# Clinical Policy: Capecitabine (Xeloda)

Reference Number: ERX.SPA.48
Effective Date: 07.01.16
Last Review Date: 05.20
Line of Business: Commercial, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
Capecitabine (Xeloda®) is a nucleoside metabolic inhibitor with antineoplastic activity.

**FDA Approved Indication(s)**
Xeloda is indicated for the treatment of:

- Adjuvant colon cancer
  - 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

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Xeloda is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

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

1. Diagnosis of one of the following (a or b):
   a. Colorectal cancer;
   b. Breast cancer and meets one of the following (i or ii):
      i. Disease is recurrent or metastatic;
      ii. Xeloda is prescribed as adjuvant therapy;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 mL/min);
5. If brand Xeloda is requested, medical justification supports inability to use generic capecitabine (e.g., contraindication to excipients in capecitabine);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,250 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** – Length of Benefit
**Medicaid** – 6 months

**B. 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;
4. Xeloda will be used concurrently with chemoradiation in combination with mitomycin;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 mL/min);
6. If brand Xeloda is requested, medical justification supports inability to use generic capecitabine (e.g., contraindication to excipients in capecitabine);
7. 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** – Length of Benefit
**Medicaid** – 6 months

**C. Neuroendocrine Tumor of the Pancreas (off-label)** (must meet all)**:**
1. Diagnosis of neuroendocrine tumor of the pancreas;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Xeloda is prescribed as a single agent or in combination with temozolomide;
5. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 mL/min);
6. If brand Xeloda is requested, medical justification supports inability to use generic capecitabine (e.g., contraindication to excipients in capecitabine);
7. 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** – Length of Benefit
**Medicaid** – 6 months

**D. Additional NCCN Recommended Uses (off-label)** (must meet all)**:**
1. Prescribed for one of the following diagnoses:
   a. Gastric, esophageal or esophagogastric junction cancer;
   b. Gestational trophoblastic neoplasia;
   c. Advanced head and neck cancer;
   d. Hepatobiliary cancer (i, ii, or iii):
      i. Extrahepatic cholangiocarcinoma;
      ii. Gallbladder cancer;
      iii. Intrahepatic cholangiocarcinoma;
   e. Neuroendocrine tumor (i or ii):
      i. Neuroendocrine tumor in the gastrointestinal tract with poorly controlled carcinoid syndrome;
      ii. Extrapulmonary neuroendocrine tumor and (a or b):
         a. Disease is poorly differentiated (i.e., high grade) neuroendocrine carcinoma;
         b. Disease is large or small cell carcinoma;
   f. Occult primary cancer (cancer of unknown origin);
   g. Ovarian, fallopian tube or primary peritoneal cancer;
   h. Pancreatic cancer;
   i. Penile cancer;
   j. Small bowel adenocarcinoma;
   k. Thymomas and thymic carcinomas;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;

4. At the time of request, member does not have severe renal impairment (creatinine clearance < 30 mL/min);
5. If brand Xeloda is requested, medical justification supports inability to use generic capecitabine (e.g., contraindication to excipients in capecitabine);
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** – Length of Benefit
**Medicaid** – 6 months

**E. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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** – Length of Benefit
**Medicaid** – 12 months

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

**IV. Appendices/General Information**

*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-warfarin interaction

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Metastatic colorectal cancer | 1,250 mg/m$^2$ PO BID for 2 weeks followed by a 1-week rest period given as 3-week cycles For adjuvant treatment of Dukes' C colon cancer, total treatment should be 24 weeks (8 cycles) | 2,500 mg/m$^2$ total daily dose |
| Adjuvant colorectal cancer | | |
| Metastatic breast cancer | | |

## VI. Product Availability

Tablets: 150 mg, 500 mg

## VII. References

1. Xeloda Prescribing Information. South San Francisco, CA: Genentech, Inc.; February 2019. Available at https://www.gene.com/patients/medicines/xeloda. Accessed February 16, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 16, 2020.
3. National Comprehensive Cancer Network. Colon Cancer Version 1.2020. Available at www.nccn.org. Accessed February 16, 2020.
4. National Comprehensive Cancer Network. Rectal Cancer Version 1.2020. Available at www.nccn.org. Accessed February 16, 2020.
5. National Comprehensive Cancer Network. Breast Cancer Version 2.2020. Available at www.nccn.org. Accessed February 16, 2020.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 05.16 | 06.16 |
| Increased approval durations from 3/6 months to 6/12 months. Split NCCN off-label uses into their own criteria sets per updated template. | 04.17 | 05.17 |
| 2Q 2018 annual review: Combined NCCN and FDA approved recommendations to one optimized criteria for each drug indication; Removed Central Nervous Cancers-Brain Metastases from off-label because it relates to the primary tumor (breast); Removed Mucinous carcinoma of the ovary as it is covered in Ovarian cancer criteria; Added COC; All approval durations modified to length of benefit; References reviewed and updated. | 02.09.18 | 05.18 |
| 2Q 2019 annual review: the following NCCN recommended uses are added: adjuvant breast cancer, gestational trophoblastic neoplasia, poorly controlled carcinoid syndrome, poorly differentiated or large/small cell neuroendocrine tumor; histologies removed from off-label uses; age added to all criteria sets if not previously listed; references reviewed and updated. | 12.19.19 | 05.19 |
| 2Q 2020 annual review: NCCN compendium-supported changes to occult primary and neuroendocrine tumors of the pancreas indications as capecitabine use as a single agent is supported for both of these indications; added NCCN compendium-supported uses of small bowel adenocarcinomas and thymomas and thymic carcinomas; added requirement for medical justification if brand Xeloda requested as generic available; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated. | 02.16.20 | 05.20 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of

physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.