CAPECITABINE

Generic	Brand	HICL	GCN	Exception/Other
CAPECITABINE	XELODA	18385		

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of Stage III (Duke's C) colon cancer?

   If yes, **approve for 12 fills by GPID as requested up to #112 (500mg tablets) and #56 (150mg tablets) per 21 days.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #2.

2. Does the patient have a diagnosis of metastatic colorectal cancer (mCRC)?

   If yes, continue to #3.
   If no, continue to #4.

3. Is Xeloda being used in combination with oxaliplatin (CapeOX or XELOX regimen) or as monotherapy?

   If yes, **approve for 12 fills by GPID as requested up to #112 (500mg tablets) and #56 (150mg tablets) per 21 days.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

4. Does the patient have a diagnosis of metastatic breast cancer?

   If yes, continue to #5.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

5. Has the patient failed an anthracycline-containing therapy (such as epirubicin or doxorubicin)?

   If yes, continue to #6.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

CONTINUED ON NEXT PAGE

CAPECITABINE

GUIDELINES FOR USE (CONTINUED)

6. Is the patient using Xeloda in combination with docetaxel?

   If yes, **approve for 12 fills by GPID as requested up to #112 (500mg tablets) and #56 (150mg tablets) per 21 days.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, continue to #7.

7. Has the patient failed paclitaxel?

   If yes, **approve for 12 fills by GPID as requested up to #112 (500mg tablets) and #56 (150mg tablets) per 21 days.**
   APPROVAL TEXT: Please note that this drug has an important FDA safety warning. For more information, please ask your doctor or pharmacist.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

DENIAL TEXT: Approval requires a diagnosis of Stage III (Duke's C) colon cancer; or a diagnosis of metastatic colorectal cancer (mCRC) and that Xeloda is being used in combination with oxaliplatin (CapeOX or XELOX regimen) or as a monotherapy; or a diagnosis of metastatic breast cancer and that Xeloda is being used as monotherapy in patients resistant to both paclitaxel and an anthracycline-containing regimen or is being used in combination with docetaxel after failure of prior anthracycline-containing therapy. The required therapies may require a prior authorization and may be covered under the medical benefit.

RATIONALE

To ensure appropriate use of Xeloda consistent with FDA approved indication and NCCN guidelines.

Xeloda (capecitabine) which is the pro-drug of 5-fluorouracil (5-FU), is administered orally with food. The daily dose is 1250mg/m^2 given in two divided doses approximately 12 hours apart at the end of a meal. Individual doses will vary by patient based on the body surface area. Xeloda is approved as first-line monotherapy for mCRC when treatment with fluoropyrimidine therapy alone is preferred and as adjuvant therapy for patients with Stage III (Duke's C) colon cancer. It is also FDA approved for the treatment of breast cancer and has demonstrated efficacy in several other cancers.

NCCN Guidelines Version 2.2013: Colon Cancer / NCCN Guidelines Version 3.2013 Rectal Cancer
Surgical removal is the preferred treatment for early stage disease. Surgery is accompanied by adjuvant chemotherapy for patients with high-risk features or more extensive cancer involvement.

CONTINUED ON NEXT PAGE

CAPECITABINE

RATIONALE (CONTINUED)
Primary treatment options for resectable synchronous metastases are:
- Chemotherapy (FOLFIRI, FOLFOX, or CapeOX) with or without Avastin
- Chemotherapy (FOLFIRI or FOLFOX) with or without Vectibix (KRAS wild-type patients only)
- Chemotherapy (FOLFIRI) with or without Erbitux (KRAS wild-type patients only)
- Staged resection
- Infusional IV 5-FU with radiation

Primary treatment options for unresectable metachronous metastases previously treated with adjuvant FOLFOX are:
- FOLFIRI with or without Avastin
- FOLFIRI with or without Zaltrap
- Irinotecan with or without Avastin
- Irinotecan with or without Zaltrap
- FOLFIRI or irinotecan with Erbitux or Vectibix (KRAS wild-type patients only)

