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| **Clinical Policy Title:** | nivolumab |
| **Policy Number:** | RxA.431 |
| **Drug(s) Applied:** | Opdivo® |
| **Original Policy Date:** | 03/06/2020 |
| **Last Review Date:** | 09/14/2021 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Nivolumab (Opdivo®) is a programmed death receptor-1 (PD-1) blocking antibody.

Opdivo® is indicated for the treatment of:

Melanoma

- Patients with unresectable or metastatic melanoma, in combination with ipilimumab.
- Patients with melanoma with lymph node involvement or metastatic disease who have undergone complete resection, in the adjuvant setting.

Non-Small Cell Lung Cancer (NSCLC)

- Adult patients with metastatic non-small cell lung cancer (NSCLC) expressing PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, as first-line treatment in combination with ipilimumab.
- Adult patients with metastatic or recurrent non-small cell lung cancer (NSCLC) with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy.
- Patients with metastatic non-small cell lung cancer (NSCLC) and progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo®.

Renal Cell Carcinoma (RCC)

- Patients with advanced renal cell carcinoma (RCC) who have received prior antiangiogenic therapy.
- Patients with advanced renal cell carcinoma, as a first-line treatment in combination with cabozantinib.
- Patients with intermediate or poor risk advanced renal cell carcinoma, as a first-line treatment in combination with ipilimumab.

Classical Hodgkin Lymphoma (cHL)

- Adult patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after:
  - autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or;
  - 3 or more lines of systemic therapy that includes autologous HSCT.

Squamous Cell Carcinoma of the Head and Neck (SCCHN)

- Patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after a platinum-based therapy.

Urothelial Carcinoma

- Patients with locally advanced or metastatic urothelial carcinoma (UC) who[a]
  - have disease progression during or following platinum-containing chemotherapy, or

- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Colorectal Cancer

- Adult and pediatric (12 years and older) patients 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, as a single agent or in combination with ipilimumab.

Hepatocellular Carcinoma (HCC)

- Patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib, as a single agent or in combination with ipilimumab.

Esophageal Cancer

- Patients with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, who have received neoadjuvant chemoradiotherapy (CRT).
- Patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

Malignant Pleural Mesothelioma

- Adult patients with unresectable malignant pleural mesothelioma, as first-line treatment in combination with ipilimumab.

Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma

- Patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma in combination with fluoropyrimidine- and platinum-containing chemotherapy.

- [a]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.

**Dosing Information**

| Drug Name | Indication | Dosing Regimen*[$] | Maximum Dose |
|---|---|---|---|
| nivolumab (Opdivo®) + ipilimumab<br>nivolumab (Opdivo®) | Melanoma - unresectable or metastatic, HCC | Monotherapy: 240 mg intravenous every 2 weeks or 480 mg intravenous every 4 weeks<br><br>With ipilimumab: 1 mg/kg intravenous, followed by ipilimumab 3 mg/kg intravenous on the same day, every 3 weeks for 4 doses, then nivolumab 240 mg intravenous every 2 weeks or 480 mg intravenous every 4 weeks | 480 mg/dose<br><br>with ipilimumab: 1 mg/kg/dose |
| | Metastatic NSCLC expressing PD-L1 | 3 mg/kg every 2 weeks with ipilimumab 1 mg/kg every 6 weeks for up to 2 years | with ipilimumab: 3 mg/kg/dose |
| | Metastatic or recurrent NSCLC, Malignant Pleural Mesothelioma | 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks and histology-based platinum doublet chemotherapy | 360 mg/dose |

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|---|---|---|---|
| | Melanoma - adjuvant treatment<br>NSCLC, RCC - advanced with previous anti-angiogenic therapy<br>CHL, SCCHN, UC, ESCC | 240 mg intravenous every 2 weeks or 480 mg intravenous every 4 weeks | 480 mg/dose |
| nivolumab (Opdivo®) | MSI-H or dMMR, CRC | Monotherapy:<br>Adult and pediatric patients age 12 years and older and weighing 40 kg or more: 240 mg every 2 weeks or 480 mg every 4 weeks.<br><br>Pediatric patients age 12 years and older and weighing less than 40 kg: 3 mg/kg every 2 weeks<br><br>With ipilimumab: 3 mg/kg intravenous, followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, followed by nivolumab monotherapy. | monotherapy:<br>480 mg/dose<br><br>with ipilimumab: 3 mg/kg/dose |
| | RCC- advanced previously untreated | Monotherapy: 240 mg IV every 2 weeks or 480 mg every 4 weeks<br><br>With ipilimumab: 3 mg/kg intravenous, followed by ipilimumab 1 mg/kg intravenous on the same day every 3 weeks for 4 doses, then nivolumab 240 mg intravenous every 2 weeks or 480 mg intravenous every 4 weeks | 480 mg/dose<br><br>with ipilimumab: 3 mg/kg/dose |
| | GC, GEJC, EAC | 240 mg every 2 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 2 weeks.<br>360 mg every 3 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 3 weeks. | 360 mg/dose |

