Clinical Policy: Capecitabine (Xeloda)

Reference Number: PA.CP.PHAR.60
Effective Date: 01/18
Last Review Date: 04/18

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by PA Health and Wellness® clinical policy for capecitabine (Xeloda®/generics).

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
It is the policy of health plans affiliated with Pennsylvania Health and Wellness® that capecitabine 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:
   i. Colorectal cancer (including colon or rectal cancer);
   ii. Recurrent or metastatic breast 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. 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*).

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. Xeloda will be used concurrently with chemoradiation in combination with mitomycin;

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 evidenc*e).

Approval duration: 6 months

C. Neuroendocrine Tumors of the Pancreas (off-label) (must meet all)**:**

1. Diagnosis of neuroendocrine tumors of the pancreas;
2. Prescribed by or in consultation with an oncologist;
3. Xeloda will be used in combination with temozolomide;
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*).

Approval duration: 6 months

D. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

1. Additional NCCN compendium uses for capecitabine, meeting NCCN categories 2a, - are covered for the following indications per the CP.PHAR.57 Global Biopharm Policy:
   a. Esophageal and esophagogastric junction cancers (squamous cell carcinoma; adenocarcinoma);
   b. Gastric cancer (adenocarcinoma);
   c. Very advanced head and neck cancer (squamous cell carcinoma with mixed subtypes);
   d. Hepatobiliary cancers:
      i. Extrahepatic cholangiocarcinoma (adenocarcinoma);
      ii. Gallbladder cancer (adenocarcinoma);
      iii. Intrahepatic cholangiocarcinoma (adenocarcinoma);
   e. Occult primary (adenocarcinoma or carcinoma not otherwise specified);
   f. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer;
   g. Pancreatic cancer (adenocarcinoma);
   h. Penile cancer.
   i. Neuroendocrine and Adrenal Tumors - Poorly Differentiated (High Grade)/Large or Small Cell
   j. Neuroendocrine and Adrenal Tumors - Neuroendocrine Tumors of the Gastrointestinal Tract, Lung and Thymus (Carcinoid Tumors) - 2A for use in poorly controlled carcinoid syndrome

2. Prescribed by or in consultation with an oncologist;

3.At the time of request, member does not have severe renal impairment (creatinine clearance < 30 ml/min);

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: 6 months

II. Continued Approval

A. All Indications (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member has none of the following reasons to discontinue capecitabine:
   a. Disease progression;
   b. Unacceptable toxicity, including severe mucocutaneous reaction possibly attributable to capecitabine treatment;
   c. Severe renal impairment (creatinine clearance < 30 mL/min);
   d. Known absent DPD activity;
   e. Hypersensitivity to capecitabine or to any product components;
   f. Hypersensitivity to 5-fluorouracil.

Approval duration: 6 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

Xeloda (capecitabine) is a fluoropyrimidine carbamate with antineoplastic activity. It is an orally administered systemic prodrug of 5'-deoxy-5-fluorouridine (5'-DFUR) which is converted to 5-fluorouracil. Enzymes convert capecitabine to 5-fluorouracil (5-FU) *in vivo*. Both normal and tumor cells metabolize 5-FU to 5-fluoro-2'-deoxyuridine monophosphate (FdUMP) and 5-fluorouridine triphosphate (FUTP). These metabolites cause cell injury by two different mechanisms. First, FdUMP and the folate cofactor, N5-10-methylenetetrahydrofolate, bind to thymidylate synthase (TS). This binding inhibits the formation of thymidylate from 2'-deoxyuridylate. Thymidylate is the necessary precursor of thymidine triphosphate, which is essential for the synthesis of DNA, so that a deficiency of this compound can inhibit cell division. Second, nuclear transcriptional enzymes can mistakenly incorporate FUTP in place of uridine triphosphate (UTP) during the synthesis of RNA. This metabolic error can interfere with RNA processing and protein synthesis.

Formulations:

Tablet, Oral:

Xeloda: 150 mg, 500 mg
Generic: 150 mg, 500 mg

Appendices

Appendix A: Abbreviation Key

DPD: dihydropyrimidine dehydrogenase
HER2: human epidermal growth factor receptor 2
HR: hormone receptor

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	Approval Date
Updated references	06/14	06/14
2Q 2018 annual review: 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; references reviewed and updated.	02/13/18	04/18

References
1. Xeldoa Prescribing Information. San Francisco, CA: Genentech, Inc.; March 2015. Available at http://www.gene.com/download/pdf/xeloda_prescribing.pdf. Accessed January 3, 2018.
2. Capecitabine. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed January 3, 2018.
3. Colon cancer (Version 2.2016). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed January 3, 2018.
4. Rectal cancer (Version 2.2016). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed January 3, 2018.