Table 11: Summary of Recommendations in Included Guidelines

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
ASCO Guideline Update, Hesketh et al. (2020)[41]	
Adult patients receiving HEC "Adults treated with cisplatin and other high-emetic risk single agents should be offered a 4-drug combination of an NK1 receptor antagonist, a serotonin ($5HT_3$) receptor antagonist*, dexamethasone, and olanzapine (day 1). Dexamethasone and olanzapine should be continued on days 2 to 4."[41] (p. 2783)	Level of evidence: High Strength of recommendation: Strong
"Adults treated with anthracycline combined with cyclophosphamide should be offered a 4-drug combination of an NK1 receptor antagonist, a $5HT_3$ receptor antagonist, dexamethasone, and olanzapine (day 1). Dexamethasone and olanzapine should be continued on days 2 to 4."[41] (p. 2783)	Level of evidence: High Strength of recommendation: Strong
Adult patients receiving MEC "Adults treated with carboplatin area under the curve (AUC) ≥ 4 mg/min should be offered a 3-drug combination of an NK1 receptor antagonist, a $5HT_3$ receptor antagonist and dexamethasone (day 1)."[41] (p. 2783)	Level of evidence: High Strength of recommendation: Strong
"Adults treated with moderate-emetic-risk antineoplastic agents (excluding carboplatin AUC ≥ 4 mg/min) should be offered a 2-drug combination of a $5HT_3$ receptor antagonist and dexamethasone (day 1)"[41] (p. 2783).	Level of evidence: High Strength of recommendation: Strong
"Adults treated with cyclophosphamide, doxorubicin, oxaliplatin, and other moderate-emetic-risk antineoplastic agents known to cause delayed nausea and vomiting may be offered dexamethasone on days to 2 to 3."[41] (p. 2783)	Level of evidence: Low Strength of recommendation: Moderate
Pediatric patients receiving HEC "(Updated) Pediatric patients treated with high-emetic-risk antineoplastic agents should be offered a 3-drug combination of a $5HT_3$ receptor antagonist, dexamethasone, and aprepitant or fosaprepitant."[41] (p. 2785)	Level of evidence: Intermediate Strength of recommendation: Strong
"(Updated) Pediatric patients treated with high-emetic-risk antineoplastic agents who are unable to receive aprepitant or fosaprepitant should be offered a 2-drug combination of a $5HT_3$ receptor antagonist and dexamethasone."[41] (p. 2785)	Level of evidence: Intermediate Strength of recommendation: Strong
"(Updated) Pediatric patients treated with high-emetic-risk antineoplastic agents who are unable to receive dexamethasone should be offered a 2-drug combination of palonosetron and aprepitant or fosaprepitant."[41] (p. 2785)	Level of evidence: Intermediate Strength of recommendation: Strong
Pediatric patients receiving MEC "Pediatric patients treated with moderate-emetic-risk antineoplastic agents should be offered a 2-drug combination of a $5HT_3$ receptor antagonist and dexamethasone."[41] (p. 2785)	Level of evidence: Intermediate Strength of recommendation: Strong
"Pediatric patients treated with moderate-emetic-risk antineoplastic agents who are unable to receive dexamethasone should be offered a 2-drug combination of a $5HT_3$ receptor antagonist and aprepitant or fosaprepitant."[41] (p. 2785)	Level of evidence: Intermediate Strength of recommendation: Strong
*$5HT_3$ receptor antagonist: Granisetron, ondansetron, palonosetron, dolasetron, tropisetron, and ramosetron	

