

# Strategies to Improve CINV Outcomes in Managed Care

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The appropriate management of chemotherapy-induced nausea and vomiting (CINV) offers opportunities to impact outcomes in 3 major areas: clinical, economic, and humanistic.<sup>1</sup> For patients, CINV can be physically and psychologically taxing. It impacts not only the patient's quality of life, but may also be a prognostic factor for overall survival and has economic implications, both in the cost of therapy and the cost of failure of therapy.<sup>2</sup> Prevention is the key; depending on the emetogenicity of the chemotherapy regimen, acute CINV may be prevented in 50% to 90% of patients.<sup>3,4</sup> However, delayed nausea and vomiting (NV), especially nausea, can still have significant impacts on patient outcomes.<sup>5</sup> CINV is likely to occur unless the interdisciplinary care team takes steps to prevent it. Healthcare providers and administrators who work in managed care systems need strategies to ensure that patients with cancer receive appropriate medications that address CINV proactively.

## Clinical Outcomes

CINV has the potential to cause severe physiologic effects, electrolyte disturbances, dehydration, malnutrition, and esophageal injury.<sup>6</sup> Symptoms often cause treatment nonadherence or dose reductions and can increase the cost of care for patients with cancer.<sup>7-11</sup> Oncology practitioners (N = 2000) indicate that 30% of all patients delay or discontinue therapy because of CINV.<sup>12</sup> Patients who have severe CINV may refuse treatment, request or require dose reductions, or seek alternative therapy options; these actions can negatively impact treatment efficacy.<sup>2,6</sup>

Poorly controlled CINV increases the possibility that the patient will develop additional NV, including anticipatory NV (ANV), a conditioned response that develops after experiencing CINV during treatment, which may also create difficulties.<sup>13,14</sup> If CINV is poorly controlled or uncontrolled, patients may begin to associate the oncology staff, the entrance to the treatment center, and the treatment room's sights and/or smells with NV. Over time, these sensory experiences alone may elicit NV in the absence of chemotherapy as a stimulus.<sup>14</sup> Once ANV develops, traditional antiemetics tend to be ineffective and patients may require psychotropic medication and/or behavioral therapy.<sup>14</sup>

## ABSTRACT

Managing chemotherapy-induced nausea and vomiting (CINV) is an opportunity for better clinical, economic, and humanistic outcomes. Clinicians working in managed care settings must understand background information about CINV's causes, likelihood, and treatment. They need to understand how CINV creates collateral damage (eg, psychological effects, electrolyte disturbances, dehydration, malnutrition, and esophageal injury). Patients with CINV are costly to treat and may be unable or unwilling to continue chemotherapy at doses needed. Several guidelines offer recommendations for selecting appropriate antiemetic medications. Most managed care organizations use or encourage their oncology staffs to use established guidelines. A trend is to tailor guidelines to address institution-specific policies, procedures, and idiosyncrasies. Patients receiving guideline-directed care for CINV tend to have better outcomes. Prophylaxis and treatment for CINV must be patient specific and consider risk factors that increase the likelihood of nausea and vomiting or, conversely, decrease the likelihood. Managed care clinicians should know that most of the guidelines do not include patient-specific factors in their prediction models for CINV. Although research has indicated that clinicians tend to underestimate and undertreat CINV, some research has indicated that clinicians can be too aggressive when providing prophylaxis for various types of CINV. Patient education is the cornerstone of good treatment planning, and educating patients on how and when to report symptoms is critical. Tools are available to help patients track symptoms. The multidisciplinary team must ensure that patients receive prophylaxis and appropriate treatment for their diagnoses, as well as treatment plans.

*Am J Manag Care.* 2018;24:S398-S404

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## Economic Outcomes

Value is a constant concern in healthcare. The cost of the treatment of CINV must be compared with the value of a successful cancer care outcome or the cost of failure to prevent CINV. Failing to prevent CINV can cause or contribute to higher costs in several ways. The clinical outcomes of nonadherence resulting in dose reductions or delays have already been discussed. There are other costs associated with CINV. Results published in 2011 of a study of 178 patients with cancer found increased costs associated with severe CINV. In the study, the average per-patient costs due to healthcare utilization for patients who reported severe nausea was \$802.40. Conversely, patients who reported moderate nausea had average costs of \$32.30 per patient, and those reporting mild nausea incurred average costs of \$6.70 per patient. These researchers estimated that uncontrolled CINV costs healthcare facilities \$778 during the first 5 days of chemotherapy.<sup>8</sup> Other study findings have revealed that uncontrolled CINV can double the cost of healthcare and can add between \$33 and \$1300 in costs.<sup>9-11</sup> A single CINV-related event in an inpatient, outpatient, or emergency department (ED) may cost more than \$5200.<sup>15</sup>

CINV also creates substantial indirect costs. The effects on patient and caregiver productivity can be tremendous, as managing CINV and making unanticipated visits consumes much time. A survey completed by 15,532 patients highlighted indirect costs. On average, patients with active cancer missed 18 workdays annually due to CINV, and visits to clinicians' offices to deal with CINV's numerous effects forced 28% of respondents to reduce their work hours from full time to part time.<sup>11</sup>

## Humanistic Outcomes

The largest impact of CINV is on the patient's quality of life. Performing daily tasks, seeing friends and family, and enjoying meals are all vital to keep morale high. These activities influence patients' outlook about chemotherapy treatment, improving motivation to complete therapy successfully. Patients already experiencing the psychological tolls of a cancer diagnosis may experience further negative impact if treatment begins and is accompanied by NV.

