TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Vandetanib

INDICATION: Non-small cell lung cancer, locally advanced or metastatic, after failure of first- or second-line chemotherapy

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, 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)]

TRUVEN HEALTH ANALYTICS

EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Herbst,R.S., et al: Vandetanib plus docetaxel versus docetaxel as second-line treatment for patients with advanced non-small-cell lung cancer (ZODIAC): a double-blind, randomised, phase 3 trial. Lancet Oncology Jul 2010; Vol 11, Issue 7; pp. 619-626.	Study methodology comments: This was a double-blind, randomized, placebo-controlled, phase III trial. Many potential confounding factors were controlled through the study design, statistical analyses, and eligibility criteria. Additional strengths of the study included: 1) defined primary and secondary outcomes and clinical response; 2) conducted power analysis; 3) provided 95% confidence intervals; 4) presented eligibility criteria; 5) confirmed diagnosis; 6) explained method of randomization; 7) compared baseline characteristics of groups; 8) conducted analyses on the intent-to-treat population; and 9) made statistical adjustments to preserve the type 1 error rate. Selection bias may have been present since subjects were not recruited in a random or consecutive manner.	S
Natale,R.B., et al: Phase III trial of vandetanib compared with erlotinib in patients with previously treated advanced non-small-cell lung cancer. Journal of Clinical Oncology Mar 10, 2011; Vol 29, Issue 8; pp. 1059-1066.	Study methodology comments: This was a double-blind, randomized, phase III trial. If the trial did not demonstrate a difference between groups, a pre-planned noninferiority analysis was conducted for progression-free survival (PFS) and overall survival (OS). Noninferiority was declared if vandetanib retained at least 50% of the efficacy of erlotinib for both PFS and OS. Many potential confounding factors were controlled through the study design, statistical analyses, and eligibility criteria. Additional strengths of the study included: 1) rigorous design; 2) defined primary and secondary outcomes; 3) defined clinical response; 4) had both inclusion and exclusion criteria; 5) conducted power analysis; 6) provided 95% confidence intervals; 7) confirmed diagnosis; 8) compared baseline characteristics of groups; 9) conducted analyses on the intent-to-treat population; and 10) confirmed response at 4 weeks. Weaknesses included 1) partial explanation of method of randomization; and 2) selection bias may have been present since subjects were not recruited in a random or consecutive manner.	S
de Boer,R.H., et al: Vandetanib plus pemetrexed for the second-line treatment of advanced non-small-cell lung cancer: a randomized, double-blind phase III trial. Journal of Clinical Oncology Mar 10, 2011; Vol 29, Issue 8; pp. 1067-1074	Study methodology comments: This was a double-blind, randomized, phase III trial. Many potential confounding factors were controlled through the study design, statistical analyses, and eligibility criteria. Additional strengths of the study included: 1) defined primary and secondary outcomes; 2) defined clinical response; 3) had both inclusion and exclusion criteria; 4) conducted power analysis; 5) provided 95% confidence intervals; 6) confirmed diagnosis; 7) compared baseline characteristics of groups; 8) conducted analyses on the intent-to-treat population; and 9) confirmed response at 4 weeks. Weaknesses included 1) partial explanation of method of randomization; and 2) selection bias may have been present since subjects were not recruited in a random or consecutive manner.	S

