Yervoy (ipilimumab)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Yervoy (ipilimumab)

APPROVAL CRITERIA

Requests for Yervoy (ipilimumab) may be approved the following criteria are met:

I. Individual is using for the treatment of Bone cancer, including osteosarcoma, Ewing Sarcoma, chondrosarcoma, and Chordoma; **AND**
   A. Individual is using in combination with nivolumab (Opdivo) for unresectable or metastatic disease; **AND**
   B. Individual has failed and progression on prior treatment; **AND**
   C. Individual has no satisfactory alternative treatment options for tissue tumor mutation burden-high (TMB-H) tumors with 10 or more mutations per megabase;

OR

II. Individual is using for the treatment of Colorectal Cancer, including advanced Appendiceal Adenocarcinoma; **AND**
   A. Individual meets one of the following criteria:
      1. Primary treatment used in combination with nivolumab (Opdivo) for unresectable metachronous metastases (defective mismatch repair/high microsatellite instability [dMMR/MSIH] only) and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months (NCCN 2A); **OR**
      2. Yervoy (ipilimumab) is used in combination with nivolumab (Opdivo) as subsequent therapy for unresectable advanced or metastatic colorectal cancer with defective mismatch repair (dMMR) or high microsatellite instability (MSIH) mutations that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, or irinotecan- based chemotherapy (Label, NCCN 2A);

   AND
   B. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; **AND**
   C. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

III. Individual has a diagnosis of unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC) (Label); **AND**
   A. Individual is using in combination with nivolumab (Opdivo); **AND**
   B. Individual is using as first-line treatment; **AND**

C. Individual has a current ECOG performance status of 0-1; **AND**
D. Individual has not received prior treatment with anti-PD-1, anti-PD-L1, any antibody or drug specifically targeting T-cell co-stimulation, or checkpoint pathways; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

IV. Individual has a diagnosis of advanced Hepatocellular Carcinoma and the following criteria are met (Label, NCCN 2A):
A. Individual is using in combination with nivolumab (Opdivo); **AND**
B. Individual is using as subsequent therapy; **AND**
C. Individual has a current ECOG performance status of 0-2; **AND**
D. Individual has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

V. Individual has a diagnosis of relapsed/refractory advanced classic Kaposi Sarcoma and the following criteria are met (NCCN 2A):
A. Individual is using in combination with nivolumab (Opdivo); **AND**
B. Individual is using as subsequent systemic therapy;

OR

VI. Individual has a diagnosis of unresectable Malignant Pleural or Peritoneal Mesothelioma and using as first line therapy (Label, NCCN 2A); **AND**
A. Individual is using in combination with nivolumab (Opdivo); **AND**
B. Individual has a ECOG performance status of 0-2; **AND**
C. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
D. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

VII. Individual has a diagnosis of Malignant Pleural or Peritoneal Mesothelioma (NCCN 2A); **AND**
A. Individual is using in combination with nivolumab (Opdivo) for subsequent therapy; **AND**
B. Individual has an ECOG performance status of 0-2; **AND**
C. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

VIII. Individual has a diagnosis of metastatic Melanoma with brain metastases (NCCN 2A); **AND**
A. Individual has a primary diagnosis of melanoma; **AND**

B. Individual has asymptomatic brain metastases (Long 2017, 2018, Tawbi 2017); **AND**
C. Individual is using in combination with nivolumab; **AND**
D. Individual has not received treatment with another anti-PD-1, anti-PD-L1 agent, or anti-CTLA-4 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

IX. Individual is using for the treatment of unresectable or metastatic Melanoma (Cutaneous and Uveal); **AND**
A. An individual has an ECOG performance status of 0-2; **AND**
B. Yervoy (ipilimumab) is used in combination with nivolumab (Opdivo) (Label);
OR
C. Yervoy (ipilimumab) is used as a single agent for one of the following:
1. First line therapy as a single course of 4 treatments; **OR**
2. Second-line or subsequent lines of therapy as a single course of 4 treatments (NCCN 2A); **OR**
3. Retreatment, consisting of a 4-dose limit, for an individual who had no significant systemic toxicity during prior Yervoy therapy and whose disease progressed after being stable for greater than 3 months following completion of a prior course of Yervoy, and for whom no intervening therapy has been administered (NCCN 2A);

OR

X. Individual is using as a single agent for the adjuvant treatment of Melanoma (Cutaneous and Uveal) in individual with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including lymphadenectomy.