## Guideline-directed Treatments

Combined, the patient outcomes and cost data call for systemic approaches that ensure antiemetics are available and can be used appropriately. Understanding CINV and its direct and indirect fiscal consequences, and the medications used to prevent and treat it, ensures that the healthcare provider's rationale is clinically and fiscally sound.<sup>2,16</sup> Researchers have analyzed the costs of antiemetics in numerous studies; however, a recent review of economic studies indicates that the cost of CINV is highly variable and attributes the range of costs to the heterogeneity of strategies used to address it. They stated that the failure to effectively treat

CINV resulted in increases in the costs of medical care associated with increases in hospitalizations, medication expenditures, and ED and clinic visits. These researchers also indicated that unbiased comparisons of treatments are extremely difficult to make.<sup>17</sup>

Educating healthcare professionals on the impact that CINV has on their patients motivates them to address CINV more proactively. Improving communication among providers and patients could help improve patient outcomes, as there appears to be a disconnect between what providers perceive and what patients experience. Research shows that 88% to 95% of oncology providers said that their patients' CINV was well controlled with their current antiemetic regimens, but also indicated that 25% of their patients experienced uncontrolled CINV. Regardless, many of these same providers indicated that they stopped or delayed their patients' chemotherapy after CINV symptoms.<sup>12</sup> This highlights a difference in providers' perceptions and patients' realities. Managed care providers need to actively engage with patients and each other regarding CINV. Open communication among all parties is especially important to address each patient's unique NV symptoms.

Many managed care organizations use guidelines to direct therapy, improve outcomes, and manage medication costs. **Table 1**<sup>18-21</sup> lists the current evidence-based guidelines for CINV. Typical processes rely on examining the rationale for inclusion/exclusion into the guidelines and determining cost-effectiveness. The general assumption is that evidence-based guidelines will lead to better overall outcomes, reduce costs, and provide the value that the patient and the system are seeking. This appears to be the case in CINV.

In a large European observational study, 1000 patients who had received guideline-consistent antiemetic treatment had significantly better CINV control than those who did not receive guideline-consistent treatment. The complete control rates were 60% versus 51%, respectively.<sup>22</sup> Results of a study conducted in the United States<sup>23</sup> and a single-center United Kingdom observational study<sup>24</sup> found similar rates of control with evidence-based treatment guidelines. In the US study, the incidence of no CINV was significantly higher among those receiving guideline-consistent CINV prophylaxis than those who did not (53.4% vs 43.8%, respectively).<sup>23</sup>

Although the findings of each study demonstrated a clear association between guideline-consistent antiemetic prophylaxis and enhanced CINV control, unfortunately they also showed low rates of utilization. The overall adherence to guidelines was just 29% in the European study. Similar results were also seen in a large study in Asia-Pacific countries. Although the serotonin receptor antagonists were generally prescribed per guidelines, corticosteroids were not consistently administered, especially in the delayed phase. In the HEC setting, the neurokinin-1 antagonists (NK<sub>1</sub>s) were also frequently underused.<sup>25</sup>

Improving adherence to guidelines has been examined by several studies, with limited success.<sup>25-29</sup> Communication of a

**TABLE 1.** Guidelines for the Management of CINV<sup>18-21</sup>

Sponsoring Organization	Access
American Society of Clinical Oncology	Antiemetics: American Society of Clinical Oncology Focused Guideline Update. <a href="https://ascopubs.org/doi/pdf/10.1200/JCO.2017.74.4789">ascopubs.org/doi/pdf/10.1200/JCO.2017.74.4789</a> . Published in 2011 and updated in 2017.
Multinational Association of Supportive Care in Cancer (MASCC) and European Society for Medical Oncology (ESMO)	2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients: results of the Perugia consensus conference. <a href="https://academic.oup.com/annonc/article/27/suppl_5/v119/2237028">academic.oup.com/annonc/article/27/suppl_5/v119/2237028</a> . Published September 23, 2016.
National Comprehensive Cancer Network (NCCN)	NCCN Clinical Practice Guidelines in Oncology: Antiemesis. Version 3. <a href="https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf">nccn.org/professionals/physician_gls/pdf/antiemesis.pdf</a> . Published June 11, 2018.

**TABLE 2.** Evolving Pharmacy & Therapeutics Committee Responsibilities and Concerns

Traditional	Evolving
<ul style="list-style-type: none"> <li>• Safety</li> <li>• Efficacy</li> <li>• Outcomes</li> <li>• Cost (all other things equal)</li> </ul>	<ul style="list-style-type: none"> <li>• Pharmacoeconomics</li> <li>• Place in the guidelines</li> <li>• The product’s demonstrated value</li> <li>• Insurer reimbursement</li> <li>• Range of dosage forms</li> <li>• Quality metrics related to the treatment indication</li> <li>• Purchasing:                             <ul style="list-style-type: none"> <li>› Is product available through the organization’s normal supply chain?</li> <li>› Does the product require a limited distribution channel?</li> <li>› Is the product available for next-day delivery? Is extended time required for shipping?</li> <li>› Are there unique storage conditions?</li> </ul> </li> <li>• Availability through 340B drug discount program</li> <li>• Presence of bar coding appropriate for automated dispensing cabinets or bedside scanning</li> </ul>

Adapted from reference 29.

patient’s CINV outcomes to the provider seems to be the key factor in improving adherence, but, often, multitargeted strategies are necessary to see an impact.

