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**COMPENDIA TRANSPARENCY TRACKING FORM**

**DATE:** 2/27/2017

**PACKET:** 1384

**DRUG:** Dabrafenib Mesylate

**USE:** Non-small cell lung cancer, metastatic with BRAF V600E mutation, in previously treated patients as monotherapy or in combination with trametinib

| 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, 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)]**

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**EVIDENCE CONSIDERED:**

*to meet requirements 2 and 4

| CITATION | STUDY-SPECIFIC COMMENTS | LITERATURE CODE |
|---|---|---|
| Planchard,D., et al: Dabrafenib plus trametinib in patients with previously treated BRAFV600E-mutant metastatic non-small cell lung cancer: an open-label, multicentre phase 2 trial. The Lancet Oncology Jul 01, 2016; Vol 17, Issue 7; pp. 984-993. | Comments: This study is part of an ongoing international, phase 2, open-label, single-arm trial. There was low risk of bias associated with selection of cohorts and assessment of outcome. Sensitivity analyses were conducted by an independent review committee on the study endpoints. All eligible patients were included in the analyses. Median follow-up was 11.6 months (IQR 8·8–15·2). A major caveat of the study was the absence of a control group or active comparator. | S |
| Planchard,D., et al: Dabrafenib in patients with BRAF(V600E)-positive advanced non-small-cell lung cancer: A single-arm, multicentre, open-label, phase 2 trial. The Lancet Oncology May 01, 2016; Vol 17, Issue 5; pp. 642-650 | Comments: This study was an international, phase 2, open-label, single-arm trial. There was low risk of bias associated with selection of cohorts and assessment of outcome. Sensitivity analyses were conducted by an independent review committee on the study endpoints. All patients were included in the analyses. Median follow-up was 10·7 months (IQR 4·5–16·2). A major caveat of the study was the absence of a control group or active comparator. | S |
| Gautschi,O., et al: Targeted therapy for patients with BRAF-mutant lung cancer results from the European EURAF cohort. Journal of Thoracic Oncology Oct 01, 2015; Vol 10, Issue 10; pp. 1451-1457. | | 3 |
| Shea,M., Costa,D.B., and Rangachari,D.: Management of advanced non-small cell lung cancers with known mutations or rearrangements: Latest evidence and treatment approaches. Therapeutic Advances in Respiratory Disease 2016; Vol 10, Issue 2; pp. 113-129. | | 4 |

| | | |
|---|---|---|
| Kim,Y.H.: Dual inhibition of BRAF and MEK in BRAF-mutated metastatic non-small cell lung cancer. Journal of Thoracic Disease 2016; Vol 8, Issue 9; pp. 2369-2371. | | 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 |
|---|---|---|---|
| Felicia Gelsey, MS | None | | |
| Stacy LaClaire, PharmD | None | | |
| Catherine Sabatos, PharmD | None | | |
| | | John D Roberts | None |
| | | Jeffrey Klein | None |
| | | Richard LoCicero | Incyte Corporation<br><br>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 |
|---|---|---|---|---|
| **MICROMEDEX** | Evidence Favors Efficacy | Class IIa: Recommended, In Most Cases | | B |
| John D Roberts | Evidence Favors Efficacy | Class I: Recommended | In two multi-center, single arm trials, dabrafenib, without or with trametinib, showed a significant response rate and tolerable toxicities in patients with BRAF V600E mutated non-small cell lung cancer. The combination showed a higher response rate, a higher incidence of toxicities, but fewer secondary skin cancers. | N/A |

| | | | | |
|---|---|---|---|---|
| Jeffrey Klein | Evidence Favors Efficacy | Class IIb: Recommended, In Some Cases | The use of Dabrafenib alone or in combination with trametinib in nsclc patients was shown to be quite effective. These patients had a BRAF genetic mutation and were previously treated with other agents. Unfortunately over 50% of these patients experienced serious adverse effects in one study. In addition screening for the BRAF mutation has limitations with costs and insurance coverage. | N/A |
| Richard LoCicero | Evidence Favors Efficacy | Class IIa: Recommended, In Most Cases | Phase II data supports the efficacy of Dabrafenib in BRAF V600E mutation positive metastatic non-small cell lung cancer with acceptable toxicity. | N/A |