IBM Watson Health

COMPENDIA TRANSPARENCY TRACKING FORM

DATE: April 5, 2022

PACKET: 2399

DRUG: Fam-Trastuzumab Deruxtecan-nxki

USE: Non-small cell lung cancer; Advanced disease, previously treated, HER2 mutation-positive

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, 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)]

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Ren S, Wang J, Ying J, et al. Consensus for HER2 alterations testing in non-small-cell lung cancer. ESMO Open. 2022 Feb;7(1):100395.		4
Li BT, Smit EF, Goto Y, et al; DESTINY-Lung01 Trial Investigators. Trastuzumab Deruxtecan in HER2-Mutant Non-Small-Cell Lung Cancer. N Engl J Med. 2022 Jan 20;386(3):241-251.	This was a prospective single-arm phase 2 clinical trial that investigated trastuzumab deruxtecan in HER2-overexpressing or HER2-mutant non-small cell lung cancer. The risk of bias due to confounding, selection of participants, classification of and deviation from intervention, measurement of outcome, and selective reporting were deemed low risk. The risk of bias associated with missing data was deemed moderate risk due to the high amount of censoring at 6 to 12 months. A major caveat of the study is the lack of a control group.	S
Tsurutani J, Iwata H, Krop I, et al. Targeting HER2 with Trastuzumab Deruxtecan: A Dose-Expansion, Phase I Study in Multiple Advanced Solid Tumors. Cancer Discov. 2020 May;10(5):688-701.		3
Kato Y, Kato Y, Minegishi Y, et al. Efficacy with Trastuzumab Deruxtecan for Non-Small-Cell Lung Cancer Harboring HER2 Exon 20 Insertion Mutation in a Patient with a Poor Performance Status: A Case Report. Onco Targets Ther. 2021 Nov 23;14:5315-5319.		3
Li BT, Michelini F, Misale S, et al. HER2-Mediated Internalization of Cytotoxic Agents in ERBB2 Amplified or Mutant Lung Cancers. Cancer Discov. 2020 May;10(5):674-687.		1

O'Rourke K. Trastuzumab deruxtecan shows durable activity in HER2-mutant non-small cell lung cancer. Cancer. 2022 Mar 1;128(5):938. doi: 10.1002/cncr.34102. PMID: 35147987.		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)

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Megan Smith	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Todd Gersten	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	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases		B
John Roberts	Effective	Class IIb: Recommended, in Some Cases	In an international, single-arm trial in 91 patient's with HER-2 mutation-positive advanced non-small cell lung cancer who had received previous treatment, fam-trastuzumab deruxtecan-nski 6.4 mg/kg every 3 weeks led to nominal tumor shrinkage in 85 (93%) and objective partial response by conventional criteria in 50 (55%) patients with a median duration of response of 9.3 months. Treatment was associated with moderate to severe toxicity, notably interstitial lung disease in 24 (26%) patients resulting in death in 2 (2%). Fam-trastuzumab deruxtecan-nski is a reasonable treatment option for similar patients who are without significant respiratory compromise. Ongoing investigations include a lower dose (5.4 mg/kg), which is the approved dose for the treatment of breast cancer.	
Richard LoCicero	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases	A single phase II multicenter clinical trial evaluating Fam-Trastuzumab Druxtecan-nxki in the treatment of previously treated HER2+ advanced non-small cell lung cancer demonstrated a 55% response rate and 9.3 month median duration of response. While no unexpected toxicities were observed, 2 of 91 patients died of lung toxicity.	
Todd Gersten	Evidence Favors Efficacy	Class IIa: Recommended, in Most Cases	Fam-Trastuzumab demonstrated promising efficacy including response rate and median overall survivorship in a Phase II study of HER-2 mutated relapsed/refractort non-squamous NSCLC.	