Initial therapy options for treatment of mCRC in patients appropriate for intensive therapy are:
- FOLFOX, with or without Avastin
- FOLFOX, with or without Vectibix (KRAS wild-type patients only)
- CapeOX with or without Avastin
- FOLFIRI with or without Avastin
- FOLFIRI with our without Erbitux or Vectibix (KRAS wild-type patients only)
- 5-FU/leucovorin or Xeloda with or without Avastin
- FOLFOXIRI

Initial therapy options for treatment of mCRC in patients not appropriate for intensive therapy are:
- Infusional 5-FU with leucovorin or Xeloda with or without Avastin
- Erbitux (KRAS wild-type patients only)
- Vectibix (KRAS wild-type patients only)

Zaltrap in combination with FOLFIRI is a recommended therapeutic regimen following progression of mCRC after an oxaliplatin containing chemotherapy regimen. Stivarga is considered a treatment option in therapy after first, second, or third progression, depending on previous lines of therapy.

Other treatment options after first or second progression include:
- Erbitux or Vectibix with irinotecan (KRAS wild-type patients only)
- FOLFOX, FOLFIRI, CapeOX, or irinotecan with or without Avastin
- Irinotecan and oxaliplatin with or without Avastin

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CAPECITABINE

RATIONALE (CONTINUED)
The Xeloda prescribing information contains one study (X-ACT) supporting its use in the adjuvant setting for patients with Stage III (Duke's C) colon cancer. A total of 1987 patients were randomized to Xeloda or 5-FU/LV. With a median follow-up of 6.9 years, Xeloda was at least equivalent to 5-FU/LV in terms of disease free survival and OS.

There were two pivotal trials of identical design that evaluated Xeloda as a first line treatment for mCRC. The first trial by Hoff randomized a total of 605 patients to treatment with either Xeloda or 5-FU/LV. The Xeloda treated patients experienced a higher overall objective tumor response rate than the 5-FU/LV patients (24.8% vs. 15.5%). The median time to disease progression (4.3 vs. 4.7 months) and median OS (12.5 vs. 13.3) were similar between treatment arms. Quality of life data was not reported. (32) The second trial led by Van Cutsem included 602 patients. The Xeloda treated patients experienced similar overall response rates (18.9% vs. 15.0%), median time to disease progression (5.2 vs. 4.7 months) and OS (13.2 vs. 12.1 months) as the 5-FU/LV group.

Later the XELOX-1 (Study NO16966) trial investigated Xeloda as a first line treatment in combination with oxaliplatin (XELOX) compared to FOLFOX-4. The trial was later amended to include Avastin resulting in four treatment arms: XELOX vs. FOLFOX-4, with either Avastin or placebo. OS was 19.8 months in the pooled XELOX/XELOX placebo/ XELOX Avastin arms vs. 19.5 months in the pooled FOLFOX4/FOLFOX4-placebo/FOLFOX4-Avastin. In the pooled XELOX/XELOX-placebo arms, median OS was 19.0 vs. 18.9 months in the pooled FOLFOX4/FOLFOX4-placebo arms.

A trial led by Ducreux evaluated XELOX vs. FOLFOX-6 for the first line treatment of mCRC. Efficacy of the two regimens was similar with median PFS of 8.8 months with XELOX and 9.3 months with FOLFOX-6, and median OS of 19.9 and 20.5 months, respectively. A quality of life analysis was performed using two scales: the Cancer Quality of Life Questionnaire-C30 (QLQ-C30) and the module 'Chemotherapy Convenience and Satisfaction Questionnaire' (CCSQ) of the Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System; which is a collection of HRQoL questionnaires related to the management of chronic illnesses, measures the health-care satisfaction of patients. Both regimens had a similar quality of life profile but XELOX was perceived as more convenient and satisfactory to patients.

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CAPECITABINE

FDA APPROVED INDICATIONS

Xeloda is approved for:

- Adjuvant Colon Cancer
  - Patients with Stage III (Duke's 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

REFERENCES

- Xeloda [Prescribing Information]. South San Francisco, CA: Genentech Inc.
- National Comprehensive Cancer Network. Colon Cancer Guideline Version 3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf [Accessed October 1, 2012].
- National Comprehensive Cancer Network. Rectal Cancer Guideline Version 3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf [Accessed October 1, 2012].

Library	Commercial	NSA
Yes	Yes	No

Part D Effective: N/A
Commercial Effective: 10/01/13

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