TRUVEN HEALTH ANALYTICS
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COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 3/20/2018

PACKET: 1656

DRUG: Pyridoxine

USE: Prophylaxis, acral erythema due to cytotoxic therapy in patients receiving capecitabine-containing chemotherapy

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: C, E *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
Zhou,Y., et al: Prophylactic pyridoxine was not able to reduce the incidence of capecitabine-induced hand-foot syndrome: A meta-analysis. Biomed.Rep. Nov 2013; Vol 1, Issue 6; pp. 873-878.		3
Yoon-Koo Kang, et al. Pyridoxine Is Not Effective to Prevent Hand-Foot Syndrome Associated With Capecitabine Therapy: Results of a Randomized, Double-Blind, Placebo-Controlled Study. J Clin Oncol 28:3824-3829.	This was a randomized, double-blind, placebo-controlled trial. Overall, this study was at low risk of biases associated with lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with poor random sequence generation and allocation concealment was unclear and not discussed in the paper.	S
Yap,Y.S., et al: Predictors of hand-foot syndrome and pyridoxine for prevention of capecitabine-induced hand-foot syndrome: a randomized clinical trial. JAMA Oncol. Nov 01, 2017; Vol 3, Issue 11; pp. 1538-1545.	This was a single-center, randomized double-blind, placebo-controlled phase 3 trial that included 210 patients receiving capecitabine single-agent only. A major caveat of the study was that the trial was terminated before reaching the original target of 296 patients due to slow accrual associated with the declining use of single agent capecitabine, especially for gastrointestinal cancers. The study was designed to have 80% power to detect a reduction in incidence of grade 2 or higher HFA from 36% to 20% with 123 patients per group. The study had 105 patients per group and did not find a between-group difference in incidence rates. Overall, this study was at low risk of biases associated with lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with poor random sequence generation and allocation concealment was unclear and not discussed in the paper. The study controlled for potential confounding factors.	S

Corrie et al. A randomised study evaluating the use of pyridoxine to avoid capecitabine dose modifications. British Journal of Cancer (2012) 107, 585–587	This multi-site, randomized, double-blind, placebo-controlled, phase 3 study was conducted at 10 UK sites. A major caveat of the study was that it did not meet it's power requirements. The study was designed to recruit 270 patients to detect a reduction in the incidence of dose modification from 30 to 15% with 80% power and allowance for dropouts. Slower than expected recruitment rate was due to decreasing numbers of patients being treated with capecitabine as a single agent and caused the study to close prematurely. Overall, this study was at low risk of biases associated with lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with poor random sequence generation and allocation concealment was unclear and not discussed in the paper.	S
Braik,T., et al: Randomized trial of vitamin B6 for preventing hand-foot syndrome from capecitabine chemotherapy. J Community Support.Oncol. Feb 2014; Vol 12, Issue 2; pp. 65-70.	This was a randomized double-blind, placebo-controlled phase 2 trial. A sample size of 47 subjects was planned in each group to provide 80% power to detect a difference of 30 percentage points between groups in the incidence of HFS (e.g., 25% vs 55%). However, because of slow accrual, 38 patients were enrolled in the vitamin B6 arm and 39 patients were enrolled in the placebo arm. The reason for the slow accrual was the tendency for most oncologists in the participating hospital group to prefer 5-FU infusion over capecitabine. Overall, this study was at low risk of biases associated with lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with poor random sequence generation and allocation concealment was unclear and not discussed in the paper.	S
Ota,M., et al: The effect of pyridoxine for prevention of hand-foot syndrome in colorectal cancer patients with adjuvant chemotherapy using capecitabine: a randomized study. Hepatogastroenterology. Jun 2014; Vol 61, Issue 132; pp. 1008-1013.		4

Yoshimura,A., et al: A randomized phase II study evaluating the use of prydoxine to prevent hand-foot syndrome associated with capecitabine therapy for advanced or metastatic breast cancer. Journal of Clinical Oncology 2014; Vol 32, Issue 15 SUPPL. 1; p. 9610.		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
Felicia Gelsey, MS	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.

ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	Evidence is Inconclusive	Class III: Not Recommended		B
John D Roberts	Evidence is Inconclusive	Class III: Not Recommended	Multiple underpowered trials show no benefit for pyridoxine in preventing acral erythema in patients receiving capcetabine-containing chemotherapy. Presumably no meta-analysis has been performed.	N/A
Jeffrey Klein	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	The use of pyridoxine to prevent erythema (hand-foot syndrome) in patients taking capecitabine was not as very effective in 3 of the 4 studies presented. One study did demonstrate some degree of reducing the severity of the skin ailment as well as preventing a dose reduction of capecitabine. Pyridoxine is a safe product with no significant adverse effects.	N/A
Richard LoCicero	Ineffective	Class III: Not Recommended	At least 4 clinical trials have been performed and published addressing the role for pyridoxine as a chemopreventive of capecitabine associated acral erythema. Pyridoxine did not improve outcomes nor was it associated with decreased capecitabine.	N/A