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Aprepitant for Chemotherapy-Induced Nausea and Vomiting

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The development of serotonin receptor antagonists in the 1990s greatly improved treatment for chemotherapy-induced nausea and vomiting. However, despite the addition of serotonin receptor antagonists, patients receiving chemotherapy continue to experience this troublesome side effect.

On March 26, 2003, the U.S. Food and Drug Administration approved aprepitant (Emend®, Merck & Co., Inc., Whitehouse Station, NJ), the first neurokinin-1 (NK-1) receptor antagonist to be approved for use in combination with standard antiemetic agents for acute and delayed nausea and vomiting with initial and repeat courses of highly emetogenic chemotherapy, including high-dose cisplatin (Merck News, 2003). Unlike other antiemetics that block neurotransmitter receptors for dopamine and serotonin, aprepitant prevents substance P from binding to the NK-1 receptor sites in the brainstem (medulla), resulting in inhibition of emesis (Bountra et al., 1996).

Chemotherapy-Induced Nausea and Vomiting

Cisplatin is a highly emetogenic chemotherapy agent, causing vomiting in more than 90% of patients (Hesketh et al., 1997). It has a biphasic pattern of emesis, with the first peak around 6–8 hours (acute emesis) and the second peak around 48–72 hours (delayed emesis) (Tavorath & Hesketh, 1996).

Although the development of serotonin receptor antagonists has greatly improved treatment for chemotherapy-induced nausea and vomiting, patients receiving chemotherapy continue to experience this troublesome side effect. On March 26, 2003, the U.S. Food and Drug Administration approved aprepitant (Emend®, Merck & Co., Inc., Whitehouse Station, NJ) for use in combination with standard antiemetic agents for acute and delayed nausea and vomiting with initial and repeat courses of highly emetogenic therapy. Aprepitant appears to provide superior control of acute and delayed emesis compared to standard antiemetic therapy. Aprepitant was well tolerated in phase III studies, with side effects similar to standard therapy. Healthcare providers need to be aware of potential drug interactions with aprepitant. Oncology nurses continue to play a key role in helping patients adhere to their antiemetic schedules, stressing the importance of prevention of nausea and vomiting.

Key Words: nausea, vomiting, antiemetics

Researchers have found that patients receiving cisplatin have better control of delayed emesis if they have complete control of acute emesis. Additionally, patients who have experienced delayed nausea and emesis are more likely to develop anticipatory symptoms and have increased difficulty with nausea and vomiting in subsequent chemotherapy cycles (de Wit et al., 1998, 2002; Morrow & Roscoe, 1997).

Standard therapy for acute nausea and vomiting associated with highly emetogenic chemotherapy is a combination of corticosteroids with a serotonin receptor antagonist (Gralla et al., 1999; National Comprehensive Cancer Network, 1997). A corticosteroid plus either a serotonin receptor antago-

nist or metoclopramide is used commonly for delayed chemotherapy-induced nausea and vomiting (Gralla et al.; Italian Group for Antiemetic Research, 1997). Acute nausea and, particularly, delayed nausea continue to be a major concern for patients with cancer (Griffin et al., 1996). In a recent study of patients receiving serotonin receptor antagonists, the frequency of occurrence of delayed nausea was almost twice that of acute nausea (Hickok et al., 2003).

Clinical Trials of Aprepitant

Substance P was discovered in 1931 and is the most abundant neurokinin in the central and peripheral nervous system (Wahlestedt, 1998). Animal studies have shown that administration of an

NK-1 receptor antagonist was effective protection against acute and delayed cisplatin-induced emesis (Rudd, Jordan, & Naylor, 1996; Tattersall et al., 1996).

A phase II clinical trial found that dexamethasone given in combination with an NK-1 receptor antagonist was statistically

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