Clinical Policy: Capecitabine (Xeloda)

Reference Number: ERX.SPMN.102
Effective Date: 07/16
Last Review Date: 06/16

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that capecitabine (Xeloda®/generics) is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Colorectal Cancer (must meet all):
      1. Diagnosis of colorectal cancer;
      2. Member meets a or b:
         a. FDA approved use:
            i. Xeloda will be used as a single agent in one of the following ways:
               a) For adjuvant treatment of Dukes’ C (stage III) colon cancer after the primary tumor has been completely resected;
               b) As first-line treatment of metastatic colorectal carcinoma;
            b. NCCN recommended use:
               i. Xeloda will be used in one of the following ways:
                  a) In CapeOX (capecitabine and oxaliplatin) regimen;
                  b) As a single agent or in combination with bevacizumab;
                  c) As a single agent with concurrent chemoradiation.

      Approval duration: 3 months

   B. Breast Cancer (must meet all):
      1. Diagnosis of recurrent or metastatic breast cancer;
      2. Member meets a or b:
         a. FDA approved use:
            i. Xeloda will be used in one of the following ways:
               a) In combination with docetaxel after failure of anthracycline-containing chemotherapy;
               b) As monotherapy for disease that is resistant to 1 or 2 (resistance is defined as progressive disease while on treatment, or relapse within 6 months of completing treatment with an anthracycline-containing adjuvant regimen):
                  1) Paclitaxel and an anthracycline-containing chemotherapy regimen;
                  2) Paclitaxel and further anthracycline therapy is not indicated (e.g., member has received cumulative doses of 400 mg/m² of doxorubicin or doxorubicin equivalents);
b. NCCN recommended use:
   i. Xeloda will be used in one of the following ways:
      a) As a single agent or in combination with docetaxel for HER2-negative disease with one of the following characteristics:
         1) Concurrent symptomatic visceral disease or visceral crisis;
         2) The disease is HR-negative - or HR-positive and endocrine therapy refractory;
      b) In combination with trastuzumab or lapatinib (if trastuzumab-exposed disease) for HER2-positive disease with one of the following characteristics:
         1) Concurrent symptomatic visceral disease or visceral crisis;
         2) The disease is HR-negative - or HR-positive and endocrine therapy refractory.

Approval duration: 3 months

C. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.
   1. Additional NCCN compendial uses for capecitabine, meeting NCCN categories 1, 2a, or 2b, are covered for the following indications per the USS.SPMN.16 Global Biopharm Policy:
      a. Anal cancer (squamous cell carcinoma);
      b. Central nervous system cancers:
         i. Limited (1-3) metastatic lesions - brain metastases;
         ii. Multiple (>3) metastatic lesions - brain metastases;
      c. Esophageal and esophagogastric junction cancers (squamous cell carcinoma; adenocarcinoma);
      d. Gastric cancer (adenocarcinoma);
      e. Very advanced head and neck cancer (squamous cell carcinoma with mixed subtypes);
      f. Hepatobiliary cancers:
         i. Extrahepatic cholangiocarcinoma (adenocarcinoma);
         ii. Gallbladder cancer (adenocarcinoma);
         iii. Intrahepatic cholangiocarcinoma (adenocarcinoma);
      g. Lung neuroendocrine tumors (carcinoid);
      h. Neuroendocrine tumors of the pancreas;
      i. Occult primary (adenocarcinoma or carcinoma not otherwise specified);
      j. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer;
      k. Pancreatic cancer (adenocarcinoma);
      l. Penile cancer.

II. Continued Approval
   A. All Indications (must meet all):
      1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
      2. No evidence of disease progression.
Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
2. Refer to ERX.SPMN.16 - 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

FDA Approved Indications:
Xeloda (capecitabine) is a nucleoside metabolic inhibitor/oral tablet formulation indicated for:
- Colorectal Cancer
  - Xeloda is indicated as a single agent for adjuvant treatment in patients with Dukes’ C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred. Xeloda was non-inferior to 5-fluorouracil and leucovorin (5-FU/LV) for disease-free survival (DFS). Physicians should consider results of combination chemotherapy trials, which have shown improvement in DFS and OS, when prescribing single-agent Xeloda in the adjuvant treatment of Dukes’ C colon cancer.
Xeloda is indicated as first-line treatment of patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred. Combination chemotherapy has shown a survival benefit compared to 5-FU/LV alone. A survival benefit over 5-FU/LV has not been demonstrated with Xeloda monotherapy. Use of Xeloda instead of 5FU/LV in combinations has not been adequately studied to assure safety or preservation of the survival advantage.

Breast Cancer

- Xeloda in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.
- Xeloda monotherapy is also indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated (e.g., patients who have received cumulative doses of 400 mg/m2 of doxorubicin or doxorubicin equivalents). Resistance is defined as progressive disease while on treatment, with or without an initial response, or relapse within 6 months of completing treatment with an anthracycline containing adjuvant regimen.

Appendices

Appendix A: Abbreviation Key
CapeOX: capecitabine and oxaliplatin
DPD: 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.

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References

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.

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