Clinical Policy: Ipilimumab (Yervoy)

Reference Number: PA.CP.PHAR.319
Effective Date: 01/18
Last Review Date: 11/17

Coding Implications
Revision Log

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

Policy/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;
2. Meets a or b:
   a. FDA approved use (i):
      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.

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**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 PA.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 PA.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 Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 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. Refer to PA.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

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.