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Aprepitant for Patients Receiving Highly Emetogenic Chemotherapy: An Economic Analysis for Singapore

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A B S T R A C T

Background: Aprepitant (a neurokinin 1 receptor antagonist), in combination with a serotonin receptor antagonist (5-HT3 RA) and dexamethasone, has demonstrated superior efficacy on end points related to chemotherapy-induced nausea and vomiting (CINV) compared with standard care (combination 5-HT3 RA and dexamethasone). **Objective:** To determine the cost-effectiveness of an aprepitant-containing regimen compared with current clinical practice for the prevention of CINV in patients receiving highly emetogenic chemotherapy (HEC) in Singapore. **Methods:** A decision-analytic model was constructed to assess the costs and outcomes associated with an aprepitant-containing regimen compared with standard care in the prevention of CINV following HEC. Three scenarios were modeled on the basis of results of four double-blind randomized clinical trials of aprepitant. CINV event probabilities were calculated on the basis of the occurrence of nausea and vomiting and the need for rescue medication in the 5 days following a single cycle of HEC. The analysis was conducted from the Singapore health care system perspective. **Results:** Aprepitant reduced emesis and nausea, resulting in small but clinically important improvements when measured in quality-adjusted life-years. The aprepitant-containing regimen was associated with higher acquisition costs but lower costs relating to patient management, hospitalization, and use of rescue medication. Across the scenarios, the incremental cost per emetic event avoided ranged from cost saving to Singapore $63 (US $51). The incremental cost-effectiveness ratio ranged from cost saving to Singapore $49,800 per quality-adjusted life-year gained (US $40,600). The analysis was relatively insensitive to changes in the inputs. **Conclusions:** Aprepitant is a clinically important and cost-effective therapy for the prevention of CINV in patients treated with HEC in Singapore.

Keywords: aprepitant, chemotherapy, cost-effectiveness, emesis, Singapore.

Introduction

Chemotherapy-induced nausea and vomiting (CINV) has been identified as one of the most distressing adverse effects for patients who are being treated with chemotherapy for malignancy [1]1. If CINV is not well controlled, it can significantly affect a patient's quality of life, leading to poor compliance with further chemotherapy treatment, which can be life-threatening. Chemotherapies are categorized into four CINV categories according to the emetogenic potential of the agent, namely, highly emetogenic agent (90% or more of the patients will experience acute emesis), moderately emetogenic agent (30%–90% of the patients will experience acute emesis), lowly emetogenic agent (10%–30% of the patients will experience acute emesis), and minimally emetogenic agent (<10% of the patients will experience acute emesis) [2]. Aprepitant, a substance P neurokinin 1 receptor antagonist [3], is indicated for use as part of an antiemetic regimen for the prevention of acute and delayed CINV associated with highly emetogenic chemotherapy (HEC) regimens such as those containing cisplatin or an anthracycline and cyclophosphamide (AC).

In clinical trials, aprepitant, in combination with a serotonin receptor antagonist (5-HT3 RA) and dexamethasone, has demonstrated superior efficacy on end points related to CINV compared with a standard care regimen (combination of 5-HT3 RA and dexamethasone) [4]. As a result, in the antiemesis guidelines issued by a few of the key international organizations, such as the Multinational Association of Supportive Care in Cancer, the European Society for Medical Oncology, the National Comprehensive Cancer Network, and the American Society of Clinical Oncology, aprepitant is recommended as part of an antiemetic regimen for patients who are receiving HEC [2,5,6]. In Singapore, aprepitant is indicated for CINV prophy-

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Table 1 – Clinical trials informing the decision-analytic model.