Institutions should use evidence-based guidelines to direct the development of institution-specific guidelines. Economic decisions may impact the guidelines because new drugs are costlier; however, many drugs in the CINV guidelines are generically available or will soon be available. When multiple products within a therapeutic category are available, which is the case with antiemetics, organizations often use drug class reviews to investigate therapeutic equivalence and keep a preferred agent or a ranked listing of preferred agents in the guidelines. Traditionally, pharmacy

and therapeutics committees have looked at safety, efficacy, outcomes, and, all things being equal, acquisition costs when deciding on drugs to add to their formulary. However, today, the healthcare environment is more complicated, and medication management has broader responsibilities and evolving concerns (see **Table 2**).<sup>29</sup> Increasingly, complex pharmacoeconomic analyses contribute heavily to the discussion, and several organizations now offer value-based frameworks to help determine cost-effectiveness and guide medication management decision making (see **Table 3**).<sup>30</sup> Keeping the institution guidelines up-to-date can be a challenge as new drugs and data emerge that change the recommended

therapy. Periodic review and updating of the guidelines should be done with analysis of instructional guideline compliance. Timely feedback of the compliance analysis and of patient outcomes should be given to the providers.

### Treatment Planning: Patient-specific Antiemetic Regimens

Although chemotherapy emetogenicity is the primary risk factor for CINV, patient-specific risk factors influence the likelihood of developing CINV.<sup>13,30</sup> Most studies of risk factors have addressed acute CINV, but results of recent research indicate that in delayed CINV, as patients’ risk factors increase, so does the likelihood of CINV and treatment failure. Female patients are at highest risk.<sup>31</sup> Current guidelines acknowledge a chemotherapeutic agent’s potential to induce emesis using a 4-level classification scheme of emetogenic risk (minimal [ $<10\%$ ], low [ $10\%$  to  $30\%$ ], moderate [ $31\%$  to  $90\%$ ], and high [ $>90\%$ ]).<sup>19,20,32-35</sup> However, each patient responds to chemotherapy differently, necessitating patient-specific antiemetic regimens.

Current guidelines (see **Table 1**<sup>18-21</sup>) do not factor patient-specific criteria into recommended antiemetic combinations because few studies tease out each risk factor’s potential impact.<sup>36</sup> For example, it would be ideal if evidence indicated that people who have fewer risk factors (ie, older men with lung cancer who have consumed alcohol regularly) could use fewer than the 3 antiemetics recommended when receiving cisplatin. It is also important for clinicians to note that delayed nausea that occurs later than usual may be related to other medications; patients who have taken maintenance medications for years may be more sensitive to their adverse effects during treatment for cancer as their bodies change and adjust. Researchers are currently looking for ways to assess these factors that personalize assessment and emphasize developing a tool that can be used efficiently in clinical practice.<sup>19,37</sup>

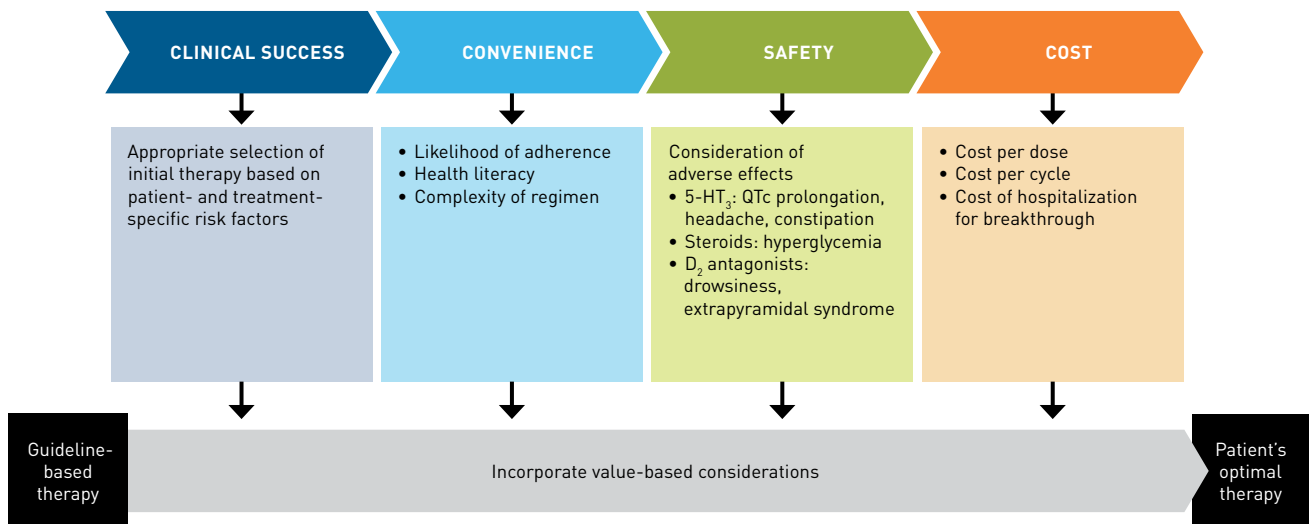
**TABLE 3.** Summary of Value Frameworks in Cancer Care<sup>30</sup>

Source	Question/Perspective	Factors Considered
American Society of Clinical Oncology's Value Framework	What is the clinical benefit in relation to cost? Perspective: providers, patients, shared decision making	Efficacy, toxicity, quality of life, bonus points, cost, context
The European Society for Medical Oncology's Magnitude of Clinical Benefit Scale	What is the clinical value? Perspective: providers, patients, society, policymakers, clinical guidelines	Efficacy, toxicity, quality of life, context
The Institute for Clinical & Economic Review's Value Assessment Framework	What is the societal value? Perspective: society, policymakers, payers	Long-term value, effectiveness, cost-effectiveness, convenience, context, budget impacts
Memorial Sloan Kettering Cancer Center's Drug Abacus	What is the just price for a cancer drug? Perspective: providers, policymakers	Efficacy, cost, toxicity, treatment novelty, cost of development, disease rarity, population burden, unmet need, prognosis
The National Comprehensive Cancer Network's Evidence Blocks	How do expert clinicians rate treatment value? Perspective: providers, patients, shared decision making	Efficacy/effectiveness, toxicity, affordability, evidence consistency

