TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Dutasteride

INDICATION: Prostate cancer prophylaxis in high risk men

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
Andriole,G.L., et al: Effect of dutasteride on the risk of prostate cancer. N Engl J Med Apr 01, 2010; Vol 362, Issue 13; pp. 1192-1202.	Study methodology comments: This was a 4-year, double-blind, placebo-controlled, randomized 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
Grubb,R.L., Andriole,G.L., Somerville,M.C., et al: The REDUCE Follow-Up Study: low rate of new prostate cancer diagnoses observed during a 2-year, observational, followup study of men who participated in the REDUCE trial. Journal of Urology Mar 2013; Vol 189, Issue 3; pp. 871-877.		S
Pinsky,P.F., et al: Projecting prostate cancer mortality in the PCPT and REDUCE chemoprevention trials. Cancer Feb 01, 2013; Vol 119, Issue 3; pp. 593-601		2
Nguyen,C.T., et al: The REDUCE metagram: a comprehensive prediction tool for determining the utility of dutasteride chemoprevention in men at risk for prostate cancer. Front Oncol 2012; Vol 2, p. 138.		3
Walsh,P.C.: GSK statement on avodart(trademark) (dutasteride) for prostate cancer risk reduction. Journal of Urology Aug 2011; Vol 186, Issue 2; p. 530.		4

Kramer,B.S., Hagerty,K.L., Justman,S., et al: Use of 5-(alpha)-reductase inhibitors for prostate cancer chemoprevention: American society of clinical oncology/American Urological Association 2008 clinical practice guideline. Journal of Clinical Oncology Mar 20, 2009; Vol 27, Issue 9; pp. 1502-1516.		4
Graham,L.: ASCO and AUA release guideline on prostate cancer chemoprevention with 5-alpha reductase inhibitors. American Family Physician Jan 01, 2010; Vol 81, Issue 1; p. 76.		4
None Listed: Medication safety and reliability: FDA warns 5-ARIs may increase the risk of high-grade prostate cancer. Formulary Aug 2011; Vol 46, Issue 8; p. 313.		4
Walsh,P.C.: Re: Usefulness of Prostate-Specific Antigen (PSA) rise as a marker of prostate cancer in men treated with dutasteride: Lessons from the REDUCE study. Journal of Urology Jan 2012; Vol 187, Issue 1; pp. 144-145		4
Schroder,F.H. and Roobol,M.J.: Editorial: The REDUCE trial. European Urology Aug 2010; Vol 58, Issue 2; pp. 253-255.		4
Walsh,P.C.: Re: Projecting prostate cancer mortality in the PCPT and REDUCE chemoprevention trials: Editorial comment. Journal of Urology Dec 2012; Vol 188, Issue 6; pp. 2226-2227.		4

Schroder,F., Bangma,C., Angulo,J.C., et al: Reply from authors re: Behfar Ehdaie, Karim A. Touijer. 5-Alpha reductase inhibitors in prostate cancer: From clinical trials to clinical practice. Eur Urol 2013;63:788-9: 5-Alpha reductase inhibitors in prostate cancer. European Urology May 2013; Vol 63, Issue 5; pp. 790-791.		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)

TRUVEN HEALTH ANALYTICS

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Margi Schiefelbein, PA	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	Thomas McNeil Beck, MD	None
Felicia Gelsey, MS	None	Thomas A. Marsland, MD	None
		James E. Liebmann, MD	None
		Jeffrey A. Bubis, DO	Other payments: Dendreon

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Edward P. Balaban, DO	Evidence is inconclusive	Class IIb - Recommended, In Some Cases	Difficult to rate. Dutasteride experience essentially the same as finasteride. Cuts down on risk of prostate cancer overall, but with an increased risk of high grade lesions. No survival data to compare. Thus, efficacy overall is a draw.	N/A
Thomas McNeil Beck, MD	Evidence is inconclusive	Class IIb - Recommended, In Some Cases	Primary end point was prostate cancer on biopsy. Survival benefit?	N/A

Thomas A. Marsland, MD	Evidence favors efficacy	Class IIa - Recommended, In Most Cases	So difficult issue paper only one study, but large multi institution randomized and blinded shows benefit for listed primary outcome concern only one trial, but supported by the PCPT which looked at a different drug in same class. Indication is for “high risk,” but was a “limited” high risk since some patients at high risk were excluded, so can these results be extrapolated to “all” high risk patients? Also I have concerns about the questions asked and objective of the study. The reduction was mostly in low grade [Gleasen < 7] tumor which may NOT be clinically significant cancers. More and more literature suggests these can be watched and not even treated. SO even though this is a positive trial, does using this drug really have an impact on the natural history of the disease? Did we change prostate cancer deaths and this is the real question that should drive the usage of the drug, but the study never addressed that (indeed there were no prostate cancer deaths in either arm)	N/A

James E. Liebmann, MD	Evidence favors efficacy	Class IIb - Recommended, In Some Cases	The results of the REDUCE trial almost exactly recapitulate the results of the Prostate Cancer Prevention Trial (PCPT) that used finasteride to reduce the risk of prostate cancer. Given that finasteride and dutasteride have similar mechanisms of action, these results are not surprising, but are reassuring in that they enhance the credibility of the PCPT results. The real question for dutasteride is, how does it compare to finasteride? Dutasteride is a reasonable option for prostate cancer prevention, but so is finasteride and there is more experience and longer follow-up data with finasteride.	N/A
Jeffrey A. Bubis, DO	Evidence is inconclusive	Class III - Not Recommended	Data demonstrating that this agent clearly reduces the risk of prostate cancer is lacking and inconclusive. There appears to be a reduction in the risk of disease overall, but an increase in high grade disease.	N/A