Scenario	Trial	Chemotherapy regimen	Aprepitant regimen	Comparator regimen	Primary end point
1	Hesketh et al. [15] (Protocol 052)	Cisplatin ≥70 mg/m^2	Day 1: APT 125 mg PO, ODN 32 mg IV, DXM 12 mg PO.	Single-day 5-HT3 comparatorDay 1: ODN 32 mg IV (GTN 3 mg IV	Proportion of patients with complete response, overall phase.
	Poli-Begelli et al. [16] (Protocol 054)	Cisplatin ≥70 mg/m^2	Days 2–3: APT 80 mg PO, DXM 8 mg PO.Day 4: DXM 8 mg PO.	for local standard care), DXM 20 mg PO.Days 2–4: DXM 8 mg PO BID.	
2	Schmoll et al. [17] (Protocol 801)	Cisplatin ≥70 mg/m^2	Day 1: APT 125 mg PO, ODN 32 mg IV, DXM 12 mg PO.Days 2–3: APT 80 mg PO, DXM 8 mg PO.Day 4: DXM 8 mg PO.	Multiday (days 2–4) 5-HT3 comparatorDay 1: ODN 32 mg IV (GTN 3 mg IV for local standard care), DXM 20 mg PO.Days 2–4: ODN 8 mg PO BID or GTN 1 mg PO BID, DXM 8 mg PO BID.	Proportion of patients with complete response, overall phase.
3	Rapoport et al. [18] (Protocol 130)	AC-based*	Day 1: APT 125 mg PO, ODN 8 mg PO BID, DXM 12 mg PO.Days 2–3: APT 80 mg PO.	Day 1: ODN 8 mg PO BID (GTN 1 mg PO BID for local standard care), DXM 20 mg PO.Days 2–3: ODN 8 mg PO BID or (GTN 1 mg PO BID for local standard care).	Proportion of patients with no emesis, overall phase.

AC, anthracycline plus cyclophosphamide; APT, aprepitant; BID, twice daily; DXM, dexamethasone; GTN, granisetron; IV, intravenous; ODN, ondansetron; PO, *per os* (oral); QD, once daily.
* Subgroup from trial treated with AC-based regimen.

laxis with any HEC or moderately emetogenic chemotherapy regimen and is not restricted for use in specific cancer types [7].

Aprepitant has been assessed and recommended for listing in several markets in the Asia-Pacific region. In 2009, New Zealand added aprepitant to its pharmaceutical schedule for patients undergoing HEC or anthracycline-based chemotherapy for the treatment of malignancy [8]. Similarly, aprepitant is reimbursed in South Korea for use with chemotherapy classified as HEC and patients receiving AC combinations [9]. In Australia, aprepitant is recommended for one cycle in patients undergoing chemotherapy with certain agents, regimens deemed to be highly emetic, and for female breast cancer patients receiving AC combinations [10].

A number of cost-effectiveness analyses of aprepitant have been published [11–13]; however, the value of aprepitant in the context of the Singapore health system has not yet been described. Currently, ondansetron is included in the government standard drug list for patients with CINV. Given that an aprepitant-based regimen has superior efficacy, it is important to understand whether this regimen will be cost-effective in Singapore. Our aim was to assess the cost-effectiveness of an aprepitant-containing regimen compared with current clinical practice for the prevention of CINV in patients receiving HEC in Singapore.

Methods

Study design

A decision-analytic model was constructed in Microsoft Excel 2002 (Microsoft Corporation, Redmond, WA) to assess the costs and outcomes associated with aprepitant-containing regimens compared with a standard regimen in the prevention of CINV in patients treated with HEC. Three scenarios were modeled by using probabilities of response from the four randomized controlled trials (Table 1).

Because the published randomized controlled trials formed the basis of the comparison, the base-case analyses assume the same patient populations and comparators as the published trials (Table 1). Because granisetron is the 5-HT3 RA used in Singapore, however, a comparable granisetron dose was used in place of ondansetron for additional local comparator analyses. Patients enrolled in the trials were older than 18 years with solid malignancies who were scheduled to receive either chemotherapy that included cisplatin (≥70 mg/m^2) or an AC-based regimen for the first time. The models assess the use of aprepitant-containing regimens in these same patient populations.

Perspective and time horizon

The analysis was conducted from the perspective of the Singapore health care system: direct medical costs of medications, outpatient physician assessments, diagnostic tests and procedures, emergency department visits, and hospitalizations were included. In line with the clinical trial study period, which captured information up to 120 hours postchemotherapy, a 5-day (120-hour) time horizon was selected for the economic analyses and assessment of CINV outcomes relating to the first cycle of chemotherapy (Table 2).

Clinical effectiveness of aprepitant compared with standard care

The results of the clinical trials are summarized in Table 2. *Complete response* was defined as no vomiting and no use of rescue medications, and patients who did not achieve complete response were considered to be incomplete responders. CINV is classified according to the time since administration of chemotherapy; the acute phase occurs between 0 and 24 hours of administration, and the delayed phase lasts from more than 24 to 120 hours. As reported by Warr and colleagues [14], the data from protocols 052 and 054 were pooled for scenario 1 because of the similarity in trial design, patient population, and antiemetic regimens.

In all trials, aprepitant demonstrated a statistically significant benefit in terms of complete response in the overall phase, as well as in the acute and delayed period.

The antiemetic prophylaxis regimens used in the aprepitant clinical trials [15–18] represent the standard regimens in