Before creating a treatment plan, the healthcare team needs to thoroughly assess patients at risk for CINV.<sup>13,31</sup> If prescribers just consider chemotherapy-related risk factors to select the antiemetic regimen, they may underestimate risk, provide inadequate prophylaxis, and fail to prevent NV.<sup>31</sup> Including both patient- and treatment-related risk factors provides the best antiemetic care possible. By using the institution's guidelines and working with patients, the team can develop an individualized treatment plan that meets the need of each patient (Figure).<sup>38</sup>

After considering patient-related risk factors, clinicians must select the best CINV treatment plan based on the chemotherapy's emetic potential and patient risk factors. This is an inexact science. The National Comprehensive Cancer Network states that the antiemetic regimen should be chosen based on the chemotherapeutic agent with the highest risk for CINV.<sup>13</sup> It is also important to provide the patient with antiemetics that will help both acute and delayed NV. Depending on the treatment regimen and patient-specific factors, antiemetic treatment may require a 5-HT<sub>3</sub> receptor

**FIGURE.** Proposed Value-Based Decision Algorithm for CINV<sup>38</sup>



5-HT indicates serotonin; CINV, chemotherapy-induced nausea and vomiting. American health & drug benefits by Engage Healthcare Communications, LLC. Reproduced with permission of Engage Healthcare Communications, LLC in the format Continuing Education via Copyright Clearance Center.

antagonist and an NK<sub>1</sub> receptor antagonist or both.<sup>13</sup> In instances where patients are undergoing chemotherapy with very high risk for CINV, such as cisplatin, a corticosteroid may also be needed.<sup>7</sup> Ensuring that clinicians have access to 5-HT<sub>3</sub> receptor antagonists, NK<sub>1</sub> receptor antagonists, olanzapine, benzodiazepines, and dexamethasone is vital.

The oncology team may need to consider additional treatment if the patient experiences ANV; researchers indicate that the difficulty treating ANV is an unmet need.<sup>39</sup> Unfortunately, due to its strong psychological component, ANV does not respond to typical antiemetic medications.<sup>14</sup> Drug options include benzodiazepines, such as lorazepam and alprazolam,<sup>13</sup> but the most effective method to combat ANV is behavioral therapies.<sup>14</sup> It is important for providers to reach out to the patient, explain ANV, and provide care if necessary.

The previous paragraphs recommend aggressive prophylaxis for CINV. Managed care clinicians should be aware that, conversely, treatment can be unnecessarily aggressive. The American Society of Clinical Oncology (ASCO) recognizes this risk in one of its recommendations on the American Board of Internal Medicine (ABIM) Foundation's Choosing Wisely website ([choosingwisely.org](http://choosingwisely.org)).<sup>8</sup> The ABIM Foundation established this site to promote conversations about care that is supported by evidence, does not duplicate tests or procedures, and is free from harm and truly necessary. Based on data accumulated by ASCO's Cost of Cancer Care Task Force, it recommends, "Don't give patients starting on a chemotherapy regimen that has a low or moderate risk of causing nausea and vomiting antiemetic drugs intended for use with a regimen that has a high risk of causing nausea and vomiting."<sup>40</sup>

This recommendation, which was vetted thoroughly by community-based oncologists, state/regional oncology societies, and advocacy groups, suggests that clinicians need to weigh their choices carefully. ASCO notes that antiemetics can be very expensive and have potential adverse effects. When the likelihood of CINV is low or moderate, more cost-effective drugs are available.<sup>40</sup>

In the managed care setting, each provider can actively engage in their patients' care, include the patient as a partner, and greatly improve outcomes. It is crucial that providers understand the types of NV, the mechanisms of action, and the various treatment modalities. Proper knowledge of the complications and the medication guidelines is critical. If healthcare professionals are not up-to-date with the newer treatment methods, the results for the patient could be disastrous.

### Behavioral Interventions: Educate Every Patient

Each patient beginning chemotherapy is likely to approach treatment with their own expectations.<sup>13</sup> Many patients fear NV more than any other aspect of treatment.<sup>41</sup> Patients may recall friends or family members who received cancer treatment struggling greatly with these symptoms in the past. Before initiating chemotherapy,

the oncology team needs to address misperceptions and educate patients about current treatment options and success rates. Describing CINV treatments, setting realistic expectations, and reviewing treatment goals help patients prepare to deal with adverse effects.

