



POLICY: Oncology – Yervoy® (ipilimumab injection for intravenous use – Bristol-Myers Squibb)

APPROVAL DATE: 09/25/2019

OVERVIEW

Yervoy, a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody, is indicated for the following conditions:

- 1) Unresectable or metastatic melanoma in adults and pediatric patients (≥ 12 years).
- 2) Adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of > 1 mm who have undergone complete resection, including total lymphadenectomy.
- 3) In combination with Opdivo® (nivolumab for intravenous injection) for the treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma (RCC).
- 4) In combination with Opdivo for the treatment of adult and pediatric patients ≥ 12 years of age 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.

The following are the recommended dosing for Yervoy for the FDA-approved indications:

- For unresectable or metastatic melanoma: Yervoy 3 mg/kg administered intravenously (IV) over 90 minutes every 3 weeks for a maximum of 4 doses.
- For adjuvant treatment of melanoma: Yervoy 10 mg/kg administered IV over 90 minutes every 3 weeks for 4 doses followed by 10 mg/kg every 12 weeks for up to 3 years. In the event of toxicity, doses are omitted, not delayed.
- Renal cell carcinoma: Yervoy is used in combination with Opdivo for RCC. Opdivo 3 mg/kg administered IV over 30 minutes, followed by Yervoy 1 mg/kg administered IV over 30 minutes on the same day, every 3 weeks for 4 doses. After completing 4 doses of the combination, administer Opdivo as a single agent, either 240 mg every 2 weeks or 480 mg every 4 weeks.
- Colon and rectal cancer: Yervoy 1 mg/kg administered IV over 30 minutes, immediately following Opdivo on the same day, every 3 weeks for up to 4 doses or until intolerable toxicity or disease progression.
- In general, if Yervoy is administered in combination with Opdivo, if Yervoy is withheld then Opdivo should also be withheld.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Yervoy. Approval is recommended for those who meet the **Criteria and Dosing** for the diagnosis provided. Extended approvals are allowed for the duration noted, if the patient continues to meet the criteria and dosing for the requested indication. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist).

Because of the specialized skills required for evaluation and diagnosis of patients treated with Yervoy as well as the monitoring required for AEs and long-term efficacy, initial approval requires Yervoy be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Yervoy is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Colon or Rectal Cancer, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR). Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

- A) The patient is 12 years of age or greater; AND
- B) The patient meets ONE of the following criteria (i or ii):
 - i. The patient has tried chemotherapy.
NOTE: Examples of chemotherapy are fluoropyrimidine such as 5-fluorouracil [5-FU], capecitabine; oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX [5-FU, leucovorin, and oxaliplatin] or CapeOX [capecitabine and oxaliplatin]; OR
 - ii. The patient has unresectable or metastatic disease and is not a candidate for intensive therapy, according to the prescribing physician; AND
- C) The medication will be used in combination with Opdivo (nivolumab intravenous injection); AND
- D) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve Yervoy dose of up to 1 mg/kg administered not more frequently than once every 3 weeks.

2. Melanoma [NOTE: This includes cutaneous melanoma, brain metastases due to melanoma, and uveal melanoma]. Approve if the patient meets ALL of the following (A, B, and C):

- A. The patient is 12 years of age or greater; AND
- B. The patient meets ONE of the following (i or ii):
 - i. Approve for 4 months if the patient has unresectable or metastatic melanoma; OR
 - ii. Approve for 1 year if Yervoy will be used as adjuvant treatment
NOTE: For example, in patients with cutaneous melanoma who have undergone complete resection, including total lymphadenectomy); AND
- C. The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve if the Yervoy dose meets one of the following criteria (A or B):

- A. Adjuvant treatment: Approve Yervoy dose up to 10 mg/kg administered IV once every 3 weeks or 12 weeks; OR
- B. Unresectable or Metastatic Melanoma: Approve Yervoy dose of up to 3 mg/kg not more frequently than once every 3 weeks.

3. Renal Cell Carcinoma. Approve for 4 months if the patient meets the following criteria (A, B, and C):

- A) The patient has advanced (e.g., relapsed, Stage IV, metastatic) disease; AND
- B) The medication will be used in combination with Opdivo (nivolumab for intravenous injection); AND
- C) The medication is prescribed by or in consultation with an oncologist.

Dosing in Renal Cell Carcinoma. Approve Yervoy dose of up to 1 mg/kg administered IV not more frequently than once every 3 weeks.

Other Uses with Supportive Evidence

- 4. Small Cell Lung Cancer.** Approve for 1 year if the patient meets BOTH of the following (A, B, and C):
- A) The patient has tried at least one other systemic chemotherapy regimen within the past 6 months.
NOTE: Examples of chemotherapy are cisplatin and etoposide, carboplatin and etoposide; AND
 - B) The medication is used in combination with Opdivo (nivolumab for intravenous injection); AND
 - C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve Yervoy dose of up to 3 mg/kg administered IV not more frequently than once every 3 weeks.

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- 5. Malignant Pleural Mesothelioma.** Approve for 1 year if the patient meets the following (A, B, and C):
- A) The patient has tried at least one other chemotherapy regimen.
NOTE: Examples of chemotherapy are cisplatin, gemcitabine, Alimta (pemetrexed for injection), carboplatin, bevacizumab; AND
 - B) The medication will be used in combination with Opdivo (nivolumab for intravenous injection); AND
 - C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve Yervoy dose of up to 3 mg/kg administered IV not more frequently than once every 3 weeks.

Limited dosing is available regarding use of Yervoy for this indication; however, doses up to 3 mg/kg administered once every 3 weeks are recommended in the product labeling for the majority of approved uses.¹

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- 6. Small Bowel Adenocarcinoma, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR).** Approve for 1 year if the patient meets the following (A, B, and C):
- A) The patient has advanced or metastatic disease; AND
 - B) The medication will be used in combination with Opdivo (nivolumab for intravenous injection); AND
 - C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve Yervoy dose of up to 3 mg/kg administered IV not more frequently than once every 3 weeks.

Limited dosing is available regarding use of Yervoy for this indication; however, doses up to 3 mg/kg administered once every 3 weeks are recommended in the product labeling for the majority of approved uses.¹

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Yervoy has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Yervoy® injection for intravenous use [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; May 2019.

2. The NCCN Drugs & Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 20, 2019. Search term: ipilimumab.
3. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 7.2019 – August 30, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 23, 2019.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New Policy	--	01/30/2019
Early annual revision	<p>For all indication moved examples to Note. Changed from specifying “Yervoy” to “The medication”. In Dosing, added “not more frequently than” once every 3 weeks for duration.</p> <ul style="list-style-type: none"> • Malignant Pleural Mesothelioma: Added new condition of approval. Previously, this condition was listed under Other Cancer-Related Indications and was eligible for review on a case by case basis. • Small Bowel Adenocarcinoma, Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR): Added new condition of approval based on compendium/guideline recommendations. • Other Cancer-Related Indicators: Deleted condition in-line with other policies. 	09/25/2019