MEDICAL MUTUAL®

Drug Policy

Policy:	**201813**	**Initial Effective Date: 6/17/2018**
Code(s):	**HCPCS J9228**	**Annual Review Date:**
SUBJECT:	**Yervoy ® (ipilimumab)**	**Last Revised Date: 07/19/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

Yervoy is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody approved by the FDA 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; and 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. 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 STATEMENT

This policy involves the use of Yervoy, Prior authorization is recommended for medical benefit coverage of Yervoy. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. **Waste Management** applies for all covered conditions. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

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. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

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RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Yervoy is recommended in those who meet the following criteria:

1. **Melanoma, unresectable or metastatic:** Approve in patients who meet the following criteria (A, B, C, and D):
   A. Patient must be at least 12 years and older; AND
   B. Yervoy is prescribed by an oncologist, hematologist, or provider who specializes in Melanoma treatment; AND
   C. Patient has unresectable or metastatic melanoma; AND
   D. Patient meets one of the following criteria (i, ii, or iii):
      i. Yervoy will be used in combination with nivolumab as first-line therapy; OR
      ii. Yervoy will be used as second-line or subsequent therapy after disease progression or maximum clinical benefit from BRAF targeted therapy if anti-PD-1 therapy (either alone or in combination with nivolumab) not previously used; OR
      iii. Yervoy will be used as second-line or subsequent therapy after disease progression or maximum clinical benefit from BRAF targeted therapy if prior anti-PD-1 therapy resulted in disease control (complete response, partial response, or stable disease) and no residual toxicity, and disease progression/relapse occurred >3 months after treatment discontinuation.

Dosing in Melanoma, unresectable or metastatic: *Dosing must meet the following:* IV: 3 mg/kg every 3 weeks for a maximum of 4 doses; doses may be delayed due to toxicity, but all doses must be administered within 16 weeks of the initial dose.

Initial Approval/ Extended Approval.
A) *Initial Approval:16 weeks*
B) *Extended Approval: not recommended*

Duration of Therapy in Melanoma, unresectable or metastatic: maximum of 4 doses or until unacceptable toxicity

Labs/Diagnostics. Evaluate liver function tests before each dose of Yervoy (ipilimumab)-Withhold for moderate and permanently discontinue for severe or life-threatening transaminase or total bilirubin elevation; Monitor clinical chemistries, ACTH level, and thyroid function tests prior to each dose; Monitor for changes in renal function. Withhold for moderate or severe and permanently discontinue for life-threatening serum creatinine elevation.

2. **Melanoma, adjuvant treatment.** Approve in patients who meet the following criteria (A, B, C, D, and E):
   A. Patient is 18 years of age or older; AND
   B. Yervoy is prescribed by an oncologist, hematologist, or provider who specializes in Melanoma treatment; AND
   C. Yervoy is being used as adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm; AND
   D. Patient has undergone complete resection, including total lymphadenectomy; AND
   E. Patient meets one of the following criteria (i, ii, or iii):
      i. Patient has stage IIIA, B/C sentinel lymph node positive metastasis >1 mm following active nodal basin surveillance or complete lymph node dissection (CLND); OR

ii. Patient has stage III disease with clinically positive node(s) following wide excision of primary tumor and a complete therapeutic lymph node dissection; OR
iii. Yervoy will be used following CLND and/or complete resection of nodal recurrence.

Dosing in Melanoma, adjuvant treatment. *Dosing must meet the following:* IV: 10 mg/kg every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks for up to 3 years unless disease progression or unacceptable toxicity occur; if toxicity occurs, doses are omitted (not delayed).

Initial Approval/ Extended Approval.
A) *Initial Approval:6 months*
B) *Extended Approval: 6 months if patient has shown a response to treatment and shows no signs of disease progression.*

Duration of Therapy in Melanoma, adjuvant treatment: 3 years unless disease progression or unacceptable toxicity occurs

Labs/Diagnostics. Evaluate liver function tests before each dose of Yervoy (ipilimumab)-Withhold for moderate and permanently discontinue for severe or life-threatening transaminase or total bilirubin elevation; Monitor clinical chemistries, ACTH level, and thyroid function tests prior to each dose; Monitor for changes in renal function. Withhold for moderate or severe and permanently discontinue for life-threatening serum creatinine elevation.

