

**COMPENDIA TRANSPARENCY TRACKING FORM**

**DATE:** June 1, 2023

**OFF-LABEL ID #:** 2555

**DRUG NAME:** Mirtazapine

**OFF-LABEL USE:** Chemotherapy-induced nausea and vomiting (Prophylaxis); Highly emetogenic 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, L** \*to meet requirement 1

| CODE | EVALUATION/PRIORITIZATION CRITERIA  |
|------|---|
| A    | Treatment represents an established standard of care or significant <b>advance</b> over current therapies |
| C    | <b>Cancer</b> or cancer-related condition   |
| E    | Quantity and robustness of <b>evidence</b> for use support consideration                                  |
| L    | <b>Limited</b> alternative therapies exist for condition of interest                                      |
| P    | <b>Pediatric</b> condition  |
| R    | <b>Rare</b> disease   |
| S    | <b>Serious</b> , 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 |
|---|-----------------|
| Filetti, M, Lombardi, P, Giusti, R, et al: Efficacy and safety of antiemetic regimens for highly emetogenic chemotherapy-induced nausea and vomiting: A systematic review and network meta-analysis. Cancer Treat Rev Jan 21, 2023; Vol 115, p. 102512.   | 3               |
| Cao, J, Ouyang, Q, Wang, S, et al: Mirtazapine, a dopamine receptor inhibitor, as a secondary prophylactic for delayed nausea and vomiting following highly emetogenic chemotherapy: an open label, randomized, multicenter phase III trial. Invest New Drugs Apr 2020; Vol 38, Issue 2; pp. 507-514. | S               |
| Maleki, A, Ghadiyani, M, Salamzadeh, J, et al: Comparison of mirtazapine and olanzapine on nausea and vomiting following anthracycline-cyclophosphamide chemotherapy regimen in patients with breast cancer. Iran J Pharm Res 2020; Vol 19, Issue 3; pp. 451-464.                                     | S               |
| Kinomura, M, Iihara, H, Fumii, H, et al: Effect of mirtazapine for the prevention of nausea and vomiting in patients with thoracic cancer receiving platinum-based chemotherapy. Anticancer Res Mar 2023; Vol 43, Issue 3; pp. 1301-1307.   | 3               |
| Kast,R.E. and Foley,K.F.: Cancer chemotherapy and cachexia: mirtazapine and olanzapine are 5-HT3 antagonists with good antinausea effects. Eur J Cancer Care (Engl) Jul 2007; Vol 16, Issue 4; pp. 351-354.   | 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)

\*to meet requirement 3

| PACKET PREPARATION        | DISCLOSURES | EXPERT REVIEW    | DISCLOSURES   |
|---------------------------|-------------|------------------|---|
| Megan Smith               | None        |                  |   |
| Stacy LaClaire, PharmD    | None        |                  |   |
| Catherine Sabatos, PharmD | None        |                  |   |
|                           |             | Todd Gersten     | 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 |
|-----------------------|--------------------------|---------------------------------------|--|----------------------|
| <b>IBM MICROMEDEX</b> | Effective                | Class IIb: Recommended, in Some Cases |  | B                    |
| Jeffrey Klein         | Evidence Favors Efficacy | Class IIa: Recommended, in Most Cases | The use of mirtazapine to prevent chemotherapy induced nausea and vomiting showed to be quite effective over the control group. The product also was effective to reduce delayed emesis. Adverse effects of drowsiness and weight gain needs to considered during treatment.   |                      |
| Richard LoCicero      | Effective                | Class IIb: Recommended, in Some Cases | In a phase III randomized trial, Mirtazapine added to standard triplet antiemetic prophylaxis improved outcome (no emesis) in patients receiving highly emetogenic chemotherapy. Additionally, in another phase III randomized trial, mirtazapine was as effective as olanzapine (currently in use for the same indication). |                      |
| Todd Gersten          | Effective                | Class IIb: Recommended, in Some Cases | Mirtazapine has been demonstrated to improve prophylactic control of delayed CINV when added to triple therapy in patients previously experiencing delayed emesis after use of a standard triple drug regimen (i.e. in the secondary prophylaxis setting = "some cases")   |                      |