TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Celecoxib

INDICATION: Prevention of sporadic colorectal adenomas, in high-risk patients

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, L**
*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
Bertagnolli,M.M., et al: Celecoxib for the prevention of sporadic colorectal adenomas. N Engl J Med Aug 31, 2006; Vol 355, Issue 9; pp. 873-884.	Study methodology comments: This was a rigorously designed randomized, multicenter, placebo-controlled trial with many strengths. A central study pathologist examined all polyps removed during study colonoscopies in a blinded manner. Additional strengths of the study included 1) defined primary and secondary outcomes; 2) conducted power analysis; 3) provided 95% confidence intervals; 4) controlled for the effect of potential confounding factors on outcomes; 5) had inclusion and exclusion criteria; and 6) compared baseline characteristics of groups. Weaknesses included: 1) possible selection bias since subjects were not recruited in a random or consecutive manner; and 2) partial explanation of method of randomization.	S
Bertagnolli,M.M., Eagle,C.J., Zauber,A.G., et al: Five-year efficacy and safety analysis of the Adenoma Prevention with Celecoxib Trial. Cancer Prev Res (Phila) Apr 2009; Vol 2, Issue 4; pp. 310-321.	Study methodology comments: This was a five-year safety and efficacy analysis of the Bertagnolli et al 2006 study.	S
Arber,N., et al: Celecoxib for the prevention of colorectal adenomatous polyps. N Engl J Med Aug 31, 2006; Vol 355, Issue 9; pp. 885-895.	Study methodology comments: This was a rigorously designed randomized, double-blind, multicenter, placebo-controlled trial with many strengths. Additional strengths of the study included 1) defined primary and secondary outcomes; 2) conducted power analysis; 3) provided 95% confidence intervals; 4) controlled for the effect of potential confounding factors on outcomes; 5) conducted a single-blind, placebo-controlled run-in period; 6) had inclusion and exclusion criteria; and 7) compared baseline characteristics of groups. Weaknesses included: 1) possible selection bias since subjects were not recruited in a random or consecutive manner; and 2) partial explanation of method of randomization.	S
Arber,N., Spicak,J., Racz,I., et al: Five-year analysis of the prevention of colorectal sporadic adenomatous polyps trial. Am J Gastroenterol Jun 2011; Vol 106, Issue 6; pp. 1135-1146.	This was a rigorously designed randomized, double-blind, multicenter, placebo-controlled trial with many strengths. Additional strengths of the study included 1) defined primary and secondary outcomes; 2) conducted power analysis; 3) provided 95% confidence intervals; 4) controlled for the effect of potential confounding factors on outcomes; 5) conducted a single-blind, placebo-controlled run-in period; 6) had inclusion and exclusion criteria; and 7) compared baseline characteristics of groups. Weaknesses included: 1) possible selection bias since subjects were not recruited in a random or consecutive manner; and 2) partial explanation of method of randomization.	S

Solomon,S.D., et al: Effect of celecoxib on cardiovascular events and blood pressure in two trials for the prevention of colorectal adenomas. Circulation Sep 05, 2006; Vol 114, Issue 10; pp. 1028-1035.	Study methodology comments: This was a combined analysis that was not prespecified in either the APC or PreSap trial protocols. The analysis used the raw data from each trial while preserving the randomization structure of each study. Before the unblinding of the both trials, the Cardiovascular Safety Committee selected the composite end point of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or heart failure as the primary cardiovascular safety end point. The results should be interpreted with much caution due to the very low event rates and wide confidence intervals. Due to the low event rates, the analyses had limited statistical power. Strengths of the analysis were 1) included all trial participants; 2) controlled for the effect of confounds; 3) maintained randomization structure of each trial; 4) compared baseline characteristics of trial participants; 5) conducted a blinded analysis of cardiovascular events; 6) trials used uniform definitions and procedures; and 7) analyses were based on adjudicated prespecified outcomes.	S
Solomon,S.D., et al: Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. N Engl J Med Mar 17, 2005; Vol 352, Issue 11; pp. 1071-1080.	Study methodology comments: The authors reviewed all potentially serious cardiovascular events among the participants in the APC trial.	2
Cooper,K., et al: Chemoprevention of colorectal cancer: systematic review and economic evaluation. Health technology assessment (Winchester, England) Jun 2010; Vol 14, Issue 32; pp. 1-206.		4
Lance,Peter: Sporadic Aberrant Crypt Foci Are Not a Surrogate Endpoint for Colorectal Adenoma Prevention. Cancer Prevention Research Jun 2008; Vol 1, Issue 1; pp. 4-8.		4
Asano,T.K. and Mcleod,r.S.: Non steroidal anti-inflammatory drugs (NSAID) and Aspirin for preventing colorectal adenomas and carcinomas. Cochrane database of systematic reviews (Online) 2004; Issue 2; p. CD004079.		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)

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CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Margi Schiefelbein, PA	None	Jeffrey A. Bubis, DO	Other payments: Dendreon
Stacy LaClaire, PharmD	None	Thomas McNeil Beck, MD	None
Felicia Gelsey, MS	None	Keith A. Thompson, MD	None
		James E. Liebmann, MD	None
		John M. Valgus, PharmD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Jeffrey A. Bubis, DO	Ineffective	Class lll: Not Recommended	Risk outweighs potential benefits and trials not completed	N/A
Thomas McNeil Beck, MD	Evidence Favors Efficacy	Class llb: Recommended, In Some Cases	Cardiovascular risk must be evaluated.	N/A
Keith A. Thompson, MD	Evidence Favors Efficacy	Class llb: Recommended, in Some Cases	Physician may consider in light of increased C.V. risk.	N/A

James E. Liebmann, MD	Ineffective	Class lll: Not Recommended	While COX-2 inhibitors clearly lower the risk of developing adenomas, there is no evidence from any study that they lower the risk of colon cancer. All trials show a consistent increased risk of cardiovascular events in groups treated with Celecoxib. Finally, it appears that the “protection” from adenomas only exists while patients are taking Celecoxib – note the increased rates of adenoma formation in the Celecoxib group between years 3 and 5 in the PreSAP Trial. It is impossible to justify use of a drug that has so little benefit and such substantial risk	N/A
John M. Valgus, PharmD	Evidence Favors Efficacy	Class llb: Recommended, In Some Cases	Data clearly demonstrates Celecoxib is effective in reducing adenomas. Safety data is also clear that this is at cost of increasing cardiovascular events. Therefore, this can only be recommended in select patients where benefits outweigh risk of cardiovascular disease	N/A