Prior Authorization Review Panel

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CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 05/01/2020**
Policy Number: PA.CP.PHAR.319	**Effective Date: 01/2018** **Revision Date: 04/15/2020**
Policy Name: Ipilimumab (Yervoy)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

2Q 2020 annual review: criteria added for hepatocellular carcinoma (HCC) in combination with nivolumab; added NCCN compendium-supported indications of small bowel adenocarcinoma, uveal melanoma, non-small cell lung cancer; condensed NCCN compendium-supported indications into one subsection; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Francis G. Grillo, MD**	**Signature of Authorized Individual:**

Clinical Policy: Ipilimumab (Yervoy)

Reference Number: PA.CP.PHAR.319
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

Description
Ipilimumab (Yervoy®) is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody.

FDA Approved Indication(s)
Yervoy is indicated for:

- Treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older)
- Adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy
- Treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with nivolumab
- Treatment of adult and pediatric patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, in combination with nivolumab
- Treatment of hepatocellular cancer (HCC) in patients who have been previously treated with sorafenib, in combination with nivolumab*

** This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.*

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Pennsylvania Health and Wellness ® that Yervoy is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cutaneous Melanoma (must meet all):

1. Diagnosis of cutaneous melanoma with pathologic involvement of regional lymph nodes;
2. Prescribed by or in consultation with an oncologist;
3. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/kg;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

B. Unresectable or Metastatic Melanoma (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Unresectable or metastatic melanoma;
   b. Brain metastasis from melanoma as primary tumor;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 3 mg/kg per dose for a maximum of 4 doses over 16 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 16 weeks (maximum of 4 doses)

C. Renal Cell Carcinoma (must meet all):
1. Diagnosis of renal cell carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Prescribed in combination with Opdivo®;
   **Prior authorization may be required for Opdivo*
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg/kg IV every 3 weeks for a maximum of 4 doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 16 weeks (maximum of 4 doses)

D. Colorectal Cancer (must meet all)**:**
1. Diagnosis of MSI-H or dMMR colorectal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Disease is unresectable or metastatic;
5. Prescribed in combination with Opdivo;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 1 mg/kg IV every 3 weeks for a maximum of 4 doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 16 weeks (maximum of 4 doses)

E. Hepatocellular Cancer (HCC) (must meet all)**:**
1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. Member has been previously treated with sorafenib (Nexavar);
5. Prescribed in combination with nivolumab (Opdivo);
   **Prior authorization may be required for Opdivo*
6. Request meets one of the following (a or b):
   a. Dose does not exceed 3 mg/kg IV every 3 weeks for a maximum of 4 doses;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 16 weeks (maximum of 4 doses)

F. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a, b, c, d, or e):
   a. Small cell lung cancer prescribed in combination with Opdivo;*
   b. Malignant pleural mesothelioma prescribed in combination with Opdivo;*
   c. MSI-H or dMMR small bowel adenocarcinoma prescribed in combination with Opdivo;*
   d. Uveal melanoma prescribed either as a single agent or in combination with Opdivo;*
   e. Non-Small Cell Lung Cancer (NSCLC) in combination with Opdivo;*

   **Prior authorization may be required.*
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. For small cell lung cancer and malignant pleural mesothelioma:Failure of a platinum-containing regimen (e.g. cisplatin, carboplatin), unless clinically significant adverse effects are experienced or all are contraindicated;*

   **Prior authorization may be required for platinum-containing regimens*
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

G. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Unresectable or Metastatic Melanoma

1. Reauthorization beyond 16 weeks is not permitted. Members will need to be re-evaluated against the initial approval criteria, at a minimum of 3 months since initial treatment discontinuation.
   a. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   b. Member is responding positively to therapy.

B. Renal Cell Carcinoma, Colorectal Cancer (must meet all):

1. Reauthorization beyond 16 weeks is not permitted. Members will need to be re-evaluated against the initial approval criteria.
   a. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   b. Member is responding positively to therapy.

C. Cutaneous Melanoma (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 10 mg/kg per dose;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 12 months or up to a total duration of 3 years, whichever is less

D. Hepatocellular Carcinoma (must meet all)**:**

1. Reauthorization beyond 16 weeks is not permitted. Members will need to be re-evaluated against the initial approval criteria.
2. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
3. Member is responding positively to therapy.

E. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Member is responding positively to therapy;
3. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

F. Other diagnoses/indications (must meet 1 or 2)**:**

4. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CRC: colorectal cancer
CTLA-4: cytotoxic T-lymphocyte antigen 4
dMMR: mismatch repair deficient
FDA: Food and Drug Administration
MSI-H: microsatellite instability-high

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Opdivo® (nivolumab)	**Renal cell carcinoma** Nivolumab 3 mg/kg IV, followed by ipilimumab 1 mg/kg IV on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks **Small cell lung cancer** 1 mg/kg to 3 mg/kg IV every 2 weeks with or without ipilimumab **MSI-H/dMMR CRC** 3 mg/kg IV, followed by ipilimumab 1 mg/kg IV on the same day, every 3 weeks for 4 doses, then nivolumab 240 mg IV as a single agent every 2 weeks until disease progression or unacceptable toxicity **MSI-H/dMMR Small bowel adenocarcinoma** 3 mg/kg IV once every 3 weeks for four doses, then 3 mg/kg IV or 240 mg IV every 2 weeks with or without ipilimumab	RCC, SCLC: 480 mg/dose CRC, small bowel adenocarcinoma: 240 mg/dose
cisplatin- or carboplatin-containing regimen	**Small cell lung cancer, malignant pleural mesothelioma** Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications and Boxed Warnings

- Bristol-Myers Squibb was released from the REMS program for Yervoy in March 2015.
- Boxed warning(s): Immune-mediated adverse reactions
- Contraindiation(s): none reported

Appendix D: General Information

- NCCN lists Yervoy in combination with Opdivo with a category 2A recommendation for use in small cell lung cancer as subsequent systemic therapy for patients with:
  - Performance status 0-2 with relapse within 6 months following complete or partial response
  - Stable disease with initial treatment
  - Patients with primary progressive disease.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Cutaneous melanoma	10 mg/kg IV every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks for up to 3 years or until documented disease recurrence or unacceptable toxicity.	10 mg/kg/dose
Unresectable or metastatic melanoma or small cell lung cancer	3 mg/kg IV every 3 weeks for a total of 4 doses	3 mg/kg/dose
Advanced renal cell carcinoma	Nivolumab 3 mg/kg IV, followed by ipilimumab 1 mg/kg IV on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	1 mg/kg/dose
Colorectal cancer	Nivolumab 3 mg/kg IV, followed by ipilimumab 1 mg/kg IV on the same day, every 3 weeks for a maximum of 4 doses, then nivolumab 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	1 mg/kg/dose
Hepatocellular Carcinoma	Nivolumab 1 mg/kg IV, followed by ipilimumab 3 mg/kg IV on the same day, every 3 weeks for 4 doses, then nivolumab 240 mg every 2 weeks or 480 mg every 4 weeks	3 mg/kg/dose

V. Product Availability

Single-use vials: 50 mg/10 mL, 200 mg/40 mL

VI. References

1. Yervoy Prescribing information. Princeton, NJ: Bristol-Myers Squibb Company; March 2020. Available at: https://packageinserts.bms.com/pi/pi_yervoy.pdf. Accessed May 11, 2020.
2. Ipilimumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 17, 2020.
3. National Comprehensive Cancer Network. Malignant Pleural Mesothelioma Version 1.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mpm.pdf. Accessed February 17, 2020.
4. National Comprehensive Cancer Network. Small Bowel Adenocarcinoma Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/small_bowel.pdf. Accessed February 17, 2020.
5. National Comprehensive Cancer Network. Uveal Melanoma Version 1.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf. Accessed February 17, 2020.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-

date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9228	Injection, ipilimumab, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
Criteria added for new FDA indication: advanced renal cell carcinoma in combination with nivolumab; removed malignant pleural mesothelioma due to NCCN 2B recommendation status; added oncologist specialist requirement for all covered indications; summarized NCCN and FDA-approved uses for improved clarity; added up to a total tx duration of 3 years for cutaneous melanoma per PI; added failure of platinum-containing chemotx for SCLC per NCCN; allowed continuity of care for continued approval; clarified continued therapy language for unresectable or metastatic melanoma that reauthorization beyond 16 weeks is not permitted from reauthorization is not permitted; references reviewed and updated.	05.18	
2Q 2019 annual review: criteria added for colorectal cancer in combination with nivolumab; added coverage for malignant pleural mesothelioma; references reviewed and updated.	04.19	
2Q 2020 annual review: criteria added for hepatocellular carcinoma (HCC) in combination with nivolumab; added NCCN compendium-supported indications of small bowel adenocarcinoma, uveal melanoma, non-small cell lung cancer; condensed NCCN compendium-supported indications into one subsection; references reviewed and updated.	04/2020	