TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Dexmethylphenidate

INDICATION: Fatigue, cancer-related

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
Moraska,Phase III, Randomized, Double-Blind, Placebo-Controlled Study of Long-Acting Methylphenidate for Cancer-Related Fatigue: North Central Cancer Treatment Group NCCTG-N05C7 Trial. J Clin Oncol 28:3673-3679.	Study methodology comments: This was a randomized, double-blind, placebo-controlled trial. Overall, this study was at low risk of biases associated with random sequence generation, lack of blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with allocation concealment was unclear and not discussed in the paper.	S
Eduardo Bruera, et al. Patient-Controlled Methylphenidate for Cancer Fatigue: A Double-Blind, Randomized, Placebo-Controlled Trial. J Clin Oncol 24:2073-2078	Study methodology comments: This was a randomized, double-blind, placebo-controlled trial. Key bias criteria evaluated were (1) random sequence generation of randomization; (2) lack of allocation concealment, (3) lack of blinding, (4) incomplete accounting of patients and outcome events, and (5) selective outcome reporting bias. The study was at low risk of bias for these key criteria, and no additional biases were identified.	S
Andrew J. Roth, et al. Methylphenidate for Fatigue in Ambulatory Men With Prostate Cancer. Cancer 2010;116:5102–10.	Study methodology comments: This was a randomized, double-blind, placebo-controlled trial. Overall, this study was at low risk of biases associated with lack of allocation concealment and blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with random sequence generation was unclear and not discussed in the paper. Interpret with caution since there were only 10 and 13 evaluable subjects per arm.	S
Gong,S., Sheng,P., Jin,H., et al: Effect of methylphenidate in patients with cancer-related fatigue: a systematic review and meta-analysis. PLoS ONE [Electronic Resource] 2014; Vol 9, Issue 1; p. e84391.	Study methodology comments: This was a meta-analysis that included five double-blind, randomized, placebo-controlled trials of 498 patients. The authors used the Jadad scale to measure the quality of the included trials. All studies were deemed of good quality with a score of 3 or more on the Jadad scale. The analyses showed low to moderate heterogeneity (I2 ranged from 0% to 40%). All of the criteria of the SR/MA worksheet were fulfilled.	S

Lower et al. Efficacy of dexmethylphenidate for the treatment of fatigue after cancer chemotherapy: a randomized clinical trial. J Pain Symptom Manage. 2009 Nov;38(5):650-62.	Study methodology comments: This was a randomized, double-blind, placebo-controlled trial. Overall, this study was at low risk for most of the key risk of bias criteria which included lack of allocation concealment and blinding, incomplete accounting of patients and outcome events, and selective outcome reporting. The risk of bias associated with random sequence generation was unclear and not discussed in the paper.	S
Butler et al. A phase III, double-blind, placebo-controlled prospective randomized clinical trial of d-threo-methylphenidate HCl in brain tumor patients receiving radiation therapy. Int J Radiat Oncol Biol Phys. 2007 Dec 1;69(5):1496-501.	Study methodology comments: This was a randomized, double-blind, placebo-controlled trial. Patient accrual terminated early due to the withdrawal of support from the sponsoring drug company. There is a possible high risk of bias associated with the large rate of attrition. Fifty-three percent of the patients dropped out of the study. The authors concluded that the early dropout was related to some of the patient covariates but not to the actual outcome measures. The study was at low risk of bias associated with lack of blinding and selective outcome reporting. The risk of bias associated with random sequence generation and allocation concealment was unclear and not discussed in the paper.	S
Peuckmann,V., Elsner,F., Krumm,N., et al: Pharmacological treatments for fatigue associated with palliative care. Cochrane Database of Systematic Reviews 2010; Vol 2010, Issue 11; p. 1.		2

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	Edward P. Balaban, DO	None
Felicia Gelsey, MS	None	Keith A. Thompson, MD	None
		Thomas McNeil Beck, MD	None
		James E. Liebmann, MD	None

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		A
Jeffrey A. Bubis, DO	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	3/5 randomized trials demonstrate benefit, though the methodologies are different. It can be considered in select patients for whom potential toxicities can be managed effectively and for whom the risk: potential benefit ratio is in favor of therapy.	N/A
Edward P. Balaban, DO	Ineffective	Class III: Not Recommended	As with methylphenidate, this drug has been studied enough with little impact.	N/A
Keith A. Thompson, MD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	None	N/A
Thomas McNeil Beck, MD	Ineffective	Class III: Not Recommended	Cancer related fatigue specifically and QOL generally were not improved. Side effects common.	N/A

James E. Liebmann, MD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	The available trials concerning this subject are small and inconclusive. However, there seems to be agreement that there is little toxicity from the use of methylphenidate in the treatment of cancer related fatigue. The meta-analysis of the trials suggested a trend towards improvement in fatigue with the use of methylphenidate. The single largest trial, by Moraska et al, while negative overall, did suggest an improvement in fatigue with methylphenidate use in the patients with the most fatigue or advanced cancers. Hence, the drug may be useful for select patients.	N/A