## Dosage Forms

- Single-dose vials: 40 mg/4 mL, 100 mg/10 mL, 240 mg/24 mL.

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

**I. Initial Approval Criteria**

**A. Melanoma** (must meet all)**:**

1. Diagnosis of melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a, b, or c):
   a. Monotherapy: Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. In combination with Yervoy®: Dose does not exceed 1 mg/kg every 3 weeks for 4 doses, followed by 240 mg every 2 weeks or 480 mg every 4 weeks;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**B. Non-Small Cell Lung Cancer** (must meet all)**:**

1. Diagnosis of metastatic NSCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for one of the following (a or b):
   a. First-line treatment of patient with metastatic NSCLC with tumors express PD-L1(≥1%), or patient with metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations
   b. Disease has progressed on or after a platinum-containing regimen (e.g., cisplatin, carboplatin);
5. Request meets one of the following (a, b, c or d):
   a. Monotherapy: Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. Metastatic NSCLC expressing PD-L1: 3 mg/kg every 2 weeks with ipilimumab 1 mg/kg every 6 weeks,
   c. Metastatic or recurrent NSCLC: 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks and histology-based platinum doublet chemotherapy every 3 weeks;
   d. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**C. Renal Cell Carcinoma** (must meet all)**:**

1. Diagnosis of RCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for one of the following (a, b, or c):
   a. In combination with ipilimumab, for the first-line treatment of patients with intermediate or poor risk advanced RCC.
   b. In combination with cabozantinib, for the first-line treatment of patients with advanced RCC.
   c. As a single agent, for the treatment of patients with advanced renal cell carcinoma (RCC) who have

received prior anti-angiogenic therapy.

5. Request meets one of the following (a, b, or c):
   a. Monotherapy: Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. In combination with Yervoy®: Dose does not exceed 3 mg/kg every 3 weeks for 4 doses, followed by 240 mg every 2 weeks or 480 mg every 4 weeks;
   c. In combination with cabozantinib: 240 mg every 2 weeks or 480 mg every 4 weeks;
   d. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**D. Classical Hodgkin Lymphoma** (must meet all):
1. Diagnosis of cHL;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has relapsed or progressed after (a or b):
   a. Autologous hematopoietic stem cell transplantation and brentuximab vedotin, or;
   b. 3 or more lines of systemic therapy that includes autologous HSCT;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**E. Squamous Cell Carcinoma of the Head and Neck** (must meet all):
1. Diagnosis of SCCHN;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has progressed on or after a platinum-containing regimen (e.g., cisplatin, carboplatin);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**F. Urothelial Carcinoma** (must meet all):
1. Diagnosis of UC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of a platinum-containing regimen (e.g., cisplatin, carboplatin), unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**G. Colorectal Cancer** (must meet all):
1. Diagnosis of unresectable or metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Tumor has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan;
4. Tumor is characterized as MSI-H or dMMR;
5. Age ≥ 12 years;
6. Dose does not exceed for one of the following (a, b, or c):
   a. Monotherapy: For adult and pediatric patient weighing 40 kg or more 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. In combination with Yervoy: 3 mg/kg every 3 weeks for 4 doses, then followed by monotherapy;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**H. Hepatocellular Carcinoma** (must meet all):
1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has had disease progression following treatment with Nexavar® (sorafenib);
   *Prior authorization may be required for Nexavar.
5. Request meets one of the following (a, b or c):
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. In combination with Yervoy®: Dose does not exceed 1 mg/kg every 3 weeks for 4 doses, followed by 240 mg every 2 weeks or 480 mg every 4 weeks;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**I. Esophageal Squamous Cell Carcinoma** (must meet all):
1. Diagnosis of unresectable advanced, recurrent or metastatic ESCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of at least one fluoropyrimidine- and platinum-based chemotherapy unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg every 2 weeks or 480 mg every 4 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration:**
**Commercial:** 6 months
**Medicaid:** 6 months

