On behalf of TESARO, I respectfully request the NCCN Antiemesis Guidelines Panel to review the enclosed data in support of the use of the NK-1 receptor antagonist (RA) VARUBI® (rolapitant) in patients receiving carboplatin.

**Change Requested:** We request the inclusion of rolapitant in combination with a 5HT₃ RA and dexamethasone as a Category 1 recommendation in all patients receiving carboplatin-containing regimens, specifically, removing the with/without caveat for carboplatin on page AE-6, which currently applies to all moderately emetogenic chemotherapy (MEC).

**FDA Clearance:** The FDA has approved oral VARUBI® (rolapitant) in combination with other antiemetic agents in adults for the prevention of delayed chemotherapy-induced nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.¹

**Rationale:** NCCN Guidelines currently recommend that a 5-HT₃ receptor antagonist (RA) and dexamethasone be used in all patients receiving MEC and that patients with additional CINV risk factors may also receive an NK-1 RA. Carboplatin has an emetic potential greater than that of many agents classified as MEC. According to a natural history study, without antiemetic prophylaxis, 89% of carboplatin-treated patients experienced some degree of nausea and 82% of patients vomited.² Recently updated NCCN antiemetic guidelines support the use of rolapitant (Category 1 level of evidence and consensus) to protect against CINV in both patients with cancer receiving HEC and select patients receiving MEC. The inclusion of rolapitant in the antiemetic guidelines was based on the results of 3 large, global, randomized, double-blind, placebo-controlled phase 3 studies demonstrating that oral rolapitant combined with a 5-HT₃ RA and dexamethasone was superior to a 5-HT₃ RA and dexamethasone alone in providing CINV protection in the delayed phase in patients receiving HEC or MEC.³,⁴

A pre-specified analysis in one of the phase 3 trials of patients receiving non-AC MEC (n=322 rolapitant; n = 307 control) showed that rolapitant provided statistically superior complete responses (CRs) across all phases: 76% versus 64% (p=0.0008) in the delayed phase, 75% versus 61% (p=0.0003) in the overall phase, and 91% versus 84% (p=0.0163) in the acute phase.³
• Sixty-four percent of patients in the rolapitant phase 3 non-AC MEC population (n = 192 rolapitant; n = 209 control) received carboplatin-containing regimens. Among the carboplatin-containing regimen subset, CR was higher with rolapitant in all phases and statistically significant in the delayed and overall phases: 82.3% vs. 65.6% (p<0.001) delayed phase; 80.2% vs 64.6% (p<0.001) overall phase.\(^5\)

The following enclosures are being submitted in support of the proposed changes:


We sincerely appreciate your considerations of these requests and welcome any additional dialogue. If any questions arise or if you require any additional information, please don’t hesitate to contact me by phone at (781) 257-2536 or email me at mhuber@tesarobio.com.

Sincerely,

[Signature]

Martin Huber, MD