Providers should discuss the various types of CINV, such as acute, delayed, and ANV, with patients.<sup>6</sup> Key talking points include describing how CINV treatment is prophylactic in nature and that it is especially important for them to continue taking the antiemetic even if they experience no nausea or vomiting.<sup>31</sup> It is also important to provide CINV education and resources to younger patients. Research indicates that 75% of patients 50 years and older remained adherent to their antiemetic plans, but only 50% of younger patients maintained adherence.<sup>13,42</sup> To ensure proper CINV control, patients need to understand the importance of beginning their antiemetic regimen before they feel nauseated and to continue taking it throughout, and possibly for several days after, each chemotherapy cycle.<sup>42</sup>

Open communication and effective questioning between patient and provider is vital. The oncology team, which should include a pharmacist, should specifically describe delayed NV carefully because it is more common than acute CINV and it often occurs at home.<sup>43,44</sup> Patients may inadvertently downplay the severity of their NV because by the time they attend the next appointment, symptoms have subsided.<sup>31</sup> Patients discharged home are less likely to report CINV,<sup>23,45</sup> prefer to report treatment benefits,<sup>46</sup> forget its magnitude, or simply do not report it to avoid dose adjustments or treatment delays.<sup>47</sup> Clinicians need tools to ensure that they monitor CINV appropriately and will find the Hematology/Oncology Pharmacy Association's Time to Talk CINV resource selection helpful. It includes clinician and patient checklists, chemotherapy adverse effect trackers, a myth and fact flyer, and various other tools.<sup>48</sup>

Due to the subjective nature of CINV, patients receive the best symptom management when they self-report their symptoms accurately.<sup>6</sup> The team needs to show patients how to monitor and note symptom severity if they experience delayed CINV.<sup>31</sup> Healthcare providers should also encourage patients to freely discuss their thoughts, fears, and experiences surrounding their CINV. Vomiting is obvious to track, but nausea is more difficult to assess because it is a subjective experience, an unpleasant sensation in the epigastrium and at the back of the throat. Several tools that measure NV are available and help patients self-report CINV accurately. A 2008 review compared 7 tools used to assess NV clinically and found that many are conceptually confusing, meaning they assess different types and phases of CINV, and often ignore functional impact. The most comprehensive tools tended to be long and difficult to interpret.<sup>49</sup> However, they found the most concise tool to be the Multinational Association of Supportive Care in Cancer (MASCC) Antiemesis Tool (MAT).<sup>49</sup> The MAT is a validated 8-item visual analog scale that is available free-of-charge as printable forms and as a smartphone



app. MASCC provides an accompanying guide for clinicians, and it is reproducible so patients can describe their nausea levels.<sup>50,51</sup>

Patients receive chemotherapy most often in outpatient settings and benefit from clear and concise instructions on proper at-home use of their antiemetics.<sup>13</sup> Pharmacists and other healthcare providers can help educate patients by discussing the medication with them before they leave the clinic and ensuring they understand how to take the medication. A critical point is that patients or their caregivers need to know who to contact and how to do so if the patients experience problems. Pharmacists who practice in ambulatory care settings can engage patients each time they fill prescriptions for antiemetics by asking about symptom control. Patients who experience severe vomiting may have difficulty with oral medications; alternatives such as sublingual and buccal formulations can provide relief. Others may be adequately controlled in the acute setting, but experience breakthrough or delayed NV.

Education on nonpharmacologic methods is also important because these may help reduce the prevalence of CINV. Simple things such as wearing loose clothing, resting when fatigued, avoiding foods that may upset the stomach, and eating smaller meals can help the patient feel more comfortable. An important point to stress is that although complementary therapies, such as ginger, can be effective, patients should not use them instead of prescribed medication.<sup>31,52-55</sup>

### Multidisciplinary Collaboration

Many patients with cancer have comorbidities that complicate the clinical picture. Healthcare practitioners working in oncology need a broad knowledge base and healthcare professionals from all disciplines (eg, nursing; pharmacy; and medical, surgical, or radiation oncology) contribute different expertise. Including multiple healthcare providers from various specialties is crucial for developing specialized CINV treatment plans. Each professional has specific responsibilities and skills in the care of patients undergoing chemotherapy and brings their accumulated knowledge.<sup>22</sup>

Most guidelines share common features, and the oncology team needs to buy into key points that emphasize prevention<sup>19,20,33,35,56</sup>:

- A 10% risk of CINV is the threshold at which patients should receive prophylaxis
- Prophylaxis should be administered or available for the entire risk period
- Oral and intravenous antiemetics have the same efficacy
- Clinicians should prescribe the antiemetic treatment most likely to be effective based on the chemotherapy's emetogenicity, the patient's history of CINV, and risk factors unique to the patient
- Patients receiving highly emetogenic agents and anthracycline-based chemotherapy regimens need 5-HT<sub>3</sub> RA and NK<sub>1</sub>-receptor antagonists with dexamethasone

Oncology pharmacists are well versed in chemotherapy drugs and the antiemetics used to combat CINV. They can aid in developing the patient care plan by assessing the risk of the chemotherapeutic agent and determining which antiemetic regimen would be of most benefit to the patient. Frequently, drug interactions occur with the increasingly complex treatment plans, and pharmacists are the best trained to manage interactions and develop plans to meet treatment goals. Due to their frequent contact with individual patients, nurses are often better placed to assess patient-specific risk factors for CINV and can help ensure that CINV is being adequately controlled.<sup>13,31</sup> Behavioral health specialists can aid with the psychological component of treatment and provide the necessary care should ANV arise. Additional providers, such as social workers and nutritionists, are valuable on the patient care team if patients experience difficulty with eating and other activities of daily living.

### Conclusions

Today, healthcare providers can prevent and relieve their patients' CINV with unprecedented success. Numerous guidelines summarize the accumulated evidence, yet there are still unmet needs.<sup>19,20,33,35</sup> The goal of guideline-directed treatments should be to have zero CINV, and patients who receive proven CINV interventions at appropriate times can come close to achieving that goal while continuing activities of daily living and pursuing pleasurable activities soon after treatment. Appropriate CINV prophylaxis maintains quality of life for patients and, more importantly, avoids chemotherapy dose reductions or discontinuation. As the body of evidence accumulates indicating that antiemetic safety, effectiveness, and outcomes are good, preventing CINV becomes a clinical responsibility. ■

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**Funding source:** This activity is supported by an independent educational grant from Helsinn Therapeutics (U.S.), Inc.

