) in this setting is 1mg/kg IV every 3 weeks for a total of 4 cycles.
3. IMDC Criteria:

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% Karnofsky Scale	Intermediate Risk = 1-2
Hemoglobin < LLN; <12 g/dL	Poor Risk= 3-6
Calcium > ULN; > 12 mg/dL	
Neutrophils > ULN	
Platelets > ULN	

**E. Colorectal Cancer**

NOTE: Yervoy (ipilimumab) is not a preferred drug per NCH Policy or NCH Pathway for unresectable/metastatic/recurrent microsatellite instability-high (MSI-H) or mismatch repair

deficient [dMMR] colorectal cancer. The preferred drug in this setting is single agent pembrolizumab. Please refer to *UMC ONC\_1263 Keytruda (pembrolizumab)* policy.

#### **F. Hepatocellular Carcinoma (HCC)**

NOTE: Yervoy (ipilimumab) is not a preferred drug per NCH Policy or NCH Pathway for the initial or subsequent treatment of hepatocellular carcinoma. Please refer to the NCH Pathway document for the most current recommended therapies for hepatocellular carcinoma. This recommendation is based on the lack of Level 1 evidence (randomized trial and/or meta-analyses) showing superior outcomes with Yervoy (ipilimumab) over the preferred first and second line therapies recommended per the NCH Pathway.

#### **G. Non-Small Cell Lung Cancer**

NOTE: The combination of [Yervoy (ipilimumab + Opdivo (nivolumab)] for metastatic Non-Small Cell Lung Cancer, in the first line/subsequent line setting, is Non-Preferred per NCH Policy and NCH Pathway. Please refer to the NCH Pathway document for the most current recommended regimens/agent for metastatic Non-Small Cell Lung Cancer. This recommendation is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) showing the superiority of the above combination over the recommended regimens for first line therapy of EGFR/ALK negative metastatic NSCLC: a.) [carboplatin/cisplatin + pemetrexed + pembrolizumab] for non-squamous NSCLC and b.) [carboplatin/cisplatin + paclitaxel + pembrolizumab] for squamous NSCLC.

#### **H. Malignant Pleural Mesothelioma**

1. Yervoy (ipilimumab) may be used in combination with Opdivo (nivolumab), as first line therapy for members with Non-epithelioid subtype (by histology) of metastatic/unresectable Malignant Pleural Mesothelioma. Yervoy (ipilimumab) is dosed at 1 mg/kg every 6 weeks until disease progression or unacceptable toxicities, in the above setting.

NOTE: Yervoy (ipilimumab) + Opdivo (nivolumab) is not recommended for use in Epithelioid metastatic/unresectable Malignant Pleural Mesothelioma. This recommendation is based on the lack of a survival benefit of the above regimen compared to [platinum + pemetrexed] in the trial by Baas et al referenced below.

### **III. EXCLUSION CRITERIA**

- A. Members who experience severe or life-threatening reactions to Yervoy (ipilimumab) including any moderate immune mediated adverse events or symptomatic endocrinopathy.
- B. Disease progression while taking Yervoy (ipilimumab).
- C. Dosing exceeds single dose limit of Yervoy (ipilimumab) 3mg/kg when Yervoy is being used as a single agent.
- D. Dosing Exceeds 1 mg/kg when Yervoy (ipilimumab) is being given in combination with Opdivo (nivolumab).
- E. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

### **IV. MEDICATION MANAGEMENT**

- A. Please refer to the FDA label/package insert and/or ASCO guidelines for management of immunotherapy toxicities.

### **V. APPROVAL AUTHORITY**

- A. Review – Utilization Management Department

- B. Final Approval – Utilization Management Committee

## VI. ATTACHMENTS

- A. None

## VII. REFERENCES

- A. Yervoy prescribing information. Princeton, NJ. Bristol-Myers Squibb Company 2020.
- B. Baas et al, The Lancet, published online January 21, 2021. DOI:[https://doi.org/10.1016/S0140-6736\(21\)00147-1](https://doi.org/10.1016/S0140-6736(21)00147-1).
- C. Weber J, et al. CheckMate 238 Collaborators. Adjuvant Nivolumab versus Ipilimumab in Resected Stage III or IV Melanoma. N Engl J Med. 2017 Nov 9;377(19):1824-1835.
- D. Motzer RJ, et al. CheckMate 214 Investigators. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. N Engl J Med. 2018 Apr 5;378(14):1277-1290.
- E. Clinical Pharmacology Elsevier Gold Standard 2021.
- F. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2021.
- G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2021.
- H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2021.