**J. Malignant Pleural Mesothelioma** (must meet all):
1. Request is for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma, in combination with ipilimumab;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 360 mg every 3 weeks with ipilimumab 1mg/kg every 6 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**K. Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma** (must meet all):
1. Diagnosis of advanced or metastatic GC, GJC and EAC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for use in combination with fluoropyrimidine- and platinum-containing chemotherapy;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 240 mg every 2 weeks or 360 mg every 3 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 2 and 3 weeks respectively;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**L. Off-label NCCN Compendium Recommended Indications** (must meet all):
1. Diagnosis of one of the following (a, b, c, d, e, f, g, or h):
   a. Anal carcinoma;
   b. Merkel cell carcinoma;
   c. Gestational trophoblastic neoplasia;
   d. Brain metastases;
   e. Small Bowel Adenocarcinoma;
   f. Extra-nodal NK/T-Cell Lymphoma, nasal type;
   g. Uterine Neoplasms - Endometrial Carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**II. Continued Therapy Approval**

**A. All Indications in Section I** (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Opdivo® for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 480 mg every 4 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Approval Duration**
**Commercial:** 12 months
**Medicaid:** 12 months

**III. Appendices**

**APPENDIX A: Abbreviation/Acronym Key**
ALK: anaplastic lymphoma kinase
CHL: classic Hodgkin lymphoma
CRC: colorectal cancer
dMMR: mismatch repair deficient
EGFR: epidermal growth factor receptor
HCC: hepatocellular carcinoma
HSCT: hematopoietic stem cell transplantation
MSI-H: microsatellite instability-high
NSCLC: non-small cell lung cancer
PD-1: programmed death receptor-1
RCC: renal cell carcinoma
SCLC: small cell lung cancer
UC: urothelial carcinoma
ESCC: Esophageal Squamous Cell Carcinoma
PD-L1: Programmed death-ligand 1
GC: Gastric Cancer
GEJC: Gastroesophageal Junction Cancer
EAC: Esophageal Adenocarcinoma

**APPENDIX B: Therapeutic Alternatives**
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Nexavar® | HCC: 400 mg orally twice daily until clinical benefit ceases or unacceptable toxicity occurs | 800 mg/day |
| Cisplatin- or carboplatin-containing chemotherapy | SCLC, UC, SCCHN: Varies | Varies |

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| Cotellic® | Melanoma, unresectable or metastatic: 60 mg once daily days 1 to 21 of each 28-day treatment cycle | 60 mg by mouth once daily for 21 days |
| Gilotrif® | NSCLC: 40 mg once daily until disease progression | 40 mg/day orally |
| Afinitor® (everolimus) | RCC: 10 mg orally once daily | 10 mg/day |
| Gleostine | CHL: 130 mg/m$^2$ orally | 30 mg/m$^2$ orally |
| Alimta® | Malignant pleural mesothelioma: 500 mg/m$^2$ intravenous over 10 minutes on day 1, followed by cisplatin (75 mg/m$^2$ intravenous over 2 hours every 21 days) | 500 mg/m$^2$ intravenous infusion every 21 days |

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

**APPENDIX D: General Information**

- The safety and effectiveness of Opdio® have not been established:
  - In pediatric patients <12 years old with MSI-H or dMMR mCRC or,
  - In pediatric patients less than 18 years old for the other approved indications.

- Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis and hepatotoxicity, immune mediated endocrinopathies, immune-mediated dermatologic adverse reactions, and immune-mediated nephritis and renal dysfunction.

**References**


1. Opdivo® Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; May 2021. Available at https://www.opdivo.com/. Accessed July 08, 2021.
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4. Non-small cell lung cancer (Version 4.2021) National Comprehensive Cancer Network. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed July 08, 2021.
5. Kidney Cancer (Version 4.2021) National Comprehensive Cancer Network. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed July 08, 2021.
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7. Esophageal and Esophagogastric Junction Cancers (Version 2.2021) National Comprehensive Cancer Network. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed July 08, 2021.
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9. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com. Accessed July 08, 2021.
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| Review/Revision History | Review/Revised Date | P&T Approval Date |
|---|---|---|
| Policy established. | 01/2020 | 03/06/2020 |
| Policy was reviewed:<br>1. Clinical Policy Title was updated.<br>2. Drug(s) applied was updated.<br>3. Line of Business Policy Applies to was updated to “All lines of business”.<br>4. Updated background for NSCLC, HCC and added ESCC information.<br>5. Updated Dosing regimen for NSCLC, HCC, CRC and added ESCC regimen.<br>6. Initial and Continued approval duration was updated to specify Medicaid, Commercial & HIM approval duration.<br>7. Initial therapy criteria were updated to include new indication ESCC.<br>8. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”.<br>9. Appendix B was updated: added ESCC & PD-L1.<br>10. References were reviewed and updated. | 07/31/2020 | 09/14/2020 |
| Policy was reviewed:<br>1. Background was updated to remove indications “BRAF V600 melanoma” and “Small cell lung cancer (SCLC)”.<br>2. Background was updated to include new indications “Melanoma”, “Non-small cell lung cancer (NSCLC)”, “Renal cell carcinoma | 07/08/2021 | 09/14/2021 |

