RXADVANCE
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|---|---|
| **Clinical Policy Title:** | capecitabine |
| **Policy Number:** | RxA.320 |
| **Drug(s) Applied:** | Xeloda® |
| **Original Policy Date:** | 03/06/2020 |
| **Last Review Date:** | 09/14/2020 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Capecitabine (Xeloda®) is nucleoside metabolic inhibitor with antineoplastic activity indicated for the treatment of:

- Adjuvant colon cancer (i.e. patients with Dukes' C colon cancer)
- Metastatic colorectal cancer
  - First-line as monotherapy when treatment with fluoropyrimidine therapy alone is preferred
- Metastatic breast cancer
  - In combination with docetaxel after failure of prior anthracycline-containing therapy
  - As monotherapy in patients resistant to both paclitaxel and an anthracycline-containing regimen

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| Capecitabine (Xeloda®) | Metastatic colorectal cancer<br>Adjuvant colon cancer<br>Metastatic breast cancer | For adjuvant treatment of Dukes' C colon cancer, total treatment should be 24 weeks (8 cycles).<br><br>Monotherapy: 1,250 mg/m$^2$ PO twice daily for 2 weeks followed by a one-week rest period in 3-week cycles.<br><br>In combination with docetaxel: 1250 mg/m$^2$ twice daily for 2 weeks followed by a 7-day rest period, combined with docetaxel at 75 mg/m$^2$ as a 1-hour IV infusion every 3 weeks.<br><br>Dosage may need to be individualized to optimize patient management.<br><br>Reduce dose by 25% in patients with moderate renal impairment. | 2,500 mg/m$^2$ total daily dose |

## Dosage Forms

- Tablets: 150 mg, 500 mg

## 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.

**I. Initial Approval Criteria**

**A. Breast Cancer** (must meet all)**:**

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. In combination with trastuzumab with or without tucatinib, lapatinib or neratinib for recurrent or stage IV HER2 positive disease or
   b. As monotherapy or in combination with doxetaxel for HER2 negative disease or
   c. As preferred adjuvant therapy for locally advanced triple-negative disease or
   d. As monotherapy or in combination with either lapatinib or neratinib in HER2 positive disease with brain metastases;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. Request meets one of the following (a or b):
   a. Dose does not exceed 1250 mg/$m^2$ twice a day on days 1 to 14, every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*). *
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**B. Colorectal and Rectal Cancer** (must meet all)**:**

1. Diagnosis of colorectal or rectal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy with radiation for inoperable disease or
   b. In combination with oxaliplatin or
   c. In combination with oxaliplatin and bevacizumab or
   d. As monotherapy with or without bevacizumab;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 1250 mg/$m^2$ twice a day on days 1 to 14, every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*). *
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**C. Anal Carcinoma (off-label)** (must meet all)**:**

1. Diagnosis of anal squamous cell carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in combination with chemoradiation and mitomycin;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*).* **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**D. Bladder Cancer (off-label)** (must meet all)**:**

1. Diagnosis of bladder cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in combination with radio-sensitizing chemotherapy and radiation therapy;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*).* **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**E. Cancer of Unknown Primary Source (Occult Primary) (off-label)** (must meet all)**:**

1. Diagnosis of occult primary cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy with or without radiation or
   b. In combination with oxaliplatin;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). * **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**F. Esophageal and Esophagogastric Junction Cancers (off-label)** (must meet all)**:**

1. Diagnosis of esophageal or esophagogastric cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy or

b. In combination with cisplatin, oxaliplatin, or paclitaxel or
c. In combination with epirubicin and either cisplatin or oxaliplatin;

5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *
**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**G. Gastric Cancer (off-label)** (must meet all)**:**

1. Diagnosis of gastric cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy or
   b. In combination with cisplatin, oxaliplatin, or paclitaxel or
   c. In combination with epirubicin and either cisplatin or oxaliplatin;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *
**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**H. Gestational Trophoblastic Neoplasia (off-label)** (must meet all)**:**

1. Diagnosis of gestational trophoblastic neoplasia;
2. Prescribed by or in consultation with an oncologist;
3. Prescribed as monotherapy;
4. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
5. 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*). *
**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**I. Head and Neck Cancers (off-label)** (must meet all)**:**

1. Diagnosis of advanced head and/or neck cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed as monotherapy;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *
**Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration**

**Commercial:** 6 months
**Medicaid:** 6 months

**J. Hepatobiliary Cancers (off-label)** (must meet all)**:**

1. Diagnosis of gallbladder cholangiocarcinoma (extrahepatic or intrahepatic);
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy or
   b. In combination with gemcitabine, cisplatin, or oxaliplatin;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**K. Neuroendocrine Tumors (off-label)** (must meet all)**:**

1. Diagnosis of neuroendocrine tumor of the GI tract, lung, pancreas, and/or thymus that is poorly differentiated;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in combination with temozolomide;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**L. Ovarian, Fallopian Tube and Peritoneal Cancers (off-label)** (must meet all)**:**

1. Diagnosis of epithelial ovarian cancer, fallopian tube cancer or peritoneal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy or
   b. In combination with oxaliplatin with or without bevacizumab;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**M. Pancreatic Cancer (off-label)** (must meet all)**:**

1. Diagnosis of pancreatic adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy with or without radiation therapy or
   b. In combination with gemcitabine with or without docetaxel or
   c. In combination with oxaliplatin;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**N. Penile Cancer (off-label)** (must meet all)**:**

1. Diagnosis of penile cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed as monotherapy with radiation;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**O. Small Bowel Cancer (off-label)** (must meet all)**:**

1. Diagnosis of small bowel cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Prescribed in one of the following ways:
   a. As monotherapy with or without radiation or
   b. In combination with oxaliplatin with or without bevacizumab or
   c. As monotherapy with or without bevacizumab or
   d. In combination with docetaxel and gemcitabine;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**P. Thymomas and Thymic Cancers (off-label)** (must meet all)**:**

1. Diagnosis of thymoma or thymic cancer;
2. Prescribed by or in consultation with an oncologist;

3. Age 18 years or older;
4. Prescribed in combination with gemcitabine;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);
6. 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*). *
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**II. Continued Therapy Approval**

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

1. Currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Xeloda® 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 2,500 mg/m$^2$ total daily dose on days 1 to 14, every 21 days;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
      **Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

**III. Appendices**

**APPENDIX A: Abbreviation/Acronym Key**
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

**APPENDIX B: Therapeutic Alternatives**
Not applicable.

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - Severe renal impairment, hypersensitivity
- Boxed warning(s):
  - Xeloda - oral coumarin-derivative interaction

**References**

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15. National Comprehensive Cancer Network. Pancreatic Cancer Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Updated November 26, 2019. Accessed August 11, 2020.
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| Review/Revision History | Review/Revised Date | P&T Approval Date |
|---|---|---|
| Policy established. | 02/2020 | 03/06/2020 |
| Policy was reviewed:<br>1. Policy title table was updated.<br>2. In initial approval and continued therapy criteria- *Prescribed regimen must be | 08/11/2020 | 09/14/2020 |

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| FDA-approved or recommended by NCCN this line was added.<br>3. Approval duration was updated in initial and continued therapy approval to specify Commercial and Medicaid plans.<br>4. Updated breast cancer initial therapy criteria prescribing methods to include “in combination with trastuzumab without or without tucatinib”.<br>5. Updated initial therapy criteria for pancreatic and penile cancer - diagnosis and prescribing methods.<br>6. Updated small bowel cancer initial therapy criteria prescribing methods to include “in combination with oxaliplatin with or without bevacizumab”.<br>7. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”.<br>8. References were updated. | | |