Clinical Policy Title:	capecitabine
Policy Number:	RxA.320
Drug(s) Applied:	Xeloda®
Original Policy Date:	03/06/2020
Last Review Date:	4/2/2024
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of advanced or metastatic breast cancer;
2. Prescribed in one of the following ways (a, or b):
   a. As a single agent if an anthracycline or taxane-containing chemotherapy is not indicated;
   b. In combination with docetaxel after disease progression on prior anthracycline-containing chemotherapy.

Initial Approval duration : 12 months, Split Fill
All line of business (except Medicare)

B. Colorectal Cancer (must meet all)**:**

1. Diagnosis of colorectal cancer and any one of the following (a, b or c):
   a. Stage III colon cancer;
   b. Locally advanced rectal cancer;
   c. Unresectable or metastatic colorectal cancer;
2. If the diagnosis is locally advanced rectal cancer, then the medication is used as perioperative therapy in combination with chemoradiotherapy.

Initial Approval duration : 12 months,
Split Fill
All line of business (except Medicare)

C. Gastric, Esophageal or Gastroesophageal Junction Cancer (must meet all):

1. Diagnosis of one of the following (a or b):
   a. Unresectable or metastatic gastric, esophageal, or esophagogastric cancer;
   b. HER2-overexpressing metastatic gastric or esophagogastric adenocarcinoma;
2. Prescribed in as one of the following ways (a or b):
   a. In combination with chemotherapy;

b. For HER2-overexpressing metastatic gastric or esophagogastric adenocarcinoma, as initial treatment in combination with chemotherapy.

Initial Approval duration : 12 months, Split
Fill
All line of business (except Medicare)

D. Pancreatic Cancer (must meet all):
1. Diagnosis of pancreatic adenocarcinoma;
2. Prescribed in combination with chemotherapy.

Initial Approval duration : 12 months, Split
Fill
All line of business (except Medicare)

II. Continued Therapy Approval (APA)

A. All Indications in Section I (must meet all)**:**
1. 1.Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.

Approval duration : 12 months
All line of business (except Medicare)

References

1. Xeloda. Package insert. Genentech, Inc; 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/020896s044s045s046s047s048s049s050s051lbl.pdf. Accessed April 2, 2024.
2. National Comprehensive Cancer Network. Colon Cancer Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed April 01, 2024.
3. National Comprehensive Cancer Network. Rectal Cancer Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed April 02, 2024.
4. National Comprehensive Cancer Network. Breast Cancer Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed April 01, 2024.
5. National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancer Version 1.2024. Available at: . Accessed April 02, 2024.
6. National Comprehensive Cancer Network. Gastric Cancer Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed April 02, 2024.
7. National Comprehensive Cancer Network. Pancreatic Adenocarcinoma Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed April 02, 2024.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	02/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. In initial approval and continued therapy criteria- *Prescribed regimen must be FDA-approved or	08/11/2020	09/14/2020

recommended by NCCN this line was added. 3. Approval duration was updated in initial and continued therapy approval to specify Commercial and Medicaid plans. 4. Updated breast cancer initial therapy criteria prescribing methods to include “in combination with trastuzumab without or without tucatinib”. 5. Updated initial therapy criteria for pancreatic and penile cancer - diagnosis and prescribing methods. 6. Updated small bowel cancer initial therapy criteria prescribing methods to include “in combination with oxaliplatin with or without bevacizumab”. 7. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 8. References were updated.		
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial Approval Criteria I.D was updated to remove off-label NCCN category-3 indication, “Bladder Cancer (off-label)”. 3. Initial Approval Criteria I.D.4 was updated from “Prescribed in one of the following ways: a. As monotherapy with or without radiation or b. In combination with oxaliplatin;” to “Prescribed as monotherapy with or without radiation or as a component of CAPEOX regimen;”. 4. Initial Approval Criteria I.D.5 was updated to include “Prescribed for symptomatic patients with performance status (PS) 1-2 or asymptomatic patients with PS 0 and aggressive disease;”. 5. Initial Approval Criteria I.E.4.b was updated from “In combination with cisplatin, oxaliplatin, or paclitaxel or” to “In combination with cisplatin or oxaliplatin”. 6. Initial Approval Criteria I.E.4.c was updated from “In combination with epirubicin and either cisplatin or oxaliplatin” to “In combination with cisplatin and trastuzumab”. 7. Initial Approval Criteria I.E.4.d was updated to include “In combination with cisplatin and pembrolizumab (PD-L1 CPS ≥ 10) for adenocarcinoma…”. 8. Initial Approval Criteria I.E.4.e was updated to include “In combination with oxaliplatin and nivolumab (PD-L1 CPS ≥ 5) for adenocarcinoma…”.	07/14/2021	09/14/2021