3. Renal cell carcinoma, advanced: Approve in patients who meet the following criteria (A, B, C, D, and E):
A. Patient is 18 years of age or older; AND
B. Yervoy is prescribed by an oncologist, hematologist, or provider who specializes in Renal cell carcinoma treatment; AND
C. Patient has been diagnosed with relapsed or surgically unresectable stage IV Renal Cell Carcinoma; AND
D. Yervoy will be given in combination with Opdivo (nivolumab); AND
E. Patient meets one of the following criteria (i or ii):
i. Yervoy will be used as preferred first-line therapy for predominant clear cell histology; OR
ii. Yervoy will be used as subsequent therapy for predominant clear cell histology.

Dosing in Renal cell cancer, advanced, combination therapy: *Dosing must meet the following:* IV: 1 mg/kg once every 3 weeks (in combination with nivolumab) for 4 doses, followed by nivolumab monotherapy (refer to nivolumab monograph for nivolumab dosing information) until disease progression or unacceptable toxicity. **Note:** If ipilimumab therapy is withheld, nivolumab should also be withheld.

Initial Approval/ Extended Approval.
A) *Initial Approval:16 weeks*
B) *Extended Approval: not recommended.*

Duration of Therapy in Renal cell cancer, advanced, combination therapy: maximum of 4 doses or until unacceptable toxicity

Labs/Diagnostics. Evaluate liver function tests before each dose of Yervoy (ipilimumab)-Withhold for moderate and permanently discontinue for severe or life-threatening transaminase or total bilirubin elevation; Monitor clinical chemistries, ACTH level, and thyroid function tests prior to each dose; Monitor for changes in renal function. Withhold for moderate or severe and permanently discontinue for life-threatening serum creatinine elevation.

4. **Colorectal Cancer, metastatic :** Approve in patients who meet the following criteria (A, B, C, D, and E):
   A. Patient is 12 years of age or older; AND
   B. Yervoy is prescribed by an oncologist or provider who specializes in Colorectal treatment; AND
   C. Patient has been diagnosed with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectalcancer; AND
   D. Cancer has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan; AND
   E. Yervoy will be given in combination with Opdivo (nivolumab).

Dosing in Colorectal Cancer, metastatic: *Dosing must meet the following:* IV: Nivolumab 3 mg/kg followed by Yervoy 1 mg/kg on the same day every 3 weeks for 4 doses, then nivolumab 240 mg every 2 weeks

Initial Approval/ Extended Approval.
A) *Initial Approval:16 weeks*
B) *Extended Approval: not recommended.*

Duration of Therapy in Colorectal Cancer, metastatic: maximum of 4 doses or until unacceptable toxicity

Labs/Diagnostics. Evaluate liver function tests before each dose of Yervoy (ipilimumab)-Withhold for moderate and permanently discontinue for severe or life-threatening transaminase or total bilirubin elevation; Monitor clinical chemistries, ACTH level, and thyroid function tests prior to each dose; Monitor for changes in renal function. Withhold for moderate or severe and permanently discontinue for life-threatening serum creatinine elevation.

Other Uses With Supportive Evidence

5. Patient has been Started on Yervoy. Approve if the patient meets the conditions for coverage required for **Dosing**, **Extended Approval**, **Duration of Therapy**, and **Labs/Diagnostics** for an approved use in this *Yervoy Utilization Review* policy.

6. **Other Cancer-Related Indications.** Forward to the Medical Director for review on a case-by-case basis. An example of other indications supported in *NCCN Compendium* with a category 1, 2A, and 2B recommendation includes: Small Cell Carcinoma; Malignant Pleural Mesothelioma; Uveal Melanoma; CNS Metastases in patients with Melanoma.

Waste Management for All Indications.
Injection: 50 mg/10 mL (5 mg/mL) and 200 mg/40 mL (5 mg/mL) in a single-use vial.

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.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS Codes J9228

REFERENCES

- Yervoy [Prescribing Information] Princeton, NJ: Bristol-Myers Squibb. July 2018.
- The NCCN Melanoma Clinical Practice Guidelines in Oncology (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed May 10, 2018.
- The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (Version 4.2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed May 10, 2018.
- The NCCN Drugs & Biologics Compendium. © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 16,, 2018. Search term: Yervoy.
- Yervoy Monograph. Lexicomp® Online, Hudson, Ohio, Lexi-Comp., Inc. Last revised 07/10/2018. Accessed on July 16, 2018.

Edits and Denials:

Prior approval: Prior approval is required for Yervoy **(HCPCS Codes J9228)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Codes** J9228 will pend with **Remark Code M3M or M4M** and will be adjudicated in accordance with the Corporate Medical Policy.
Liability: A participating provider will be required to write off charges denied as not medically necessary.

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HCPCS Code(s):	
J9228	Injection, ipilimumab, 1 mg