TRUVEN HEALTH ANALYTICS

## COMPENDIA TRANSPARENCY TRACKING FORM

**DRUG:** Capecitabine

**INDICATION:** Stage lll colon cancer, adjuvant, in combination with oxaliplatin

| COMPENDIA TRANSPARENCY REQUIREMENTS | |
|---|---|
| 1 | Provide criteria used to evaluate/prioritize the request (therapy) |
| 2 | Disclose evidentiary materials reviewed or considered |
| 3 | Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest |
| 4 | Provide meeting minutes and records of votes for disposition of the request (therapy) |

**EVALUATION/PRIORITIZATION CRITERIA:** **A, C, S**
*to meet requirement 1

| CODE | EVALUATION/PRIORITIZATION CRITERIA |
|---|---|
| **A** | Treatment represents an established standard of care or significant **advance** over current therapies |
| **C** | **Cancer** or cancer-related condition |
| **E** | Quantity and robustness of **evidence** for use support consideration |
| **L** | **Limited** alternative therapies exist for condition of interest |
| **P** | **Pediatric** condition |
| **R** | **Rare** disease |
| **S** | **Serious**, life-threatening condition |

**Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]**

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## EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

| CITATION | STUDY-SPECIFIC COMMENTS | LITERATURE CODE |
|---|---|---|
| Haller,D.G., et al: Capecitabine Plus Oxaliplatin Compared With Fluorouracil and Folinic Acid As Adjuvant Therapy for Stage III Colon Cancer. Journal of Clinical Oncology Apr 10, 2011; Vol 29, Issue 11; pp. 1465-1471. | Study methodology comments:<br>This was a randomized, open-label, multicenter, comparative trial with many strengths. Strengths of the study included 1) defined primary and secondary outcomes; 2) confirmed the diagnosis; 3) power analysis; 4) conducted analyses on the intent-to-treat population; 5) had both inclusion and exclusion criteria; 6) compared baseline characteristics of treatment groups; 7) controlled for the effect of many potential confounding factors on treatment outcome; 8) randomization was done centrally; and 9) presented 95% confidence intervals. Weaknesses were 1) possible selection bias since patients were not recruited in a random or consecutive manner; 2) open-label design without the use of independent reviewers; and 3) partial explanation of randomization procedure. | S |
| Schmoll,H.J., et al: Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: A planned safety analysis in 1,864 patients. Journal of Clinical Oncology Jan 01, 2007; Vol 25, Issue 1; pp. 102-109. | Study methodology comments:<br>This paper presented the results of the safety analysis of the study above. | S |

| | | |
|---|---|---|
| Schmoll,H.J., et al: Final safety findings from a randomized phase III trial of capecitabine plus oxaliplatin (XELOX) vs. bolus 5-FU/LV as adjuvant therapy for patients (pts) with stage III colon cancer. Journal of Clinical Oncology Jun 20, 2006; Vol 24, Issue 18; pp. 163S-163S. | Study methodology comments:<br>Abstract | 3 |
| Jonker,D.J., Spithoff,K., and Maroun,J.: Adjuvant Systemic Chemotherapy for Stage II and III Colon Cancer after Complete Resection: An Updated Practice Guideline. Clinical Oncology Jun 2011; Vol 23, Issue 5; pp. 314-322. | | 4 |

**Literature evaluation codes: S = Literature selected; 1 = Literature rejected = Topic not suitable for scope of content; 2 = Literature rejected = Does not add clinically significant new information; 3 = Literature rejected = Methodology flawed/Methodology limited and unacceptable; 4 = Other (review article, letter, commentary, or editorial)**

## CONTRIBUTORS:

*to meet requirement 3

| PACKET PREPARATION | DISCLOSURES | EXPERT REVIEW | DISCLOSURES |
|---|---|---|---|
| Margi Schiefelbein, PA | None | Edward P. Balaban, DO | None |
| Stacy LaClaire, PharmD | None | James E. Liebmann, MD | None |
| Felicia Gelsey, MS | None | Gerald J. Robbins, MD | None |
| | | Keith A. Thompson, MD | None |
| | | John M. Valgus, PharmD | None |

## ASSIGNMENT OF RATINGS:

*to meet requirement 4

| | EFFICACY | STRENGTH OF RECOMMENDATION | COMMENTS | STRENGTH OF EVIDENCE |
|---|---|---|---|---|
| **MICROMEDEX** | --- | | | B |
| **Edward P. Balaban, DO** | Evidence favors efficacy | Class IIb - Recommended, In Some Cases | When compared to Leucovorin / 5-FU- the results would predictably favor oxaliplatin – based programs like (Capox) and would be similar to results seen with other Oxaliplatin – based programs (FOLFOX). Therefore Capox is efficacious in this population. But lack of confirmatory data and adverse effects keep it recommended for only “some cases.” | N/A |

| | | | | |
|---|---|---|---|---|
| **James E. Liebmann, MD** | Effective | Class I - Recommended | Xeloda is already FDA-approved as adjuvant therapy of colon cancer (Stage lll) when treatment with 5-FU would be preferred. No16968 is the logical extension of assessing Xeloda and Oxaliplatin (Xelox) vs 5-FU, analogous to previous studies of FOLFOX vs 5-FU. Like FOLFOX, Xelox resulted in about a 4-5% absolute improvement in DFS compared to 5-FU. Toxicity of Xelox is what one would expect from Oxaliplatin. It is likely that Xelox = FOLFOX as adjuvant therapy of stage lll colon cancer. | N/A |
| **Gerald J. Robbins, MD** | Effective | Class I - Recommended | If you consider Capecitabine equivalent to 5FU/LV regimens, but with different toxicity profile, then study really compares Oxaliplatin vs no Oxaliplatin. However, proves that Xelox better than 5FU/FA but comparison to FOLFOX open. Would recommend regimen, but choice open to toxicity and cost compared to FOLFOX. | N/A |
| **Keith A. Thompson, MD** | Evidence favors efficacy | Class IIa - Recommended, In Most Cases | None | N/A |
| **John M. Valgus, PharmD** | Evidence favors efficacy | Class IIa - Recommended, In Most Cases | Haller trial suggests superiority vs FU/LV. Current NCCN guidelines have as category 1 recommendation based on this data. Abstract data suggest Capox may be more toxic than FOLFOX. | N/A |