Consideration of evidence on antiemetic drugs for nausea and vomiting associated with chemotherapy or radiation therapy in adults

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Record Status
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Citation

Authors' conclusions
For the maximal patient outcome of total control (no emesis, no use of rescue medication, no or only mild nausea), the evidence was strongest in support of a significant increase with mixed oral and injectable three-drug regimens containing aprepitant compared to two-drug regimens without aprepitant during the overall study period, as well as during both the acute and delayed treatment periods in adults undergoing highly emetogenic chemotherapy. However, the benefit of a multi-day, three-drug, aprepitant-containing regimen was minimal during the acute period and only became larger in magnitude during the overall and delayed periods when the control group was administered the 5-HT3 antagonist on day 1 only. For all-oral regimens, comparisons of regimens with or without aprepitant or between two-drug regimens without aprepitant, there was low-strength evidence of no significant differences for the outcome of total control. No conclusions could be reached about total control for the comparison among different mixed two-drug regimens, without aprepitant, as evidence was unavailable for this outcome.

For complete response (no emesis, no use of rescue medication), there was predominantly high-strength evidence indicating a significant increase in benefit with three-drug regimens containing aprepitant compared to two-drug regimens without aprepitant during all study periods, regardless of whether the antiemetics were all given by an oral route or mixed oral and intravenous routes. Again, however, in the case where mixed routes were used in patients undergoing primarily highly emetogenic chemotherapy, the benefit of a multi-day, three-drug, aprepitant-containing regimen was minimal during the acute period and only became larger in magnitude during the overall and delayed periods when the control group was administered the 5-HT3 antagonist on day 1 only. There was only low-strength evidence of no significant differences in complete response between different mixed oral and intravenous route two-drug regimens, without aprepitant. No conclusions could be reached about complete response for the comparison among different all-oral, two-drug regimens, without aprepitant, as evidence was unavailable for this outcome.

Overall, comparative evidence on the impact of antiemetic regimens on the patient's ability to tolerate subsequent chemotherapy sessions was low strength. Based on a single study of Chinese women undergoing moderately emetogenic chemotherapy, an all-oral, three-drug, aprepitant-containing regimen resulted in significantly fewer patients needing to delay subsequent chemotherapy sessions compared to an all-oral two-drug regimen not containing aprepitant. Applicability of these findings to a broader population was not clear. For mixed oral and intravenous regimens, no difference in the rate of completion of six cycles of chemotherapy was found between three-drug, aprepitant-containing regimens and two-drug regimens, based on a pooled analysis of data from extensions phases of two short-term randomized controlled trials. Further studies designed with this outcome as primary are needed to reliably answer this question.

There was no significant differences found between any regimens in incidence of overall adverse events for three-drug, aprepitant-containing regimens compared with two-drug regimens without aprepitant both when all-oral regimens were compared in patients undergoing moderately emetogenic chemotherapy (moderate-strength evidence) and when mixed oral and intravenous regimens were compared in patients undergoing highly emetogenic chemotherapy (high-strength evidence). There was only low-strength evidence of no significant differences in incidence of overall adverse events between different two-drug regimens without aprepitant, regardless of whether they were all given orally, or using a mixed oral and intravenous regimen.

The applicability of this evidence to patients age 65 and older is still somewhat limited, with only four studies reporting subgroup analyses. When compared to a two-drug regimen where the 5-HT3 antagonist was administered on day 1 only,
a mixed oral and intravenous three-drug regimen containing aprepitant was superior in rates of complete response across the five-day period from start of chemotherapy. These findings were limited in that they only related to this specific comparison and to only one outcome measure, did not include evidence on comparative harms, and some of these data were unpublished. The evidence base had strong applicability to women, with approximately 60% of all enrolled patients across the studies being female. While women experienced higher rates of chemotherapy induced nausea and vomiting than men, it appeared that both oral and mixed intravenous/oral three-drug regimens were superior to two-drug regimens in women, with women achieving a slightly higher rate of complete response compared to men. However, there was inadequate evidence on any differences in harms to make conclusions.

Insufficient evidence was available for evaluating disparate effects on socioeconomic status or ethnicity/race. Although we attempted to identify studies in patients undergoing radiation, only one study was available, and it was rated poor quality.

As with other types of research, the limitations of this systematic review are important to recognize as well. These can be divided into two groups: those relating to generalizability of the results and those relating to methodology within the scope of this review. The generalizability of the results was affected by the scope of the key questions and inclusion criteria. The impact on generalizability determined by scope was separate to the applicability provided by the included studies themselves, as discussed above. In accordance with the specific programmatic interests of CMS, the scope of this systematic review was limited to studies of three-drug regimens including aprepitant, a 5-HT3 antagonist (e.g., dolasetron, granisetron, ondansetron, palonosetron), and a corticosteroid (e.g., dexamethasone, prednisone) or two-drug regimens including a 5-HT3 antagonist and a corticosteroid. Further, the primary focus was on comparing regimens where all drugs were given by the oral route to each other or to regimens where all drugs were given by the intravenous route, and to regimens given by mixed oral and intravenous routes. Consequently, evaluation of the evidence from the numerous studies that compared regimens where all drugs are given by intravenous routes was not represented here. Methodological limitations of the review within the defined scope included the exclusion of studies published in languages other than English and lack of a specific search for unpublished studies.

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