**COMPENDIA TRANSPARENCY TRACKING FORM**

**DATE:** June 21, 2024

**OFF-LABEL ID #:** 2677

**DRUG NAME:** Temozolomide

**OFF-LABEL USE:** Neuroendocrine tumor of pancreas Advanced, progressive disease, as monotherapy or in combination with capecitabine

| 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, E** *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 | LITERATURE CODE |
|---|---|
| Kunz PL, Graham NT, Catalano PJ, et al. Randomized Study of Temozolomide or Temozolomide and Capecitabine in Patients With Advanced Pancreatic Neuroendocrine Tumors (ECOG-ACRIN E2211). J Clin Oncol. 2023;41(7):1359-1369. doi:10.1200/JCO.22.01013 | S |
| Del Rivero J, Perez K, Kennedy EB, et al. Systemic Therapy for Tumor Control in Metastatic Well-Differentiated Gastroenteropancreatic Neuroendocrine Tumors: ASCO Guideline. J Clin Oncol. 2023;41(32):5049-5067. doi:10.1200/JCO.23.01529 | S |
| Pavel M, Öberg K, Falconi M, et al. Gastroenteropancreatic neuroendocrine neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020;31(7):844-860. doi:10.1016/j.annonc.2020.03.304 | 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 |
|---|---|---|---|
| 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 |
|---|---|---|---|---|
| **MERATIVE MICROMEDEX** | Effective | Class I: Recommended | | B |
| Warren Brenner | Effective | Class I: Recommended | This study by Kuntz was a well conducted randomised phase II trial - in my opinion based on the study temozolomide is an effective agent in advanced PNET which is a cancer with a high unmet need. The combination of tern/cap is clearly more effective than Tern alone with clinical meaningful PFS benefit although OS was not improved - given its overall efficacy and relatively favorable side effect profile based on the data I concluded the agent is effective and would give a class I recommendation. | |

| | | | | |
|---|---|---|---|---|
| Todd Gersten | Effective | Class I: Recommended | Temozolamide has activity in this rare tumor type with few other treatment options. The response rate of > 30% (with or without capecitabine) and ability to control disease (DOR) for > 1 year support this notion…as does as disease stabilization rate of over 40% (with or without capecitabine). | |
| Jeffrey Klein | Evidence Favors Efficacy | Class IIa: Recommended, in Most Cases | The use of Temozolamide in combination with capecitabine demonstrated a higher degree of progression free survival then temozolamide alone. Adverse effects were more pronounced with combination therapy. | |