TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Acitretin

INDICATION: Prophylaxis of skin cancers, in high-risk renal transplant recipients

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, R, 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
Bouwes Bavinck,Jan N.: Prevention of skin cancer and reduction of keratotic skin lesions during acitretin therapy in renal transplants recipients: A double-blind, placebo-controlled study. Journal of Clinical Oncology 1995; Vol 13, Issue 8; pp. 1933-1938.	Study methodology comments: This was a double-blind, randomized, placebo-controlled trial. Additional strengths of the study included 1) had both inclusion and exclusion criteria; 2) controlled for the effect of confounding factors on outcomes; 3) conducted a power analysis; 4) compared baseline characteristics of groups; 5) explained method of randomization; 6) each subject was evaluated by the same assessor; 7) confirmed lesions; and 8) presented 95% confidence intervals. Selection bias may have been present since patients were not recruited in a random or consecutive manner.	S
Harwood,C.A.: Low-dose retinoids in the prevention of cutaneous squamous cell carcinomas in organ transplant recipients: A 16-year retrospective study. Archives of Dermatology Apr 01, 2005; Vol 141, Issue 4; pp. 456-464.	Study methodology comments: This was a retrospective cohort study that should be interpreted with some caution. Strengths of the study included 1) had both inclusion and exclusion criteria; 2) histologically confirmed CIS; 3) presented 95% confidence intervals; and 4) reduced selection bias by recruiting all presenting subjects. Weaknesses included 1) open-label design without the use of independent assessors; 2) absence of a power analysis; 3) no control group; and 4) did not examine the effect of potential confounding factors on outcomes.	S
de Sévaux RG, et al. Acitretin treatment of premalignant and malignant skin disorders in renal transplant recipients: clinical effects of a randomized trial comparing two doses of acitretin. J Am Acad Dermatol. 2003 Sep;49(3):407-12.	Study methodology comments: This was an open-label, randomized, comparative trial that should be interpreted with caution. Strengths of the study included 1) had both inclusion and exclusion criteria; 2) defined outcomes; 3) controlled for the effect of confounding factors on outcomes; 4) compared baseline characteristics of groups; and 5) employed one assessor. Weaknesses included 1) open-label design without the use of independent assessors; 2) absence of a power analysis; 3) partial explanation of method of randomization; 4) small sample size; and 5) possible selection bias since the subjects were not recruited in a random or consecutive manner.	3
George R, et al. Acitretin for chemoprevention of non-melanoma skin cancers in renal transplant recipients. Australas J Dermatol. 2002 Nov;43(4):269-73.	Study methodology comments: This was an open-label, randomized, cross-over trial that should be interpreted with much caution. A major weakness of the trial was the high dropout rate. Additional weaknesses included 1) open-label design without the use of independent assessors; 2) absence of a power analysis; 3) did not explain method of randomization; 4) did not examine the effect of potential confounding factors on outcomes; and 5) possible selection bias since patients were not recruited in a random or consecutive manner. Strengths of the study included 1) had both inclusion and exclusion criteria; 2) had a control; and 3) analyzed the intent-to-treat population.	S

Rogozinski,T.: Acitretin in the treatment and prevention of viral, premalignant and malignant skin lesions. Journal of Dermatological Treatment Dec 01, 1989; Vol 1, Issue 2; pp. 91-93.		3
McNamara,Iain Robert, Muir,James, and Galbraith,Andrew John: Acitretin for prophylaxis of cutaneous malignancies after cardiac transplantation. Journal of heart and lung transplantation - the official publication of the International Society for Heart Transplantation Nov 2002; Vol 21, Issue 11; pp. 1201-1205.		3
Yuan ZF, Davis A, Macdonald K, Bailey RR. Use of acitretin for the skin complications in renal transplant recipients. N Z Med J. 1995 Jun 28;108(1002):255-6.		2
McKenna DB, Murphy GM. Skin cancer chemoprophylaxis in renal transplant recipients: 5 years of experience using low-dose acitretin.Br J Dermatol. 1999 Apr;140(4):656-60.		2
Stasko T, et al. Guidelines for the management of squamous cell carcinoma in organ transplant recipients. Dermatol Surg. 2004 Apr;30(4 Pt 2):642-50.		S

None Listed: European best practice guidelines for renal transplantation. Section IV: Long-term management of the transplant recipient. IV.6.2. Cancer risk after renal transplantation. Skin cancers: prevention and treatment. Nephrology, dialysis, transplantation - official publication of the European Dialysis and Transplant Association - European Renal Association 2002; Vol 17 Suppl 4 p31-6, pp. 31-666.		4
Bath-Hextall,F., et al: Interventions for preventing non-melanoma skin cancers in high-risk groups. Cochrane Database of Systematic Reviews (Online) 2007; Issue 4; p. CD005414.		4
Hofbauer,G.F., et al: Swiss clinical practice guidelines for skin cancer in organ transplant recipients. Swiss medical weekly - official journal of the Swiss Society of Infectious Diseases, the Swiss Society of Internal Medicine, the Swiss Society of Pneumology Jul 25, 2009; Vol 139, Issue 29-30; pp. 407-415.		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
Catherine Sabatos, PharmD	None	Edward P. Balaban, DO	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	Jeffrey F. Patton, MD	None
		Gerald J. Robbins, 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	There appears to be justifications in organ transplant recipients that appear prone to keratotic skin lesions; with some associated side effects. The recommendation: In this patient subset is somewhere between Class IIa – IIb.	N/A

James E. Liebmann, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	While studies of Acitretin in this population are small, they strongly support the hypotheses that the drug lowers the risk of developing squamous cell skin cancers in renal transplant patients. The benefit, however, must be weighed against 1) high incidence of side effects, 2) “rebound” high incidence of scc upon discontinuation of the drug, 3) based on #2 above, need for life-long use of the drug with no information on long term risks, 4) no evidence of impact of the drug on over-all survival. Based on the evidence, the drug is reasonable to try, but only in a patient who has a history of squamous cell skin cancer who understands the potential side effects and need for life-long treatment.	N/A
Jeffrey F. Patton, MD	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	Although the supporting trials are small, they support efficacy.	N/A
Gerald J. Robbins, MD	Effective	Class IIa: Recommended, in Most Cases	Although total numbers of patients small, use and clinical trials over many years consistently positive.	N/A
John M. Valgus, PharmD	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	Evidence is not rigorous, but all evidence favors efficacy. Acceptable toxicity profile. Would need larger controlled trials for higher rating.	N/A