Yervoy

Description

Yervoy (ipilimumab)

Background
Yervoy (ipilimumab) is a monoclonal antibody used to treat patients with unresectable or metastatic (late-stage) melanoma, cutaneous melanoma (stage III) with pathologic involvement of regional lymph nodes, central nervous system (CNS) metastases if active against primary tumor (melanoma), small cell lung cancer, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, and malignant pleural mesothelioma. Yervoy blocks a molecule known as CTLA-4 (cytotoxic T-lymphocyte antigen). CTLA-4 may play a role in slowing down or turning off the body’s immune system, affecting its ability to fight off cancerous cells. Yervoy may work by allowing the body’s immune system to recognize, target, and attack cells in melanoma tumors. The drug is administered intravenously (1-2).

Regulatory Status
FDA-approved indication: Yervoy is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody indicated for: (1)

1. Treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older)
2. 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
3. Treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with nivolumab
4. 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 that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, in combination with nivolumab.

**Off Label Uses:** (2)
1. Retreatment of melanoma in patients who experience disease control but who relapse or progress greater than 3 months after treatment discontinuation.
2. Central nervous system (CNS) metastases if active against primary tumor (melanoma).

Yervoy has a boxed warning of severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of ipilimumab. Permanently discontinue Yervoy and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions. Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy and evaluate clinical chemistries including liver function tests, adrenocorticotropic hormone (ACTH) level, and thyroid function tests at baseline and before each dose (1).

Safety and effectiveness of Yervoy for pediatric patients less than 12 years of age have not been established (1).

**Related policies**
Opdivo

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Yervoy may be considered medically necessary in patients 12 years of age or older for unresectable melanoma or metastatic melanoma, cutaneous melanoma, central nervous system (CNS) metastases, small cell lung cancer (SCLC), advanced renal cell carcinoma,
microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, or malignant pleural mesothelioma; and if the conditions indicated below are met.

Yervoy may be considered investigational in patients less than 12 years of age and all other indications.

## Prior-Approval Requirements

### Age

12 years of age or older

### Diagnoses

Patient must have **ONE** of the following:

1. Unresectable or metastatic melanoma

2. Cutaneous melanoma (Stage III)
   a. Used as adjuvant therapy
   b. Pathologic involvement of regional lymph nodes of more than 1 mm
   c. Patient has undergone complete resection, including total lymphadenectomy

3. Central nervous system (CNS) metastases
   a. Yervoy was active against the primary tumor (melanoma)
   b. Member has recurrent disease

4. Small cell lung cancer (SCLC)
   a. Used in combination with nivolumab (Opdivo)

5. Malignant pleural mesothelioma
   a. Used in combination with nivolumab (Opdivo)

6. Advanced renal cell carcinoma
   a. Patient is considered to have an intermediate or poor prognosis
      i. Used in combination with nivolumab (Opdivo)
7. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
   a. Disease progression following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan
   b. Diagnosis has to be confirmed by PCR-based assay genetic testing
   c. Used in combination with nivolumab (Opdivo)

AND ALL of the following:
1. Clinical chemistries, including adrenocorticotropic hormone (ACTH) level, and liver and thyroid function tests are evaluated at baseline and before each dose.
2. Agree to permanently discontinue Yervoy and initiate corticosteroid therapy for severe immune-mediated reactions.

Prior – Approval Renewal Requirements

Age
12 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Unresectable or metastatic melanoma
   a. Patient has had disease progression or relapse after stable disease of at least three months duration after their first course of Yervoy

2. Cutaneous melanoma (Stage III)
   a. NO disease progression or unacceptable toxicity

3. Central nervous system (CNS) metastases
   a. NO disease progression or unacceptable toxicity

4. Small cell lung cancer (SCLC)
   a. Used in combination with nivolumab (Opdivo)
   b. NO disease progression or unacceptable toxicity

5. Malignant pleural mesothelioma
   a. Used in combination with nivolumab (Opdivo)
   b. NO disease progression or unacceptable toxicity
6. Advanced renal cell carcinoma  
   a. Used in combination with nivolumab (Opdivo) 
   b. NO disease progression or unacceptable toxicity

7. Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer  
   a. Used in combination with nivolumab (Opdivo) 
   b. NO disease progression or unacceptable toxicity

AND ALL of the following:
1. Clinical chemistries, including adrenocorticotropic hormone (ACTH) level, and liver and thyroid function tests are evaluated before each dose.

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**

Duration 6 months

**Prior – Approval **Renewal **Limits**

Duration 12 months

**Rationale**

**Summary**
Yervoy is a monoclonal antibody used to treat patients with unresectable or metastatic (late-stage) melanoma, cutaneous melanoma (stage III), central nervous system (CNS) metastases if active against primary tumor (melanoma), small cell lung cancer, advanced renal cell carcinoma, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer, or malignant pleural mesothelioma. Yervoy has a boxed warning of severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation.
The most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Yervoy while maintaining optimal therapeutic outcomes.

References

Policy History

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<td>January 2011</td>
<td>New Policy</td>
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<tr>
<td>March 2013</td>
<td>Annual editorial and reference update</td>
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<td>Addition of age requirement of 18 years or older</td>
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<tr>
<td>September 2013</td>
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<td>December 2014</td>
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<td>Removal of REMS requirement</td>
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<td>November 2015</td>
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<td>March 2016</td>
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<td>Policy number change from 5.04.13 to 5.21.13</td>
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<td>Addition of age requirement to Renewal Criteria</td>
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<td>August 2017</td>
<td>Addition of central nervous system (CNS) metastases if active against primary tumor (melanoma), malignant pleural mesothelioma and small cell lung cancer. Addition of unresectable or metastatic in renewal section Removal of agreement to permanently discontinue Yervoy if full treatment course is not completed within 16 weeks of administration of first dose for melanoma. Age change from 18 to 12 years of age.</td>
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<td>May 2018</td>
<td>Addition of indication: Intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with ipilimumab. Addition of monitoring of adrenocorticotropic hormone (ACTH) level to initiation and renewal criteria (per boxed warning in package insert). Addition of renewal requirements to small cell lung cancer (SCLC), and malignant pleural mesothelioma of used in combination with nivolumab (Opdivo).</td>
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<td>June 2018</td>
<td>Annual review. Removal of the requirement: no disease progression or unacceptable toxicity from Unresectable or metastatic melanoma renewal section.</td>
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<td>July 2018</td>
<td>Addition of indication: microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, in combination with nivolumab and changed initiation duration from 4 months to 6 months.</td>
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**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.