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
NCCN Guideline Update (2020)[42]	
Adult patients receiving HEC parenteral anticancer agents Day 1: Choose 1 of the following 3 treatment options and start before anticancer therapy • Treatment option A (preferred): A 4-drug combination of olanzapine, NK_1 RA (choose 1: aprepitant, fosaprepitant, netupitant, fosnetupitant, rolapitant), 5-HT_3 RA (choose 1: dolasetron. granisetron, ondansetron, palonosetron), and dexamethasone. • Treatment option B: A 3-drug combination of olanzapine, palonosetron, and dexamethasone. • Treatment option C: A 3-drug combination of NK_1 RA (choose 1: aprepitant, fosaprepitant, netupitant, fosnetupitant, rolapitant), 5-HT_3 RA (choose 1: dolasetron. granisetron, ondansetron, palonosetron), and dexamethasone. Days 2, 3, 4: • Treatment option A: Olanzapine, aprepitant, dexamethasone. • Treatment option B: Olanzapine. • Treatment option C: Aprepitant, dexamethasone.	All recommendations are category 2A (Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate)
Adult patients receiving MEC parenteral anticancer agents Day 1: Choose 1 of the following 3 treatment options: • Treatment option D: A 2-drug combination of 5-HT_3 RA (choose 1: dolasetron. granisetron, ondansetron, palonosetron), and dexamethasone. • Treatment option E: A 3-drug combination of olanzapine, palonosetron, and dexamethasone. • Treatment option F: A 3-drug combination of NK1 RA (choose 1: aprepitant, fosaprepitant, netupitant, fosnetupitant, rolapitant), 5-HT_3 RA (choose 1: dolasetron. granisetron, ondansetron, palonosetron), and dexamethasone. Days 2, 3: • Treatment option D: Dexamethasone OR 5-HT_3 RA monotherapy (granisetron, ondansetron or dolasetron). • Treatment option E: Olanzapine. • Treatment option F: Aprepitant ± dexamethasone.	
Adult patients receiving HEC or MEC oral anticancer agents • Start before anticancer therapy and continue daily with a 5-HT_3 RA (choose 1: dolasetron. granisetron, ondansetron).	
CCO Guideline Update (2019)[43]	
Adult patients receiving HEC, a single day IV chemotherapy • Day 1: A 4-drug combination of a NK1 RA (choose 1: aprepitant OR fosaprepitant OR NEPA), a 5-HT_3 RA (choose 1: granisetron, ondansetron, palonosetron), dexamethasone, and olanzapine. • Subsequent days: Aprepitant (days 2 and 3) if started on day 1, dexamethasone (days 2 to 4), and olanzapine (days 2 to 4). **Adult patients receiving MEC, a single day IV chemotherapy** • Day 1: A 2-drug combination of a 5-HT_3 RA (choose 1: granisetron, ondansetron,	None

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
palonosetron) and dexamethasone. • Subsequent days: No 5-HT_3 RA or dexamethasone recommended after day of chemotherapy. **Adult patients receiving HEC, multiple day IV chemotherapy** • Day 1: A 4-drug combination of aprepitant, a 5-HT_3 RA (choose 1: granisetron, ondansetron), dexamethasone and olanzapine. • Subsequent days: Aprepitant, dexamethasone, and olanzapine. These drugs are given up to 2 days after last dose of chemotherapy. **Adult patients receiving MEC, multiple day IV chemotherapy** • A 2-drug combination of a 5-HT_3 RA (choose 1: granisetron, ondansetron), and dexamethasone. • Subsequent days: No 5-HT_3 RA or dexamethasone recommended after day of chemotherapy.	
POGO Guideline Update (2017)[44]	
Children receiving HEC "We recommend that children ≥ 6 months old receiving HEC which is not known or suspected to interact with aprepitant receive granisetron or ondansetron or palonosetron + dexamethasone + aprepitant."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Strong
"We recommend that children < 6 months old receiving HEC receive granisetron or ondansetron or palonosetron + dexamethasone."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Strong
"We recommend that children ≥ 6 months old receiving HEC which is known or suspected to interact with aprepitant receive granisetron or ondansetron or palonosetron + dexamethasone."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Strong
"We recommend that children ≥ 6 months old receiving HEC which is not known or suspected to interact with aprepitant, and who cannot receive dexamethasone for CINV prophylaxis receive palonosetron + aprepitant."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Strong
"We suggest that children < 6 months old receiving HEC and who cannot receive dexamethasone for CINV prophylaxis receive palonosetron."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Weak
"We suggest that children receiving HEC, which is known or suspect to interact with aprepitant, and who cannot receive dexamethasone receive palonosetron."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Weak
Children receiving MEC "We recommend that children receiving MEC receive granisetron or ondansetron or palonosetron + dexamethasone."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Strong
"We suggest that children ≥ 6 months receiving MEC who cannot receive dexamethasone for CINV prophylaxis receive granisetron or ondansetron or palonosetron + aprepitant."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Weak
"We suggest that children < 6 months receiving MEC who cannot receive dexamethasone for CINV prophylaxis receive palonosetron."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Weak
"We suggest that children receiving MEC, which is known or suspected to interact with aprepitant, and who cannot receive dexamethasone receive palonosetron."[44] (p. 3)	Level of evidence: Moderate Strength of recommendation: Weak