**Author disclosure:** Dr Soefje has reported the following relevant financial relationships with commercial interests: Consultant, Heron Therapeutics; Honoraria, PTCE CINV talk at 2018 HOPA Annual meeting.

**Authorship information:** Drafting of the manuscript, critical revision of the manuscript for important intellectual content, and supervision.

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Dr Soefje gratefully acknowledges Jeannette Y. Wick, RPh, MBA, FASCP, for her contributions to the development of this article.

### REFERENCES

1. Kozma CM, Reeder CE, Schulz RM. Economic, clinical, and humanistic outcomes: a planning model for pharmaco-economic research. *Clin Ther*. 1993;15(6):1121-1132.
2. McCullough SW. Chemotherapy-induced nausea and vomiting: roles of pharmacists and formulary decision makers. *Am J Manag Care*. 2017;23(suppl 14):S266-S271.
3. Cohen L, de Moor CA, Eisenberg P, Ming EE, Hu H. Chemotherapy-induced nausea and vomiting: incidence and impact on patient quality of life at community oncology settings. *Support Care Cancer*. 2007;15(5):497-503. doi: 10.1007/s00520-006-0173-z.
4. Koth SM, Kolesar J. New options and controversies in the management of chemotherapy-induced nausea and vomiting. *Am J Health Syst Pharm*. 2017;74(11):812-819. doi: 10.2146/ajhp160227.