9. Initial Approval Criteria I.E.4.f was updated to include “In combination with oxaliplatin and pembrolizumab (PD-L1 CPS ≥ 10) for adenocarcinoma…”. 10. Initial Approval Criteria I.E.5 was updated to include “Prescribed for patients with Karnofsky performance score ≥ 60% or ECOG performance score ≤ 2;”. 11. Initial Approval Criteria I.F.4.b was updated from “In combination with cisplatin, oxaliplatin, or paclitaxel or” to “In combination with cisplatin, trastuzumab, pembrolizumab, or oxaliplatin”. 12. Initial Approval Criteria I.F.4.c was updated from “In combination with epirubicin and either cisplatin or oxaliplatin” to “In combination with oxaliplatin and nivolumab (PD-L1 CPS ≥ 5) (if no prior tumor progression while on therapy with a checkpoint inhibitor)”. 13. Initial Approval Criteria I.F.6 was updated to include “Prescribed for patients with Karnofsky performance score ≥ 60% or ECOG performance score ≤ 2;”. 14. Initial Approval Criteria I.G.3 was updated to include age criteria, “Age ≥ 18 years;”. 15. Initial Approval Criteria I.I.4.a was updated from “As monotherapy” to “As monotherapy with or without concurrent chemoradiation”. 16. Initial Approval Criteria I.I.4.c was updated to include “Treatment for resected disease”. 17. Initial Approval Criteria I.J indication was updated from “Neuroendocrine Tumors (off-label)” to “Neuroendocrine and Adrenal Tumors (off-label)”. 18. Initial Approval Criteria I.J.4 was updated to include “…or as a component of CAPEOX regimen”. 19. Initial Approval Criteria I.L.4.a was updated from “As monotherapy with or without radiation therapy” to “As monotherapy for patients with locally advanced disease and good performance status (ECOG PS 0-1) or following neoadjuvant therapy”. 20. Initial Approval Criteria I.L.4.b was updated to include “With radiation therapy”. 21. Initial Approval Criteria I.L.4.c was updated from “In combination with gemcitabine with or without docetaxel” to “In combination with gemcitabine”. 22. Initial Approval Criteria I.L.4.d was updated to include “…with good performance status (ECOG PS 0-1) and disease progression who were previously treated with gemcitabine-based therapy”. 23. Initial Approval Criteria I.M.4 was updated to include “…for non-metastatic disease”.		

24. Initial Approval Criteria I.P was updated to include off-label NCCN category-2A indication, “Squamous Cell Skin Cancer (off-label)”. 25. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." 26. Appendix A was updated to include abbreviations PS, ECOG, HER2, INR, and PD-L1 CPS. 27. Appendix D was updated to include “Patients receiving concomitant Xeloda® and oral coumarin-derivative…”, “Occurrence: Within several days and up to several months…”, and “Predisposing factors: age > 60 years and diagnosis of cancer”. 28. Appendix D was updated to include “Reference for CPS” and subsequent data table. 29. Appendix D was updated to include “Reference index for performance score” and subsequent data table. 30. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.4: Updated to remove phrase “with or without” and included margetuximab-cmkb. 2. Initial Approval Criteria, I.A.4.d: Updated age criteria from As monotherapy or in combination with either lapatinib or neratinib in HER2 positive disease with brain metastases to As monotherapy or in combination with either lapatinib or neratinib, trastuzumab and tucatinib in HER2 positive disease with brain metastases. 3. Initial Approval Criteria, I.F.4.c: Updated to include new combination criteria “cisplatin or oxaliplatin, trastuzumab and pembrolizumab.” 4. Initial Approval Criteria, I.G.4: Updated to include criteria a and b, high risk disease or recurrent/progressive tumor. 5. Initial Approval Criteria, I.I.4.b: Updated to remove cisplatin. 6. Initial Approval Criteria, I.I.4.c: Updated to remove treatment for unresected disease. 7. Initial Approval Criteria, I.K.4.b: Update to remove bevacizumab. 8. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C.	02/10/2022	04/18/2022

