# Clinical Policy: Ipilimumab (Yervoy)

Reference Number: CP.PHAR.319
Effective Date: 03/17
Last Review Date: 03/17

Coding Implications
Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for ipilimumab for injection (Yervoy®).

**Policy/Criteria**
It is the policy of health plans affiliated with Centene Corporation® 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;
2. Meets a or b:
   a. FDA approved use (i or ii):
      i. Adjuvant treatment of cutaneous melanoma when disease is positive for regional lymph node metastasis of > 1 mm following complete resection;
   b. Off-label NCCN recommended use:
      i. Adjuvant treatment as a high-dose single agent (a or b):
         a) Stage III (any T, ≥N1, M0*) disease with clinically positive node(s) following wide excision of primary tumor and a complete therapeutic lymph node dissection;
         b) Following complete lymph node dissection and/or complete resection of nodal recurrence.

**American Joint Committee on Cancer (AJCC) TNM staging classification (7th ed., 2010) as reported in NCCN Melanoma: T (primary tumor characteristics); N (regional lymph nodes); M (metastatic disease).*

**Approval duration: 3 months**

**B. Unresectable or Metastatic Melanoma** (must meet all):
3. Diagnosis of unresectable or metastatic melanoma;
4. Prescribed dose does not exceed 3 mg/kg per dose times a maximum of 4 doses over 16 weeks.

**Approval duration: 4 doses over 16 weeks**

**C. Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy.
1. The following NCCN recommended uses for Yervoy, meeting NCCN categories 1, 2a, or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
   a. Small cell lung cancer (SCLC).

**II. Continued Approval**

**A. Cutaneous Melanoma** (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Immune-mediated adverse reactions:
      i. Endocrine (e.g., hypophysitis [inflammation of the pituitary], adrenal insufficiency/crisis, hyper/hypothyroidism):
         a) Symptomatic reactions lasting ≥ 6 weeks;
         b) Inability to reduce corticosteroid dose to 7.5 mg prednisone or equivalent per day;
      ii. Ophthalmologic: grade 2* (moderate) through grade 4* (life-threatening) reactions:
         a) Not improving to grade 1* (mild) within 2 weeks while receiving topical therapy;
         b) Requiring systemic treatment;
      iii. Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full thickness dermal ulceration, or necrotic, bullous, or hemorrhagic manifestations;
      iv. All other adverse reactions:
         a) Inability to reduce corticosteroid dose to 7.5 mg prednisone or equivalent per day;
         b) Grade 2* (moderate) reactions lasting ≥ 6 weeks;
         c) Grade 3* (severe) or Grade 4* (life-threatening) reactions, including enterocolitis, hepatotoxicity (total bilirubin > 3 times the upper limit of normal), and neuropathy such as Guillain-Barre-like syndromes.

**Grading is based on the Common Terminology Criteria for Adverse Events*

**Approval duration: 6 months**

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

**Background**

*Description/Mechanism of Action:*

CTLA-4 is a negative regulator of T-cell activity. Ipilimumab is a monoclonal antibody that binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation, including the activation and proliferation of tumor infiltrating T-effector cells. Inhibition of CTLA-4 signaling can also reduce T-regulatory cell function, which may contribute to a general increase in T cell responsiveness, including the anti-tumor immune response.

*Formulations:*
Yervoy is available as follows:
- One 50 mg vial (5 mg/mL), single-use vial
- One 200 mg vial (5 mg/mL), single-use vial

*FDA Approved Indications:*
Yervoy is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody/intravenous formulation indicated for:
- Treatment of unresectable or metastatic melanoma
- Adjuvant treatment of melanoma
  - 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.

**Appendices**
**Appendix A: Abbreviation Key**
CTLA-4: Cytotoxic T-lymphocyte antigen 4
SCLC: Small cell lung cancer

**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 |
|---|---|---|
| Policy split from CP.PHAR.182 Excellus Oncology.<br>Off-label NCCN recommended uses added. | 01/17 | 03/17 |

**References**
1. Yervoy prescribing information. Princeton, NJ: Bristol-Myers Squibb Company; October 2015. Available at http://packageinserts.bms.com/pi/pi_yervoy.pdf. Accessed January 25, 2017.
2. Ipilimumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed January 25, 2017.
3. Melanoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 25, 2017.
4. Central nervous system cancers (Version 1.2016). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 27, 2017.

**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.



**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members,** to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.