5. Bloechl-Daum B, Deuson RR, Mavros P, Hansen M, Herrstedt J. Delayed nausea and vomiting continue to reduce patients' quality of life after highly and moderately emetogenic chemotherapy despite antiemetic treatment. *J Clin Oncol*. 2006;24(27):4472-4478. doi: 10.1200/JCO.2006.05.6382.
6. Gu L, Li J. The assessment and management of chemotherapy-induced nausea and vomiting among cancer patients in a chemotherapy ward: a best practice implementation project. *JBI Database System Rev Implement Rep*. 2016;14(3):235-246. doi: 10.11124/JBISRIIR-2016-2626.
7. Hesketh PJ, Palmas M, Nicolas P. Preventing chemotherapy-induced nausea and vomiting in patients with lung cancer: efficacy of NEPA (netupitant-palonosetron), the first combination antiemetic. *Support Care Cancer*. 2018;26(4):1151-1159. doi: 10.1007/s00520-017-3936-9.
8. Haiderali A, Menditto L, Good M, Teitelbaum A, Wegner J. Impact on daily functioning and indirect/direct costs associated with chemotherapy-induced nausea and vomiting (CINV) in a US population. *Support Care Cancer*. 2011;19(6):843-851. doi: 10.1007/s00520-010-0915-9.
9. Knoth RL, Chang E, Broder MS, Powers A. Examining healthcare costs in chemotherapy induced nausea and vomiting: a retrospective analysis. Presented at: Academy of Managed Care Pharmacy Annual Meeting; April 2-5, 2013; San Diego, CA. [pharllc.com/wp-content/uploads/2013/03/Knoth-AMCP-2011a.pdf](http://pharllc.com/wp-content/uploads/2013/03/Knoth-AMCP-2011a.pdf).
10. Shih YCT, Xu Y, Elting LS. Costs of uncontrolled chemotherapy-induced nausea and vomiting among working-age cancer patients receiving highly or moderately emetogenic chemotherapy. *Cancer*. 2007;110(3):678-685. doi: 10.1002/cncr.22823.
11. Henry DH, Viswanathan HN, Elkin EP, Traina S, Wade S, Cella D. Symptoms and treatment burden associated with cancer treatment: results from a cross-sectional national survey in the U.S. *Support Care Cancer*. 2008;16(7):791-801. doi: 10.1007/s00520-007-0380-2.
12. Van Laar ES, Desai JM, Jatoi A. Professional educational needs for chemotherapy-induced nausea and vomiting (CINV): multinational survey results from 2388 healthcare providers. *Support Care Cancer*. 2015;23(1):151-157. doi: 10.1007/s00520-014-2325-x.
13. Thompson N. Optimizing treatment outcomes in patients at risk for chemotherapy-induced nausea and vomiting. *Clin J Oncol Nurs*. 2012;16(3):309-313. doi: 10.1188/12.CJON.309-313.
14. Kamen C, Tejani MA, Chandwani K, et al. Anticipatory nausea and vomiting due to chemotherapy. *Eur J Pharmacol*. 2014;722:172-179. doi: 10.1016/j.ejphar.2013.09.071.
15. Burke TA, Wisniewski T, Ernst FR. Resource utilization and costs associated with chemotherapy-induced nausea and vomiting (CINV) following highly or moderately emetogenic chemotherapy administered in the US outpatient hospital setting. *Support Care Cancer*. 2011;19(1):131-140. doi: 10.1007/s00520-009-0797-x.
16. Haiderali A, Menditto L, Good M, Teitelbaum A, Wegner J. Impact on daily functioning and indirect/direct costs associated with chemotherapy-induced nausea and vomiting (CINV) in a U.S. population. *Support Care Cancer*. 2011;19(6):843-851. doi: 10.1007/s00520-010-0915-9.
17. Sommariva S, Pongiglione B, Tarricone R. Impact of chemotherapy-induced nausea and vomiting on health-related quality of life and resource utilization: a systematic review. *Crit Rev Oncol Hematol*. 2016;99:13-36. doi: 10.1016/j.critrevonc.2015.12.001.
18. Basch E, Prestrud AA, Hesketh PJ, et al; American Society of Clinical Oncology. Antiemetics: American Society of Clinical Oncology clinical practice guideline update [erratum in *J Clin Oncol*. 2014;32(19):2117]. *J Clin Oncol*. 2011;29(31):4189-4198. doi: 10.1200/JCO.2010.34.4614.
19. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2017;35(28):3240-3261. doi: 10.1200/JCO.2017.74.4789.
20. NCCN Clinical Practice Guidelines in Oncology. Antiemesis, version 3.18. Fort Washington, PA: Harborside Press; 2018. [nccn.org/professionals/physician\\_gls/pdf/antiemesis.pdf](http://nccn.org/professionals/physician_gls/pdf/antiemesis.pdf).
21. Aapro M, Gralla RJ, Herrstedt J, Molassiotis A, Roila F. MASCC/ESMO Antiemetic Guidelines 2016. V.1.2. Multinational Association for Supportive Care in Cancer website. [mascc.org/antiemetic-guidelines](http://mascc.org/antiemetic-guidelines). Updated March 2016. Accessed July 7, 2018.
22. Aapro M, Molassiotis A, Dico M, et al; PEER Investigators. The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): Pan European Emesis Registry (PEER). *Ann Oncol*. 2012;23(8):1986-1992. doi: 10.1093/annonc/mds021.
23. Gilmore JW, Peacock NW, Gu A, et al. Antiemetic guideline consistency and incidence of chemotherapy-induced nausea and vomiting in US community practice: INSPIRE Study. *J Onc Pract*. 2013;10(1):68-74. doi: 10.1200/JOP.2012.000816.
24. Molassiotis A, Saunders MP, Valle J, et al. A prospective observational study of chemotherapy-related nausea and vomiting in routine practice in a UK cancer centre. *Support Care Cancer*. 2008;16(2):201-208. doi: 10.1007/s00520-007-0343-7.
25. Yu S, Burke TA, Chan A, et al. Antiemetic therapy in Asia Pacific countries for patients receiving moderately and highly emetogenic chemotherapy—a descriptive analysis of practice patterns, antiemetic quality of care, and use of antiemetic guidelines. *Support Care Cancer*. 2015;23(1):273-282. doi: 10.1007/s00520-014-2372-3.
26. Mertens WC, Higby DJ, Brown D, et al. Improving the care of patients with regard to chemotherapy-induced nausea and emesis: the effect of feedback to clinicians on adherence to antiemetic prescribing guidelines. *J Clin Oncol*. 2003;21(7):1373-1378. doi: 10.1200/JCO.2003.08.118.
27. Dranitsaris G, Leung P, Warr D. Implementing evidence based antiemetic guidelines in the oncology setting: results of a 4-month prospective intervention study. *Support Care Cancer*. 2001;9(8):611-618.
28. Roila F. Transferring scientific evidence to oncological practice: a trial on the impact of three different implementation strategies on antiemetic prescriptions. *Support Care Cancer*. 2004;12(6):446-453. doi: 10.1007/s00520-003-0553-6.
29. Kaiser R. Antiemetic guidelines: are they being used? *Lancet Oncol*. 2005;6(8):622-625. doi: 10.1016/S1470-2045(05)70284-9.
30. Young A, Dielenseger P, Fernandez Ortega P, et al. Helping patients discuss CINV management: development of a Patient Charter. *Eccancermedicallscience*. 2013;7:296. doi: 10.3332/ecancer.2013.296.
