COMPENDIA TRANSPARENCY TRACKING FORM

DATE: June 1, 2023

OFF-LABEL ID #: 2574

DRUG NAME: Cidofovir

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
Lawrie, TA, Nordin, A, Chakrabarti, M, et al: Medical and surgical interventions for the treatment of usual-type vulval intraepithelial neoplasia. Cochrane Database Syst Rev Jan 05, 2016; Vol 2016, Issue 1; p. CD011837.	2
Pepas, L, Kaushik, S, Bryant, A, et al: Medical interventions for high grade vulval intraepithelial neoplasia. Cochrane Database Syst Rev Apr 13, 2011; Vol 2011, Issue 4; p. CD007924.	1
Tristram, A, Hurt, CN, Madden, T, et al: Activity, safety, and feasibility of cidofovir and imiquimod for treatment of vulval intraepithelial neoplasia (RT3VIN): a multicentre, open-label, randomised, phase 2 trial. Lancet Oncol Nov 2014; Vol 15, Issue 12; pp. 1361-1368.	S
Hurt, CN, Jones, S, Madden, T-A, et al: Recurrence of vulval intraepithelial neoplasia following treatment with cidofovir or imiquimod: results from a multicentre, randomised, phase II trial (RT3VIN). BJOG Aug 2018; Vol 125, Issue 9; pp. 1171-1177.	S
Stier, EA, Goldstone, SE, Einstein, MH, et al: Safety and efficacy of topical cidofovir to treat high-grade perianal and vulvar intraepithelial neoplasia in HIV-positive men and women. AIDS Feb 20, 2013; Vol 27, Issue 4; pp. 545-551.	3
Tristram, A and Fiander, A: Clinical responses to Cidofovir applied topically to women with high grade vulval intraepithelial neoplasia. Gynecol Oncol Dec 2005; Vol 99, Issue 3; pp. 652-655.	3

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	Two phase II randomized trials have demonstrated efficacy of cidofovir for the treatment of VIN. Cidofovir is one of other effective options for treatment.	
Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	The use of Cidofovir to reduce the recurrence of Vulval intraepithelial neoplasia is quite effective. Adverse effects were minimal. The long term use of cidofovir to reduce the need for surgery was also favorable.	

Howard Goodman	Effective	Class IIa: Recommended, in Most Cases	Vulvar Intraepithelial Neoplasia (VIN) is a premalignant lesion of the vulvar skin felt to be caused by HPV. Classically, surgical excision or laser ablation have been the accepted treatment. These modalities can be associated with significant pain, scarring, change in anatomy, and change in function. Recently 2 topical agents have demonstrated efficacy in treating VIN. Cidofovir is a nucleoside analogue with antiviral properties that has shown activity in a comparable disease (cervical intraepithelial neoplasia). Tristam et al randomized 180 patients to treatment with either Cidofovir or Imiquimod. Histologically confirmed CR was noted in 46% of each group. Patients in both groups with a CR demonstrated persistent resolution of disease with short term follow up at 12 monhts, 87% in the Cidofovir group and 78% in the Imiquomod group. Grade 3 and above toxicity was similar in both groups. A follow up study by Hurt et al. analyzing longer term follow up of the same study group as Tristam et al. demonstrated robust resolution of disease in both groups but a trend towards improved long term efficacy in the Cidofovir cohort. The incidence of grade 2+ toxicity similar in both groups, with no Grade 4+ toxicity reported. Cidofovir appears to be an active agent for the treatmnt of VIN, with similar toxicity to Imiquomod, and a trend towards higher long term response. Imiquomod topical cream commercially available hence easier to prescribe than Cidofovir which requires a compounding pharmacy to formulate. Further study of these agents with larger cohorts may confirm the trend for increased long term efficacy of Cidofovir over Imiquomod.	