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| (RCC)", "Squamous cell carcinoma of the head and neck (SCCHN)", "Urothelial carcinoma", "Colorectal cancer", "Hepatocellular carcinoma (HCC)", "Esophageal cancer", and "Malignant pleural mesothelioma".<br>3. Background was updated to include "Patients with completely resected esophageal or gastroesophageal junction cancer …", "Adult patients with unresectable malignant pleural mesothelioma, as first-line treatment…", "Patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer…", and "[a]This indication is approved under accelerated approval based on overall response rate and duration…".<br>4. Dosing Information was updated to include new indications Malignant Pleural Mesothelioma, GC, GEJC, and EACas well as their respective dosing regimen and maximum dose information.<br>5. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy.<br>6. Initial Approval Criteria was updated to remove HIM approval duration.<br>7. Initial Approval Criteria I.C was updated to remove indication, "Small Cell Lung Cancer".<br>8. Initial Approval Criteria I.C.4 was updated to include "Request is for one of the following (a, b, or c)…".<br>9. Initial Approval Criteria I.C.4.a was updated to include "In combination with ipilimumab, for the first-line treatment …".<br>10. Initial Approval Criteria I.C.4.b was updated to include "In combination with cabozantinib, for the first-line treatment…".<br>11. Initial Approval Criteria I.C.4.c was updated to include "As a single agent, for the treatment of patients with advanced…".<br>12. Initial Approval Criteria I.C.5.c was updated to include "In combination with cabozantinib: 240 mg…".<br>13. Initial Approval Criteria I.D.4.a was updated from "Autologous hematopoietic stem cell transplantation" to "Autologous hematopoietic stem cell transplantation and | | |

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| brentuximab vedotin, or…".<br>14. Initial Approval Criteria I.D.4.b was updated to include "3 or more lines of systemic therapy that includes autologous HSCT…"<br>15. Initial Approval Criteria I.G.2 was updated to include prescriber criteria, "Prescribed by or in consultation with an oncologist."<br>16. Initial Approval Criteria I.G.3 was updated to include "Tumor has progressed following treatment…".<br>17. Initial Approval Criteria I.G.6.a was updated to include "240 mg every 2 weeks or…"<br>18. Initial Approval Criteria I.H.4 was updated to include generic drug name sorafenib.<br>19. Initial Approval Criteria I.J was updated to include new indication "Malignant Pleural Mesothelioma".<br>20. Initial Approval Criteria I.K was updated to include new indication "Gastic Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma".<br>21. Initial Approval Criteria I.L.1.g was updated to include off-label indication, "Uterine Neoplasms - Endometrial Carcinoma".<br>22. Continued Therapy Approval Criteria was updated to remove HIM approval duration.<br>23. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...".<br>24. Appendix A was updated to remove abbreviations BRAF and FDA.<br>25. Appendix A was updated to include abbreviations GC, GEJC, and EAC.<br>26. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..".<br>27. Appendix B was updated to remove inactive/unavailable generic drug names "sorafenib" and "lomustine."<br>28. Appendix B was updated to include brand-name drugs "Cotellic", "Gilotrif", "Afinitor", "Gleostine", and "Alimta" as well as their respective dosing regimens and maximum doses.<br>29. Statement about drug listing format in Appendix B is rephrased to "Therapeutic | | |

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| alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only".<br>30. Appendix D was updated to include warnings and precautions, “The safety and effectiveness of Opdivo… … In pediatric patients <12 years old with MSI-H… … In pediatric patients less than 18 years old…” and “Immune-mediated adverse reactions, which may be severe or fatal, can occur…”.<br>31. References were reviewed and updated. | | |