TRUVEN HEALTH ANALYTICS

COMPENDIA TRANSPARENCY TRACKING FORM

DRUG: Gefitinib

INDICATION: Head and neck cancer, Squamous cell, recurrent or metastatic, as single-agent therapy

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**
*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
Simon,J.S.W., et al: Phase III study of gefitinib 250 compared with intravenous methotrexate for recurrent squamous cell carcinoma of the head and neck. Journal of clinical oncology - official journal of the American Society of Clinical Oncology Apr 10, 2009; Vol 27, Issue 11; pp. 1864-1871.	Study methodology comments: This was a randomized comparative trial with many strengths. There were two major strengths of the study. First, gefitinib was compared to a standard comparator. Second, patients and investigators were blinded to gefitinib dose and EGFR biomarkers were assessed by blinded examiners. Additional strengths were 1) had inclusion and exclusion criteria; 2) defined primary, secondary, and exploratory endpoints; 3) defined response; 4) responses had to be sustained for 4 weeks; 5) conducted a power analysis; 6) compared baseline characteristics of groups; 7) provided 95% confidence intervals; 8) controlled for the effect of potential confounding factors on outcomes; and 9) made adjustments to the statistical analyses to preserve the type I error rate. Weaknesses included: 1) possible selection bias since subjects were not recruited in a random or consecutive manner; and 2) did not discuss the method of randomization.	S
Cohen E.E.W., et al. Phase II trial of ZD1839 in recurrent or metastatic squamous cell carcinoma of the head and neck. Clin Oncol. 2003 May 15;21(10):1980-7.	Study methodology comments: This was a time-series trial that was conducted with a two-stage design. A major strength of the study was that an independent committee reviewed the data of all patients who responded, including those with prolonged stable disease, and a single, blinded pathologist assessed the histologic data. Other strengths included 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary and secondary outcomes; 3) defined response; 4) responses were confirmed at 4 weeks; 5) presented 95% confidence intervals; 6) had both inclusion and exclusion criteria; 7) power analysis; and 8) examined the effect of potential confounding factors on treatment outcomes. A major weakness of the study was the absence of a control group which would have controlled for the effect of potential confounding factors on outcomes. Selection bias may have been present since the patients were not recruited in a random or consecutive manner.	S
Cohen E.E.W., et al. Phase II trial of gefitinib 250 mg daily in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck. Clin Cancer Res 2005;11(23):8418-24.	Study methodology comments: This was an open-label, time-series trial. A major weakness of the study was the absence of a control group which would have controlled for the effect of potential confounding factors on outcomes. Other weaknesses included 1) open-label study without the use of independent assessors; and 2) possible selection bias since the patients were not recruited in a random or consecutive manner. Strengths included 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary and secondary outcomes; 3) defined response; 4) responses were confirmed at 4 weeks; 5) presented 95% confidence intervals; 6) had both inclusion and exclusion criteria; 7) power analysis; 8) confirmed diagnosis; and 9) examined the effect of potential confounding factors on treatment outcomes.	S

Kirby,A.M., et al: Gefitinib (ZD1839, Iressa) as palliative treatment in recurrent or metastatic head and neck cancer. Br J Cancer Mar 13, 2006; Vol 94, Issue 5; pp. 631-636.	Study methodology comments: This was an open-label, time-series trial that should be interpreted with some caution. A major weakness of the study was the absence of a control group which would have controlled for the effect of potential confounding factors on outcomes. Additional weaknesses included 1) absence of a power analysis; 2) possible selection bias since the patients were not recruited in a random or consecutive manner; and 3) open-label design without the use of independent reviewers. Strengths of the study were 1) the use of a within-subject design to control for confounding effects of patient characteristics; 2) defined primary and secondary outcomes; 3) defined radiological and clinical response; 4) responses were confirmed at 4 and 12 weeks; 5) conducted analyses on the intent-totreat population; 6) had both inclusion and exclusion criteria; 7) confirmed diagnosis; 8) presented 95% confidence intervals; and 9) examined the effect of potential confounding factors on treatment outcome.	S
Chua, D.T., et al. Phase II study of gefitinib for the treatment of recurrent and metastatic nasopharyngeal carcinoma. Head Neck. 2008 Jul;30(7):863-7.		3
Hainsworth,J.D., et al: Neoadjuvant chemotherapy/gefitinib followed by concurrent chemotherapy/radiation therapy/gefitinib for patients with locally advanced squamous carcinoma of the head and neck. Cancer May 15, 2009; Vol 115, Issue 10; pp. 2138-2146.		1
Caponigro,F., et al: A phase I/II trial of gefitinib and radiotherapy in patients with locally advanced inoperable squamous cell carcinoma of the head and neck. Anti-Cancer Drugs Aug 2008; Vol 19, Issue 7; pp. 739-744.		3
Chen,C., et al: Phase I trial of gefitinib in combination with radiation or chemoradiation for patients with locally advanced squamous cell head and neck cancer. J Clin Oncol Nov 01, 2007; Vol 25, Issue 31; pp. 4880-4886.		3

