PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Capecitabine (Xeloda) Prior Authorization Policy
- Xeloda® (capecitabine tablets – Genentech, generic)

REVIEW DATE: 07/14/2021

OVERVIEW

Capecitabine, a fluoropyrimidine carbamate with antineoplastic activity, is indicated for the following uses:[1]

- **Breast cancer**:
  - In combination with docetaxel for metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.
  - Monotherapy for 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.
- **Colorectal cancer**, when treatment with fluoropyrimidine therapy alone is preferred as:
  - A single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor.
  - First-line treatment of patients with metastatic colorectal carcinoma.

Guidelines

Capecitabine is recommended (all category 2A unless otherwise noted) in guidelines from National Comprehensive Cancer Network (NCCN):[2]

- **Anal Carcinoma:** The NCCN guidelines for anal carcinoma (version 2.2021 – June 30, 2021) advise the use of capecitabine in combination with mitomycin (preferred) with concurrent chemoradiation for primary treatment of locoregional anal canal cancer and non-metastatic perianal cancer.[3] Systemic therapy with capecitabine is also recommended for inguinal node recurrence.
- **Breast Cancer:** The NCCN guidelines for breast cancer (version 5.2021 – June 28, 2021) consider capecitabine monotherapy or in combination with other therapies as a preferred regimen for multiple settings in breast cancer.[4] Combination therapy with capecitabine is also recommended as a second-, third-, or fourth-line therapy (category 1 or 2A) for patients in certain situations.
- **Central Nervous System Cancers:** The NCCN guidelines for central nervous system cancers (version 1.2021 – June 4, 2021) support the use of capecitabine monotherapy or in combination therapy (category 1 or 2A) for brain metastases from breast cancer.[5]
- **Colon Cancer:** The NCCN guidelines for colon cancer (version 2.2021 – January 21, 2021) recommend capecitabine (category 2A or 2B) monotherapy or in combination with other agents as primary treatment, neoadjuvant therapy, or adjuvant therapy for numerous conditions in colon cancer.[6]
- **Esophageal and Esophagogastric Junction Cancers:** The NCCN guidelines for esophageal and esophagogastric junction cancers (version 3.2021 – June 22, 2021) recommend capecitabine (category 1, 2A, or 2B) as monotherapy or in combination with other agents for chemoradiation (e.g., preoperative, concurrent, definitive, postoperative), peri- or postoperative chemotherapy, or palliative therapy for several circumstances.[7]
- **Gastric Cancer:** The NCCN guidelines for gastric cancer (version 3.2021 – June 22, 2021) recommend capecitabine (category 1, 2A, or 2B) as monotherapy or in combination with other agents involving various conditions related to chemoradiation (e.g., palliative, preoperative,

perioperative, postoperative), chemotherapy, surgically unresectable disease, and palliative therapy.[8]

