Clinical Policy: Capecitabine (Xeloda)

Reference Number: CP.PHAR.60
Effective Date: 05.01.11
Last Review Date: 05.22
Line of Business: HIM, Medicaid

Coding Implications
Revision Log

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

Description

Capecitabine (Xeloda®) is 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.

It is the policy of health plans affiliated with Centene Corporation® that Xeloda is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Colorectal Cancer and 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, metastatic, or unresponsive to preoperative systemic therapy;
      ii. Xeloda is prescribed as adjuvant or maintenance 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. Member must use generic capecitabine, unless contraindicated or clinically significant adverse effects are experienced;

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: 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 is prescribed 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. Member must use generic capecitabine, unless contraindicated or clinically significant adverse effects are experienced;
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: 6 months

C. Additional NCCN Recommended Uses (off-label) (must meet all)**:**
1. Prescribed for one of the following diagnoses (a - l):
   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 of the pancreas, gastrointestinal tract, lung, or thymus;
   f. Occult primary cancer (cancer of unknown origin);
   g. Ovarian or fallopian tube or primary peritoneal cancer;
   h. Pancreatic cancer;
   i. Penile cancer;
   j. Small bowel adenocarcinoma;
   k. Thymoma or thymic carcinoma;
   l. Squamous cell skin cancer;
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. Member must use generic capecitabine, unless contraindicated or clinically significant adverse effects are experienced;
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: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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. Member must use generic capecitabine, unless contraindicated or clinically significant adverse effects are experienced;
4. 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: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, 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 one week rest period in 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 colon cancer		
Metastatic breast cancer		

VI. Product Availability

Tablets: 150 mg, 500 mg

VII. References

1. Xeloda Prescribing Information. South San Francisco, CA: Genentech, Inc.; May 2021. Available at https://www.gene.com/download/pdf/xeloda_prescribing.pdf. Accessed February 21, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 21, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J8520	Capecitabine, oral, 150 mg
J8521	Capecitabine, oral, 500 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: added HIM line of business; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; removed central nervous cancers-brain metastases from off-label because it is addressed by the primary tumor (breast cancer criteria); removed mucinous carcinoma of the ovary as it is covered in ovarian cancer criteria; added continuity of care statement; references reviewed and updated.	02.13.18	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; references reviewed and updated.	02.16.20	05.20
2Q 2021 annual review: revised medical justification language for not using generic capecitabine to “must use” language and added this to continued therapy criteria; removed the criteria for prescribing as single agent or in combination with temozolomide for the indication of neuroendocrine tumor of the pancreas as capecitabine can be	02.22.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
prescribed as part of other regimens per NCCN; removed the differentiation of neuroendocrine tumor of the gastrointestinal tract, lung, or thymus as there are several different supported indications per NCCN; added NCCN-supported indication of squamous cell skin cancer; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.		
2Q 2022 annual review: added "maintenance therapy" and "unresponsive to preoperative systemic therapy" uses of Xeloda in breast cancer per NCCN; collapsed off-label criteria for neuroendocrine tumor of the pancreas into the off-label criteria set; WCG.CP.PHAR.60 was retired and initial approval duration was consolidated to 6 months; references reviewed and updated.	02.22.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	11.23.22	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.