

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: May 11, 2023

OFF-LABEL ID #: 2520

DRUG NAME: Imiquimod

OFF-LABEL USE: Vulval intraepithelial neoplasia (VIN); High-grade, squamous

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: A, 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)]

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	LITERATURE CODE
Preti, M, Joura, E, Vieira-Baptista, P, et al: The European Society of Gynaecological Oncology (ESGO), the International Society for the Study of Vulvovaginal Disease (ISSVD), the European College for the Study of Vulval Disease (ECSVD) and the European Federation for Colposcopy (EFC) consensus statements on pre-invasive vulvar lesions. Int J Gynecol Cancer Jul 04, 2022; Vol 32, Issue 7; pp. 830-845.	S
Management of vulvar intraepithelial neoplasia. Committee Opinion No. 675. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;128:e178–82.	S
Lebreton, M, Carton, I, Brousse, S, et al: Vulvar intraepithelial neoplasia: Classification, epidemiology, diagnosis, and management. J Gynecol Obstet Hum Reprod Nov 2020; Vol 49, Issue 9; p. 101801.	4
Lawrie TA, Nordin A, Chakrabarti M, et al. Medical and surgical interventions for the treatment of usual-type vulvar intraepithelial neoplasia. Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD011837.	S
Tristram, A, Hurt, CN, Madden, T, et al: Activity, safety, and feasibility of cidofovir and imiquimod for treatment of vulvar intraepithelial neoplasia (RT3VIN): a multicentre, open-label, randomised, phase 2 trial. Lancet Oncol Nov 2014; Vol 15, Issue 12; pp. 1361-1368.	2
Trutnovsky, G, Reich, O, Joura, EA, et al: Topical imiquimod versus surgery for vulvar intraepithelial neoplasia: a multicentre, randomised, phase 3, non-inferiority trial. Lancet May 07, 2022; Vol 399, Issue 10337; pp. 1790-1798.	S
van Seters, M, van Beurden, M, ten Kate, FJW, et al: Treatment of vulvar intraepithelial neoplasia with topical imiquimod. N Engl J Med Apr 03, 2008; Vol 358, Issue 14; pp. 1465-1473.	2
Terlou A, van Seters M, Ewing PC, et al. Treatment of vulvar intraepithelial neoplasia with topical imiquimod: seven years median follow-up of a randomized clinical trial. Gynecol Oncol. 2011;121(1):157-162.	2
Mathiesen, O, Buus, SK, and Cramers, M: Topical imiquimod can reverse vulvar intraepithelial neoplasia: a randomised, double-blinded study. Gynecol Oncol Nov 2007; Vol 107, Issue 2; pp. 219-222.	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)

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		Howard Goodman	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
IBM MICROMEDEX	Effective	Class IIa: Recommended, in Most Cases		B
Richard LoCicero	Effective	Class IIb: Recommended, in Some Cases	Topical imiquimod was compared to surgical therapy in a phase III non-inferiority clinical trial in women with vulvar high grade squamous intraepithelial lesions. Imiquimod was found to be safe and as effective as the standard management of surgery.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of topical Imiquimod in VIN patients as alternative to surgery appears to be safe and effective in most patient types. The long term benefit of the treatment, as well as the size of the lesions needs to be accounted for. The product seems to be safe as well.	

Howard Goodman	Effective	Class I: Recommended	<p>VIN, or vulvar intraepithelial neoplasia, is a pre cancerous lesion of the vulva classically treated with surgical resection. Depending on size and location, surgery or laser ablation may be associated with scarring, loss of function, or loss of sensation. Imiquimod is a non specific immune modulator that has shown promise as a medical treatment, although not currently approved for this indication by the FDA.</p> <p>Trutnofsky et al. reported a randomized trial demonstrating imiquimod therapy was not inferior to surgical resection. Lawrie et al. performed a Cochrane review of imiquimod use demonstrating durable response and non inferiority to cidofovir.</p> <p>In 2016 the COMMITTEE ON GYNECOLOGIC PRACTICE AMERICAN SOCIETY FOR COLPOSCOPY AND CERVICAL PATHOLOGY added imiquimod to surgical resection and laser ablation as options for treatment for VIN.</p>	
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