Natale,R.B., et al: Vandetanib versus gefitinib in patients with advanced non-small-cell lung cancer: results from a two-part, double-blind, randomized phase ii study. J Clin Oncol May 20, 2009; Vol 27, Issue 15; pp. 2523-2529.	Study methodology comments: Literature analyst CB comments	3
Heymach,J.V., et al: Randomized, placebo-controlled phase II study of vandetanib plus docetaxel in previously treated non small-cell lung cancer.[Erratum appears in J Clin Oncol. 2008 Jan 1;26(1):165-6]. Journal of Clinical Oncology Sep 20, 2007; Vol 25, Issue 27; pp. 4270-4277.	Study methodology comments: Literature analyst CB comments	2
Kiura,K., et al: A randomized, double-blind, phase IIa dose-finding study of Vandetanib (ZD6474) in Japanese patients with non-small cell lung cancer. Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer Apr 2008; Vol 3, Issue 4; pp. 386-393.		3
de,Boer R., et al: An open-label study of vandetanib with pemetrexed in patients with previously treated non-small-cell lung cancer. Annals of Oncology Mar 2009; Vol 20, Issue 3; pp. 486-491.		3
Heymach,J.V., et al: Randomized phase II study of vandetanib alone or with paclitaxel and carboplatin as first-line treatment for advanced non-small-cell lung cancer. Journal of Clinical Oncology Nov 20, 2008; Vol 26, Issue 33; pp. 5407-5415.		1

Blackhall,F.H., et al: A phase I study of Vandetanib in combination with vinorelbine/cisplatin or gemcitabine/cisplatin as first-line treatment for advanced non-small cell lung cancer. Journal of Thoracic Oncology: Official Publication of the International Association for the Study of Lung Cancer Aug 2010; Vol 5, Issue 8; pp. 1285-1288.		1
Fava,P., et al: Therapeutic hotline. A rare vandetanib-induced photo-allergic drug eruption. Dermatologic Therapy Sep 2010; Vol 23, Issue 5; pp. 553-555.		4
Hirsh,V.: Systemic therapies in metastatic non-small-cell lung cancer with emphasis on targeted therapies: The rational approach. Current Oncology Apr 26, 2010; Vol 17, Issue 2; pp. 13-23.		4
Lee,D. and Lee,David: Phase II data with ZD6474, a small-molecule kinase inhibitor of epidermal growth factor receptor and vascular endothelial growth factor receptor, in previously treated advanced non-small-cell lung cancer. [Review] [5 refs]. Clinical Lung Cancer Sep 2005; Vol 7, Issue 2; pp. 89-91.		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
Margi Schiefelbein, PA	None	Thomas McNeil Beck, MD	None
Stacy LaClaire, PharmD	None	James E. Liebmann, MD	None
Felicia Gelsey, MS	None	Jeffrey A. Bubis, DO	Other payments: Dendreon
		Keith A. Thompson, MD	None
		John M. Valgus, PharmD	None

ASSIGNMENT OF RATINGS:
*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	---	---		B
Thomas McNeil Beck, MD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	Drug should be moved to testing earlier in treatment plans.	N/A

James E. Liebmann, MD	Evidence is Inconclusive	Class lll: Not Recommended	The studies under review show little advantage to Vandetanib compared to other 2nd or 3rd line therapies for metastatic NSCLC. The Herbst Trial shows a trivial improvement in PFS (3 weeks) with no effect on OS by the addition of Vandetanib to Docetaxel. It is difficult to assess the clinical significance of an improvement in TDS, given the increase in AEs in the Vandetanib group. Vandetanib plus Pemetrexed showed no improvement of PFS or OS compared to Pemetrexed alone. It is encouraging that there was no additional toxicity when Vandetanib was added to Pemetrexed, but it is not clear that there was significant benefit either. Finally, when compared with Erlotinib, Vandetanib appears equivalent and non-inferior in terms of efficacy, but is significantly more toxic than Erlotinib at the 300 mg dose.	N/A
Jeffrey A. Bubis, DO	Effective	Class l: Recommended	OS benefit in trial.	N/A
Keith A. Thompson, MD	Evidence is Inconclusive	Class llb: Recommended, In Some Cases	None	N/A
John M. Valgus, PharmD	Evidence Favors Efficacy	Class llb: Recommended, In Some Cases	Combination trial only resulted in slight increase in PFS vs Docetaxel alone and with additional ADEs. No survival advantage. No improvement over Erlotinib monotherapy.	N/A