Chun,PY., et al: Synergistic effects of gemcitabine and gefitinib in the treatment of head and neck carcinoma. Cancer Research Jan 15, 2006; Vol 66, Issue 2; pp. 981-988.		1
Baselga,J., et al: Phase I safety, pharmacokinetic, and pharmacodynamic trial of ZD1839, a selective oral epidermal growth factor receptor tyrosine kinase inhibitor, in patients with five selected solid tumor types. Journal of Clinical Oncology - Official Journal of the American Society of Clinical Oncology Nov 301, 2002; Vol 20, Issue 21; pp. 4292-4302.		3
Van,Waes C., et al: Molecular and Clinical Responses in a Pilot Study of Gefitinib with Paclitaxel and Radiation in Locally Advanced Head-and-Neck Cancer. Int J Radiat Oncol Biol Phys Oct 29, 2009; Vol EPub, p. 1.		3
Wheeler,R.H., et al: Clinical and molecular phase II study of gefitinib in patients (pts) with recurrent squamous cell cancer of the head and neck (H&N Ca). Journal of Clinical Oncology Jun 01, 2005; Vol 23, Issue N16,1,S; pp. 507S-507S.		3
Tan,E.H., et al: Phase II study of gefitinib in combination with cisplatin and concurrent radiotherapy in patients with stage III/IV squamous cell head and neck cancer and to analyse the effect of gefitinib on tumour gene expression. EJC Supplements Oct 2008; Vol 6, Issue N12; pp. 65-66.		3

Cohen,E.E.W., et al: Integration of gefitinib (G), into a concurrent chemoradiation (CRT) regimen followed by G adjuvant therapy in patients with locally advanced head and neck cancer (HNC) - a Phase II Trial. Journal of Clinical Oncology Jun 01, 2005; Vol 23, Issue N16,1,S; pp. 501S-501S.		3
Nyati,Mukesh K., Chun,Patrick Y., and Lawrence,Theodore S.: Optimum scheduling for better therapeutic outcome is required for gefitinib and gemcitabine treatment for head and neck cancer. Proceedings of the American Association for Cancer Research Annual Meeting Apr 2005; Vol 46, Issue Suppl. S; p. 285.		3
Raben,D., et al: Preliminary report on toxicity of a phase I trial of gefitinib (Iressa (TM)) in combination with radiation/chemotherapy for patients with locally advanced head and neck cancer (LAHNC). Clinical Cancer Research Dec 01, 2003; Vol 9, Issue N16,2,S; pp. 6249S-6249S.		3
Weber, R.S., et al. Gefitinib for advanced cutaneous squamous cell carcinoma of head and neck: Phase II trial. 2009 ASCO abstract.		3
Rueda, A. et al. Gefitinib plus concomitant boost accelerated radiation (AFX-CB) and concurrent weekly cisplatin for locally advanced unresectable squamous cell head and neck carcinomas (SCCHN): A phase II study. 2007 ASCO abstract.		3

Rodriguez, C.P., et al. Multiagent concurrent chemoradiotherapy (MACCRT) and gefitinib in locoregionally advanced head and neck squamous cell cancer (HNSCC). 2009 ASCO abstract.		3
Doss, H.H., et al. Induction chemotherapy + gefitinib followed by concurrent chemotherapy/radiation therapy/gefitinib for patients (pts) with locally advanced squamous carcinoma of the head and neck: A phase I/II trial of the Minnie Pearl Cancer Research Network. 2006 ASCO abstract.		3
Morris, J.C., et al. Pilot phase I study of gefitinib (GEF) in combination with paclitaxel (PAC) and radiation therapy (RT) in patients with locally advanced head and neck squamous cell carcinoma (HNSCC) and effects on epidermal growth factor receptor (EGFR) signaling pathway. 2007 ASCO abstract.		3
Wheeler, R.H., et al. Clinical and molecular phase II study of gefitinib in patients (pts) with recurrent squamous cell cancer of the head and neck (H&N Ca). 2005 ASCO abstract.		3
Stewart, J.S., et al. A phase III randomized parallel-group study of gefitinib (IRESSA) versus methotrexate (IMEX) in patients with recurrent squamous cell carcinoma of the head and neck. 2007 AACR meeting abstract.		3

Argiris, A. Docetaxel + gefitinib in recurrent or metastatic head and neck cancer. Signal. 2006; 6(3):15-17.		4
Posner,M.R.: Gefitinib therapy feasible/tolerable with chemoradiation for head and neck cancer. Oncology Report Mar 01, 2005; Vol -, Issue SPRING; pp. 75-76.		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
Amy Hemstreet, PharmD	None	Thomas McNeil Beck, MD	None
Stacy LaClaire, PharmD	None	Susan Goodin, PharmD	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
Thomas McNeil Beck, MD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	None	N/A
Susan Goodin, PharmD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	Stewart, et al Phase III Study of gefitinib had no impact on O.S. or ORR. Kirby et al Phase II reported improved symptom control but single agent when compared to previous reports had no significant activity for ORR, TTP or survival. Cohen et al Phase II reported minimal activity.	N/A
Jeffrey F. Patton, MD	Evidence Favors Efficacy	Class IIb: Recommended, In Some Cases	None	N/A
Gerald J. Robbins, MD	Ineffective	Class III: Not Recommended	This was not an “equivalence” study and did not show improvement in O.S.	N/A

John M. Valgus, PharmD	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	Geftinib does demonstrate activity in HN Ca but less than desired. Did not show difference in OS compared with chemo so could be used in select pts who are not candidates for conventional chemo.	N/A