9. References were reviewed and updated.		
Policy was reviewed: 1. Background: Updated to remove prior information regarding Adjuvant Colon Cancer, Metastatic Colorectal Cancer and Metastatic Breast Cancer • Adjuvant colon cancer (i.e., 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." 2. Background: Updated to include new information regarding Colorectal Cancer, Breast Cancer, Gastric, Esophageal, or Gastroesophageal Junction Cancer and Pancreatic Cancer. 3. Dosing Information, Indication, Dosing Regimen and Maximum dose: Updated to include new dosing information for indications, Breast Cancer, Colorectal Cancer, Pancreatic Cancer and Gastric, Esophageal or Gastroesophageal Junction Cancer. 4. Initial Approval Criteria, I.A.1: Updated diagnostic criteria to include "advanced or metastatic". 5. Initial Approval Criteria, I.A.4: Updated to include new prescribing criteria: a. As single agent if an anthracycline- or taxane-containing chemotherapy is not indicated; b. In combination with docetaxel after disease progression on prior anthracycline-containing chemotherapy. 6. Initial Approval Criteria, I.A.6.b: Updated to include new dosing criteria, Dose does not exceed 1250 mg/m2 twice a day on days 1 to 14, every 21 days in combination with docetaxel 75 mg/m2 on day 1 of each cycle. 7. Initial Approval Criteria, I.B.1: Updated diagnostic criteria from Diagnosis of colorectal or rectal cancer to Diagnosis of colorectal cancer and any one of the following (a, b or c): a. Stage III colon cancer; b. Locally advanced rectal cancer; c. Unresectable or metastatic colorectal cancer.	04/04/2023	04/13/2023

8. Initial Approval Criteria, I.B.4.e: Updated to include new prescribing criteria As a single agent or as a component of a combination chemotherapy regimen. 9. Initial Approval Criteria, I.B.6: Updated dosing criteria to: a. Adjuvant Treatment of Colon Cancer (maximum of 8 cycles) and Unresectable or Metastatic Colorecta Cancer (i or ii): i. Single agent: Dose does not exceed 1250 mg/m2 twice a day on days 1 to 14, every 21 day; ii. In combination with Oxaliplatin-Containing Regimens: Dose does not exceed 1000 mg/m2 twice a day on days 1 to 14, every 21 days in combination with oxaliplatin 130 mg/m2 on day 1 of each cycle; b. Perioperative Treatment of Rectal Cancer (i or ii): i. With concomitant radiation therapy: 825 mg/m2 orally twice daily; ii. Without radiation therapy: 1,250 mg/m2 orally twice daily 10. Initial Approval Criteria, I.D: Updated to include approval criteria for indication, Gastric, Esophageal or Gastroesophageal Junction Cancer. 11. Initial Approval Criteria, I.E: Updated to include approval criteria for indication, Pancreatic Cancer. 12. Initial Approval Criteria, I.F: Created a single approval criteria for all the off label indication as "Additional NCCN Recommended Uses (off-label)". 13. Continued Therapy Approval Criteria, II.A.3: Updated to include new dosing criteria for indications, Breast Cancer, Colorectal Cancer, Pancreatic Cancer and Gastric, Esophageal or Gastroesophageal Junction Cancer. 14. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed. 1. Removed age criteria. 2. Removed dosing criteria. 3. Removed reauthorization requirement for positive response to therapy.	12/5/2023	11/30/2023
Policy was reviewed: 1. Removed off-label indications.	4/2/2024	

2. Changed approval duration to 12 months for all indications. 3. Removed creatinine clearance restrictions. 4. References were reviewed and updated. 5. Removed prescriber restrictions		