TRUVEN HEALTH ANALYTICS™
an IBM Company

**COMPENDIA TRANSPARENCY TRACKING FORM**

**DATE:** 7/29/16

**PACKET:** 1340

**DRUG:** Sorafenib Tosylate

**USE:** Gastrointestinal stromal tumor Advanced or metastatic disease, after failing treatment with imatinib and sunitinib

| 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)]**

TRUVEN HEALTH ANALYTICS™
an IBM Company

## EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

| CITATION | STUDY-SPECIFIC COMMENTS | LITERATURE CODE |
|---|---|---|
| Italiano A, Cioff A, Coco P, et al. Patterns of Care, Prognosis, and Survival in Patients with Metastatic Gastrointestinal Stromal Tumors (GIST) Refractory to First-Line Imatinib and Second-Line Sunitinib. Ann Surg Onool (2012) 19:1551-1559 | Comments: This was an international, multi-site, retrospective study that included all treated patients. There was low risk of bias associated with selection of cohorts and assessment of outcome. Data was gathered from medical records. Statistical analyses were performed to control for the effect of potential confounding factors on outcomes. All subjects were included in the analyses. Median follow-up for living patients was 27 months (range 22-32). A major caveat of the study was the absence of a control group or active comparator. | S |
| Montemurro,M., Gelderblom,H., Bitz,U., et al: Sorafenib as third- or fourth-line treatment of advanced gastrointestinal stromal tumour and pretreatment including both imatinib and sunitinib, and nilotinib: A retrospective analysis. European Journal of Cancer Mar 2013; Vol 49, Issue 5; pp. 1027-1031 | Comments: This was an international, multi-site, retrospective study that included all treated patients. There was low risk of bias associated with selection of cohorts and assessment of outcome. Data was gathered from medical records. Statistical analyses were performed to control for the effect of potential confounding factors on outcomes. All subjects were included in the analyses. Median follow-up was 7.9 months (range, 0.3-39.7 months). A major caveat of the study was the absence of a control group or active comparator. | S |
| Park,S.H., Ryu,M.H., Ryoo,B.Y., et al: Sorafenib in patients with metastatic gastrointestinal stromal tumors who failed two or more prior tyrosine kinase inhibitors: A phase II study of Korean gastrointestinal stromal tumors study group. Investigational New Drugs Dec 2012; Vol 30, Issue 6; pp. 2377-2383. | Comments: This was a multi-site, single-arm, phase II study. There was low risk of bias associated with selection of cohorts and assessment of outcome. All patients were included in the analyses. Only one patient withdrew from the study due to grade 3 fatigue and was considered as a nonresponder in the ITT analyses. Median follow-up was 11.0 months (range, 9.3-15.8 months). A major caveat of the study was the absence of a control group or active comparator. | S |

| | | |
|---|---|---|
| Ozer-Stillman,I., Strand,L., Chang,J., et al: Meta-analysis for the association between overall survival and progression-free survival in gastrointestinal stromal tumor. Clinical Cancer Research Jan 2015; Vol 21, Issue 2; pp. 295-302. | | 1 |
| Kefeli,U., et al: Efficacy of sorafenib in patients with gastrointestinal stromal tumors in the third- or fourth-line treatment: A retrospective multicenter experience. Oncology Letters Aug 2013; Vol 6, Issue 2; pp. 605-611. | Comments: This was a multi-site, retrospective study that included all treated patients. There was low risk of bias associated with selection of cohorts and assessment of outcome. Data was collected from clinical records and histopathology reports. Statistical analyses were performed to control for the effect of potential confounding factors on outcomes. All subjects were included in the analyses. All patients were followed up after the administration of treatment at regular intervals until mortality or the time the study manuscript was written. A major caveat of the study was the absence of a control group or active comparator. | 1 |
| Kindler,H.L., Campbell,N.P., Wroblewski,K., et al: Sorafenib (SOR) in patients (pts) with imatinib (IM) and sunitinib (SU)-resistant (RES) gastrointestinal stromal tumors (GIST): Final results of a University of Chicago Phase II Consortium trial. Journal of Clinical Oncology 2011; Vol 29, Issue 15 SUPPL.; p. 10009. | Abstract | 4 |
| Ryu,M., Park,S.H., Ryoo,B., et al: A phase II study of sorafenib in patients with metastatic or unresectable gastrointestinal stromal tumors with failure of both imatinib and sunitinib: A KGSG study. Journal of Clinical Oncology 2011; Vol 29, Issue 15 SUPPL. 1. | Abstract | 4 |

| | | |
|---|---|---|
| Roubaud,G., Kind,M., Coindre,J.-M., et al: Clinical activity of sorafenib in patients with advanced gastrointestinal stromal tumor bearing PDGFRA exon 18 mutation: A case series. Annals of Oncology Mar 2012; Vol 23, Issue 3; pp. 804-805. | | 4 |
| Bitz,U., et al: Progression free survival and overall survival in patients with metastastic gastrointestinal stromal tumor (GIST) treated with sorafenib as 3rd- or 4th-line therapy. Journal of Cancer Research and Clinical Oncology Feb 2012; Vol 138 SUPPL. 1, p. 40. | Abstract | 4 |
| Joensuu,H., Hohenberger,P., and Corless,C.L.: Gastrointestinal stromal tumour. The Lancet 2013; Vol 382, Issue 9896; pp. 973-983. | | 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 | | |
| | | Jeffrey Klein | None |
| | | John Roberts | 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 IIb: Recommended, In Some Cases | | B |
| Jeffrey Klein | Evidence Favors Efficacy | Class IIa: Recommended, In Most Cases | Three separate trials demonstrated clinical efficacy for sorafenib as a 3rd or 4th line agent in metastatic GI stromal tumors. It is not an agent for all patients and perhaps best supportive care might be the better choice but that should be done as a case by case basis. | N/A |

| | | | | |
|---|---|---|---|---|
| John Roberts | Evidence is Inconclusive | Class III: Not Recommended | Sorafenib induces occasional responses in advanced or metastatic gastrointestinal stromal tumors with moderate bother but modest serious toxicity. In the absence of prospective, comparative trials, whether sorafenib treatment is better than best supportive care is unknown. | N/A |
| Richard LoCicero | Evidence Favors Efficacy | Class IIb: Recommended, In Some Cases | Limited data has demonstrated low response rates with acceptable toxicity. | N/A |