OR

XI. Individual is using for first line treatment of recurrent, advanced, or metastatic Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1, 2A); **AND**
A. Individual is using in combination with nivolumab; **AND**
B. Individual does not have presence of actionable molecular markers*; **AND**
C. Individual has PD-L1 expression positive (≥ 1%) tumor; **AND**
D. Current ECOG performance status of 0-2; **AND**
E. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
F. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XII. Individual is using for continuation treatment of recurrent, advanced or metastatic Non-Small Cell Lung Cancer (NSCLC) (NCCN 1, 2A); **AND**
A. Individual is using In combination with nivolumab (Opdivo); **AND**
B. Individual achieved a response or has stable disease following first line therapy of nivolumab + ipilimumab +/- chemotherapy given; **AND**
C. Individual does not have presence of actionable molecular markers*; **AND**

D. Current ECOG performance status of 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XIII. Individual is using for first line treatment of recurrent, advanced, or metastatic Non-Small Cell Lung Cancer (NSCLC) (Label, NCCN 1, 2A); **AND**
A. Individual is using in combination with nivolumab *and* 2 (two) cycles of platinum-doublet chemotherapy (i.e., platinum-based chemotherapy with pemetrexed, or carboplatin with paclitaxel);

AND

B. Individual does not have presence of actionable molecular markers*; **AND**
C. Current ECOG performance status of 0-2; **AND**
D. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XIV. Individual is using for the treatment intermediate- or poor-risk, advanced Renal Cell Carcinoma (RCC); **AND**
A. Yervoy (ipilimumab) is used in combination with nivolumab (Opdivo) for four cycles followed by single agent nivolumab (Opdivo), as first-line therapy for previously untreated RCC; **OR**
B. Yervoy (ipilimumab) is used in subsequent therapy with nivolumab (Opdivo) for four cycles followed by single agent nivolumab (Opdivo),if no checkpoint blockade (PD-1, PD-L1, or CTLA-4) antibody treatment has been previously administered (NCCN 2A);

AND

C. Histologic confirmation of RCC with clear-cell component; **AND**
D. Individual has an ECOG performance status 0-2; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XV. Individual has a diagnosis of Small Bowel Adenocarcinoma (SBA) (NCCN 2A); **AND**
A. Individual has advanced or metastatic disease (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] only); **AND**
B. Individual is using in combination with nivolumab as subsequent therapy; **AND**
C. Current ECOG performance status of 0-2; **AND**
D. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant;

OR

XVI. Individual has a diagnosis of Small Bowel Adenocarcinoma (SBA)—Advanced ampullary cancer and meets the following criteria (NCCN 2A);
   A. Individual has advanced or metastatic disease (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] only); **AND**
   B. Individual is using as initial or subsequent therapy in combination with nivolumab; **AND**
   C. Current ECOG performance status of 0-2; **AND**
   D. Has not received treatment with another anti-PD-1 or anti-PD-L1 agent; **AND**
   E. Individual is not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant.

***Note:** Actionable molecular markers include EGFR, ALK, ROS1, BRAF, NTRK, MET, RET, and ERBB2 (HER2) mutations. The NCCN panel recommends testing prior to initiating therapy to help guide appropriate treatment. If there is insufficient tissue to allow testing for all of these markers, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes (NCCN 1, 2A).

Requests of Yervoy (ipilimumab) may not be approved for the following:

I. Individual has an autoimmune disease which requires treatment with immunosuppressant drugs; **OR**
II. When the above criteria are not met and for all other indications.

Key References:

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3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden. N Engl J Med. 2018; 378(22):2093-2104.
5. Hellmann MD, Paz-Ares L, Bernabe Caro R, et al. Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. *N Eng J Med.* 2019;381:2020-31.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
7. Long GV, Atkinson V, Lo S, et al. Combination nivolumab and ipilimumab or nivolumab alone in melanoma brain metastases: a multicenter randomized phase 2 study. *Lancet Oncol.* 2018;19:672-81.
8. Long GV, Atkinson V, Menzies AM, et al. A randomized phase II study of nivolumab or nivolumab combined with ipilimumab in patients with melanoma brain metastases: the Anti-PD1 Brain Collaboration. *J Clin Oncol.* 2017;35:9508[abstract]. Available at: https://ascopubs.org/doi/abs/10.1200/JCO.2017.35.15_suppl.9508.

9. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed January 17, 2023.
    a. Ampullary Adenocarcinoma. V2.2022. Revised December 6, 2022.
    b. Bone Cancer. V2.2023. Revised September 28, 2022.
    c. Central Nervous System Cancers. V1.2023. Revised September 29, 2022.
    d. Colon Cancer. V2.2022. Revised October 27, 2022.
    e. Esophageal and Esophagogastric Junction Cancers. V5.2022. Revised December 5, 2022.
    f. Hepatobiliary Cancers. V5.2022. Revised January 13, 2023.
    g. Kaposi Sarcoma. V1.2023. Revised December 20, 2022.
    h. Kidney Cancer. V4.2023. Revised January 18, 2023.
    i. Malignant Peritoneal Mesothelioma. V1.2023. Revised December 15, 2022
    j. Malignant Pleural Mesothelioma. V1.2022. Revised December 22, 2021.
    k. Cutaneous Melanoma. V1.2023. Revised December 22, 2022.
    l. Neuroendocrine and Adrenal Tumors. V2. 2022. Revised December 21, 2022.
    m. Non-Small Cell Lung Cancer. V1.2023. Revised December 22, 2022.
    n. Rectal Cancer. V3.2022. Revised October 27, 2022.
    o. Small Bowel Adenocarcinoma V1.2023. Revised January 9, 2023.
    p. Uveal Melanoma. V2.2022. Revised December 22, 2022.
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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.