- **Gestational Trophoblastic Neoplasia:** The NCCN guidelines for gestational trophoblastic neoplasia (version 2.2021 – March 31, 2021) recommend capecitabine-based regimens as useful in certain circumstances.[9]
- **Head and Neck Cancers:** The NCCN guidelines for head and neck cancers (version 3.2021 – April 27, 2021) recommend capecitabine for recurrent, unresectable, or metastatic disease as a first line or subsequent-line option.[10]
- **Hepatobiliary Cancers:** The NCCN guidelines for hepatobiliary cancers (version 3.2021 – June 15, 2021) recommend capecitabine (category 1, 2A, or 2B) monotherapy or in combination with other agents as primary treatment, neoadjuvant therapy, adjuvant therapy, or used with concurrent radiation.[11]
- **Neuroendocrine and Adrenal Tumors:** The NCCN guidelines for neuroendocrine and adrenal tumors (version 2.2021 – June 18, 2021) recommend capecitabine as neoadjuvant, adjuvant therapy, or chemotherapy alone for resectable, locoregional unresectable, or metastatic disease of the gastrointestinal tract, lung, pancreas, and thymus.[12]
- **Occult Primary:** The NCCN guidelines for occult primary (cancer of unknown primary) [version 2.2021 – February 8, 2021] recommend capecitabine as monotherapy or in combination with other agents in asymptomatic and symptomatic patients.[13]
- **Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer:** The NCCN guidelines for ovarian cancer/fallopian tube cancer/primary peritoneal cancer (version 1.2021 – February 26, 2021) recommend capecitabine (category 2A or 2B) monotherapy for persistent disease or recurrence; or in combination with other agents as adjuvant treatment.[14]
- **Pancreatic Adenocarcinoma:** The NCCN guidelines for pancreatic adenocarcinoma (version 2.2021 – February 25, 2021) recommend capecitabine (category 1, 2A, or 2B) monotherapy or in combination with other agents as primary, chemoradiation, or adjuvant treatment for progression on primary, maintenance, or recurrence therapy for a variety of conditions.[15]
- **Penile Cancer:** The NCCN guidelines for penile cancer (version 2.2021 – June 30, 2021) recommend capecitabine (category 2A or 2B) chemoradiotherapy as a single agent for primary treatment or recurrence in many specific circumstances.[16]
- **Rectal Cancer:** The NCCN guidelines for rectal cancer (version 1.2021 – December 22, 2020) recommend capecitabine (category 2A or 2B) monotherapy or in combination with other agents as primary, adjuvant, or neoadjuvant treatment for chemotherapy or chemoradiation.[17]
- **Small Bowel Adenocarcinoma:** The NCCN guidelines for small bowel adenocarcinoma (version 1.2021 – February 16, 2021) recommend capecitabine monotherapy or in combination with other agents as primary, subsequent, or adjuvant treatment for numerous conditions.[18]
- **Squamous Cell Skin Cancer:** The NCCN guidelines for squamous cell skin cancer (version 1.2021 – February 5, 2021) recommend capecitabine monotherapy useful in certain circumstances if ineligible for or progressed on immune checkpoint inhibitors and clinical trials for specific conditions.[19]
- **Thymomas and Thymic Carcinomas:** The NCCN guidelines for thymomas and thymic carcinomas (version 1.2021 – December 4, 2020) recommend capecitabine in combination with gemcitabine as first- and second-line therapy for certain patients.[20]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of generic capecitabine tablets and Xeloda. If the patient does not meet the criteria regarding brand Xeloda, auto-approvals will be given for generic capecitabine tablets when patients meet conditions for coverage of capecitabine as defined in this policy. All approvals are provided for the duration noted below.

Documentation: Documentation is required for use of generic capecitabine as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of generic capecitabine tablets and Xeloda is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Breast Cancer.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

2. **Colon Cancer.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

Other Uses with Supportive Evidence

3. **Anal Carcinoma.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

4. **Central Nervous System Cancers.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

5. **Esophageal and Esophagogastric Junction Cancers.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

6. **Gastric Cancer.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

7. **Gestational Trophoblastic Neoplasia.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

8. **Head and Neck Cancers.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND
     - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

9. **Hepatobiliary Cancers.** Approve for 3 years if the patient meets the following (A or B):
   - **A)** Generic capecitabine tablets are requested; OR
   - **B)** Patient meets both of the following (i and ii):
     - **i.** Patient has tried generic capecitabine tablets; AND

ii. Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

10. **Neuroendocrine and Adrenal Tumors.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

11. **Occult Primary.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

12. **Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

13. **Pancreatic Adenocarcinoma.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

14. **Penile Cancer.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

15. **Rectal Cancer.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

16. **Small Bowel Adenocarcinoma.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

17. **Squamous Cell Skin Cancer.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

18. **Thymomas and Thymic Carcinomas.** Approve for 3 years if the patient meets the following (A or B):
    - **A)** Generic capecitabine tablets are requested; OR
    - **B)** Patient meets both of the following (i and ii):
        - **i.** Patient has tried generic capecitabine tablets; AND
        - **ii.** Patient cannot take generic capecitabine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of generic capecitabine tablets and Xeloda is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Xeloda® tablets [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; June 2021.
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