31. Leber MB. Formulary considerations: the past, present, and future. *Am J Manag Care*. 2017;23(12 Spec No.):SP490-SP491.
32. Sekine I, Segawa Y, Kubota K, Saeki T. Risk factors of chemotherapy-induced nausea and vomiting: Index for personalized antiemetic prophylaxis. *Cancer Sci*. 2013;104(6):711-717. doi: 10.1111/cas.12146.
33. Kris MG, Uribá SG, Schwartzberg LS. Clinical roundtable monograph: treatment of chemotherapy-induced nausea and vomiting: a post-MASCC 2010 discussion. *Clin Adv Hematol Oncol*. 2011;9(1):1-15.
34. Molassiotis A, Stamataki Z, Kontopantelis E. Development and preliminary validation of a risk prediction model for chemotherapy-related nausea and vomiting. *Support Care Cancer*. 2013;21(10):2759-2767. doi: 10.1007/s00520-013-1843-2.
35. Hesketh PJ, Bohlke K, Lyman GH, et al. Antiemetics: American Society of Clinical Oncology focused guideline update. *J Clin Oncol*. 2016;34(4):381-386. doi: 10.1200/JCO.2017.74.4789.
36. Roila F, Herrstedt J, Aapro M, et al; ESMO/MASCC Guidelines Working Group. Guideline update for MASCC and ESMO in the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting: results of the Perugia consensus conference. *Ann Oncol*. 2010;21(suppl 5):v232-v243. doi: 10.1093/annonc/mdq194.
37. Hu Z, Liang W, Yang Y, et al. Personalized estimate of chemotherapy-induced nausea and vomiting: development and external validation of a nomogram in cancer patients receiving highly/moderately emetogenic chemotherapy. *Medicine (Baltimore)*. 2016;95(2):e2476. doi: 10.1097/MD.0000000000002476.
38. Rao KV, Faso A. Chemotherapy-induced nausea and vomiting: optimizing prevention and management. *Am Health Drug Benefits*. 2012;5(4):232-240.
39. Aapro M. CINV: still troubling patients after all these years. *Support Care Cancer*. 2018;26(suppl 1):5-9. doi: 10.1007/s00520-018-4131-3.
40. American Society of Clinical Oncology recommendations: antiemetic drugs for chemotherapy. ChoosingWisely, American Board of Internal Medicine Foundation website. [choosingwisely.org/clinicians/americansociety-clinical-oncology-antiemetic-drugs-for-chemotherapy](http://choosingwisely.org/clinicians/americansociety-clinical-oncology-antiemetic-drugs-for-chemotherapy). Published October 29, 2013. Accessed July 7, 2018.
41. Mellin C, Lexa M, Leak Bryant A, Mason S, Mayer DK. Antiemetic guidelines: using education to improve adherence and reduce incidence of CINV in patients receiving highly emetogenic chemotherapy. *Clin J Oncol Nurs*. 2018;22(3):297-303. doi: 10.1188/18.CJON.297-303.
42. Shih V, Wan HS, Chan A. Clinical predictors of chemotherapy-induced nausea and vomiting in breast cancer patients receiving adjuvant doxorubicin and cyclophosphamide. *Ann Pharmacother*. 2009;43(3):444-452. doi: 10.1345/aph.1L437.
43. Schnell FM. Chemotherapy-induced nausea and vomiting: the importance of acute antiemetic control. *Oncologist*. 2003;8(2):187-198. doi: 10.1634/theoncologist.8-2-187.
44. Escobar Y, Cajaraville G, Virizuela JA, et al. Incidence of chemotherapy-induced nausea and vomiting with moderately emetogenic chemotherapy: ADVICE (Actual Data of Vomiting Incidence by Chemotherapy Evaluation) study [erratum in *Support Care Cancer*. 2015;23(9):2841]. *Support Care Cancer*. 2015;23(9):2833-2840. doi: 10.1007/s00520-015-2809-3.
45. Jordan K, Gralla R, Jahn F, Molassiotis A. International antiemetic guidelines on chemotherapy induced nausea and vomiting (CINV): content and implementation in daily routine practice. *Eur J Pharmacol*. 2014;722:197-202. doi: 10.1016/j.ejphar.2013.09.073.
46. Di Maio M, Gallo C, Leigh NB, et al. Symptomatic toxicities experienced during anticancer treatment: agreement between patient and physician reporting in three randomized trials. *J Clin Oncol*. 2015;33(8):910-915. doi: 10.1200/JCO.2014.57.9334.
47. Vidall C, Dielenseger P, Farrell C, et al. Evidence-based management of chemotherapy-induced nausea and vomiting: a position statement from a European cancer nursing forum. *Eccancermedicallscience*. 2011;5:211. doi: 10.3332/ecancer.2011.211.
48. Time to talk CINV. Hematology/Oncology Pharmacy Association website. [hoparx.org/patient-education/time-to-talk-cinv](http://hoparx.org/patient-education/time-to-talk-cinv). Accessed July 10, 2018.
49. Brearley SG, Clements CV, Molassiotis A. A review of patient self-report tools for chemotherapy-induced nausea and vomiting. *Support Care Cancer*. 2008;16(11):1213-1229. doi: 10.1007/s00520-008-0428-y.
50. Molassiotis A, Coventry PA, Stricker CT, et al. Validation and psychometric assessment of a short clinical scale to measure chemotherapy-induced nausea and vomiting: the MASCC antiemesis tool. *J Pain Symptom Manag*. 2007;34(2):148-159. doi: 10.1016/j.jpainsymman.2006.10.018.
51. MASCC antiemesis tool. Multinational Association of Supportive Care in Cancer website. [mascc.org/mat](http://mascc.org/mat). Updated 2018. Accessed July 7, 2018.
52. Li X, Qin Y, Liu W, Zhou XY, Li YN, Wang LY. Efficacy of ginger in ameliorating acute and delayed chemotherapy-induced nausea and vomiting among patients with lung cancer receiving cisplatin-based regimens: a randomized controlled trial. *Integr Cancer Ther*. 2018;17(3):747-754. doi: 10.1177/1534735417753541.
53. Marx W, McCarthy AL, Ried K, et al. The effect of a standardized ginger extract on chemotherapy-induced nausea-related quality of life in patients undergoing moderately or highly emetogenic chemotherapy: a double blind, randomized, placebo controlled trial. *Nutrients*. 2017;9(8):pii:E867. doi: 10.3390/nu9080867.
54. Bossi P, Cortinovis D, Fatigoni S, et al. A randomized, double-blind, placebo-controlled, multicenter study of a ginger extract in the management of chemotherapy-induced nausea and vomiting (CINV) in patients receiving high-dose cisplatin. *Ann Oncol*. 2017;28(10):2547-2551. doi: 10.1093/annonc/mdx315.
55. Konnum J, Danwilai K, Ngamphaiboon N, Sripanidkulchai B, Sookprasert A, Subongkot S. A phase II randomized double-blind placebo-controlled study of 6-gingerol as an anti-emetic in solid tumor patients receiving moderately to highly emetogenic chemotherapy. *Med Oncol*. 2017;34(4):69. doi: 10.1007/s12032-017-0931-4.
56. Roila F, Hesketh PJ, Herrstedt J; Antiemetic Subcommittee of the Multinational Association of Supportive Care in Cancer. Prevention of chemotherapy- and radiotherapy-induced emesis: results of the 2004 Perugia International Antiemetic Consensus Conference. *Ann Oncol*. 2006;17(1):20-28. doi: 10.1093/annonc/mdj078.