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
Recommended dose of palonosetron for children • "1 month to < 17 years: 0.02 mg/kg IV once (maximum: 1.5 mg/dose) prechemotherapy."[44] (p. 3) • ≥ 17 years: 0.25 mg/dose IV or 0.5 mg/dose PO once prechemotherapy."[44] (p. 3)	• Level of evidence: Moderate • Strength of recommendation: Weak
MASCC/ESMO Guideline Update (2016)[45-47]	
Adult patients receiving HEC "For the prevention of non-AC highly emetogenic chemotherapy, a three-drug regimen including single doses of a 5-HT_3 RA (granisetron, ondansetron, dolasetron, tropisetron or palonosetron), dexamethasone and an NK_1 RA (aprepitant, fosaprepitant, netupitant or rolapitant), given before chemotherapy is recommended."[45] (p. v122)	MASCC Level of confidence: High Level of consensus: High ESMO Level of evidence: I Grade of recommendation: A
"In patients receiving non-AC highly emetogenic chemotherapy treated with a combination of an NK_1 RA, 5-HT_3 RA and dexamethasone to prevent acute nausea and vomiting, dexamethasone on days 2-4 is suggested to prevent delayed nausea and vomiting."[45] (p. v122)	MASCC Level of confidence: High Level of consensus: Moderate ESMO Level of evidence: I Grade of recommendation: B
"In women with breast cancer treated with a combination of a 5-HT_3 RA, dexamethasone and an NK_1 RA (aprepitant, fosaprepitant, netupitant or rolapitant), given before chemotherapy is recommended."[45] (p. v123)	MASCC Level of confidence: High Level of consensus: High ESMO Level of evidence: I Grade of recommendation: A
"In women with breast cancer treated with a combination of a 5-HT_3 RA, dexamethasone and an NK_1 RA to prevent acute nausea and vomiting, aprepitant or dexamethasone should be used on days 2 and 3 but not if fosaprepitant, netupitant or rolapitant has been used on day 1."[45] (p. v123)	MASCC Level of confidence: Moderate Level of consensus: Moderate ESMO Level of evidence: II Grade of recommendation: B
"Olanzapine may be considered with a 5-HT_3 RA plus dexamethasone, particularly when nausea is an issue, but using a 10 mg dose, patient sedation may be a concern."[45] (p. v124)	MASCC Level of confidence: Low Level of consensus: Low ESMO Level of evidence: II Grade of recommendation: B

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
Adult patients receiving MEC "For the prevention of acute emesis in MEC-treated patients, a 5-HT_3 RA plus dexamethasone is recommended."[45] (p. v125)	MASCC Level of confidence: Moderate Level of consensus: Moderate ESMO Level of evidence: II Grade of recommendation: B
"In patients receiving MEC with a known potential for delayed emesis, the use of dexamethasone for days 2-3 can be considered."[45] (p. v125)	MASCC Level of confidence: Low Level of consensus: Moderate ESMO Level of evidence: III Grade of recommendation: C
"No routine prophylaxis for delayed emesis can be recommended for all other patients receiving MEC."[45] (p. v125)	MASCC Level of confidence: No confidence possible Level of consensus: High ESMO Level of evidence: IV Grade of recommendation: D
Children receiving HEC "In children receiving chemotherapy of high emetic risk, an antiemetic prophylaxis with a 5-HT_3 RA (granisetron, ondansetron, tropisetron or palonosetron) plus dexamethasone plus aprepitant is recommended."[45] (p. v130)	MASCC Level of confidence: High Level of consensus: High ESMO Level of evidence: II Grade of recommendation: B
"Children who cannot receive dexamethasone should receive a 5-HT_3 RA plus aprepitant."[45] (p. v130)	MASCC Level of confidence: Moderate Level of consensus: High ESMO Level of evidence: II Grade of recommendation: B
"When aprepitant administration is not feasible or desirable, the guideline recommends a 5-HT_3 RA plus dexamethasone be given to children receiving highly emetogenic chemotherapy."[45] (p. v130)	MASCC Level of confidence: Moderate Level of consensus: High ESMO Level of evidence: II Grade of recommendation: B

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
Children receiving MEC "Children receiving MEC should receive antiemetic prophylaxis with a 5-HT_3 RA plus dexamethasone."[45] (p. v130)	MASCC Level of confidence: Moderate Level of consensus: High ESMO Level of evidence: II Grade of recommendation: B
"Children who cannot receive dexamethasone should receive a 5-HT_3 RA and aprepitant."[45] (p. v130)	MASCC Level of confidence: Moderate Level of consensus: High ESMO Level of evidence: II Grade of recommendation: B

AC = anthracycline/cyclophosphamide; ASCO = American Society of Clinical Oncology; CCO = Cancer Care Ontario; ESMO = European Society of Medical Oncology; GRADE = Grades of Recommendation Assessment, Development and Evaluation; 5-HT_3 RA = 5-hydroxytryptamine-3 receptor antagonist; HEC = high emetogenic chemotherapy; IV = IV; MASCC = Multinational Association of Supportive Care in Cancer; MEC = moderate emetogenic chemotherapy; NCCN = National Comprehensive Cancer Network; NEPA = netupitant/palonosetron; NK 1 RA = neurokinin 1 receptor antagonist; PO = by mouth; POGO = Pediatric Oncology Group of Ontario.