

# Cancer Care Ontario Practice Guidelines Initiative

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Ontario Ministry of Health and Long-Term Care



## Use of 5-HT<sub>3</sub> receptor antagonists in patients receiving moderately or highly emetogenic chemotherapy

### Practice Guideline Report #12-3

**ORIGINAL GUIDELINE: March 7, 2000**  
**MOST RECENT LITERATURE SEARCH: January 2003**  
**NEW EVIDENCE ADDED TO GUIDELINE REPORT: January 2003**

**New evidence found by update searches since completion of the original guideline is consistent with the recommendations below.**

### SUMMARY

#### Guideline Questions

1. Are the 5-HT<sub>3</sub> receptor antagonists ondansetron, granisetron and dolasetron equivalent in terms of efficacy and adverse effects?
2. Should 5-HT<sub>3</sub> receptor antagonists be administered for more than 24 hours following chemotherapy to prevent delayed-onset emesis?

#### Target Population

- These recommendations apply to adult cancer patients receiving moderately or highly emetogenic chemotherapy.
- Current standard antiemetic therapy for patients receiving moderately to highly emetogenic chemotherapy includes the use of a 5-HT<sub>3</sub> receptor antagonist and dexamethasone for the first 24 hours following chemotherapy.

#### Recommendations

- Intravenous dolasetron, granisetron and ondansetron should be regarded as equally efficacious and well tolerated.
- As a first-line approach, 5-HT<sub>3</sub> receptor antagonists should be administered for 24 hours following chemotherapy.
- There are insufficient data to draw conclusions about the equivalence of the 5-HT<sub>3</sub> receptor antagonists when given orally. A single study comparing dolasetron and ondansetron suggests that a higher than recommended dose of oral dolasetron is at least as efficacious as oral ondansetron.

## **Methods**

The literature was searched using MEDLINE (1966 through January 2003), CANCERLIT (1983 through October 2002), the Cochrane Library (Issue 4, 2002), the Physician Data Query database, the Canadian Medical Association Infobase, the National Guideline Clearinghouse, and abstracts published in annual meeting proceedings of the American Society of Clinical Oncology (1995-2002). Article bibliographies and personal files were also searched to January 2003 for evidence relevant to this practice-guideline report.

Evidence was selected and reviewed by a medical oncologist, members of the Cancer Care Ontario Practice Guidelines Initiative's (CCOPGI) Systemic Treatment Disease Site Group (ST DSG) and methodologists. This practice guideline has been reviewed and approved by the ST DSG, which comprises medical oncologists, pharmacists and one community representative.

External Review by Ontario practitioners was obtained through a mailed survey. Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee (PGCC). The CCOPGI has a formal standardized process to ensure the currency of each guideline report. This consists of periodic review and evaluation of the scientific literature, and where appropriate, integration of this literature with the original guideline information.

## **Key Evidence**

- When 5-HT<sub>3</sub> receptor antagonists are administered for more than 24 hours, the results of a meta-analysis indicate a small (4.1%) decrease in the absolute proportion of patients with delayed-onset emesis.
- A randomized trial showed no advantage when prolonged ondansetron administration was compared with metoclopramide 20 mg orally four times daily.
- No studies have compared the same 5-HT<sub>3</sub> receptor antagonist when given by the oral versus the intravenous route. Two studies of high-dose intravenous ondansetron versus oral granisetron suggest that the recommended dose of the latter is effective and may be regarded as equivalent to administration by the intravenous route.

## **UPDATE**

- Two clinical practice guidelines (1u,2u), two meta-analyses (3u,4u), and four double-blind randomized controlled trials (5u-8u) were identified in the update search and were eligible for review.
- Two clinical practice guidelines from other practice guideline development groups produced recommendations which were consistent with the recommendations outlined above.
- A meta-analysis of 14 randomized trials (including seven non-blinded trials) did not detect statistically significant differences between granisetron and ondansetron for the prevention of acute or delayed nausea or vomiting for either moderately or highly emetogenic chemotherapy. Another meta-analysis, published in abstract form, with data from 28 randomized controlled trials detected no significant differences in acute or delayed nausea or vomiting between ondansetron, granisetron and tropisetron.

## **Treatment Alternatives**

- Alternative approaches to delayed-onset emesis are the prolonged administration of dexamethasone 4 to 8 mg twice daily, or domperidone 20 mg orally four times daily.

### **Prepared by the Systemic Treatment Disease Site Group**

For further information about this practice guideline, please contact: Dr. Brent Zanke, Chair,  
Systemic Treatment Disease Site Group, Cancer Care Ontario, 620 University Avenue Toronto,  
Ontario, Canada M5G 2L7 Tel: 416-9800 x2229 sec x1328 Fax: 416-217-1281  
E-mail: [brent.zanke@cancercare.on.ca](mailto:brent.zanke@cancercare.on.ca)

## **PREAMBLE: About Our Practice Guideline Reports**

The Cancer Care Ontario Practice Guidelines Initiative (CCOPGI) is a project supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care, as part of the Program in Evidence-based Care. The purpose of the Program is to improve outcomes for cancer patients, to assist practitioners to apply the best available research evidence to clinical decisions, and to promote responsible use of health care resources. The core activity of the Program is the development of practice guidelines by multidisciplinary Disease Site Groups of the CCOPGI using the methodology of the Practice Guidelines Development Cycle.<sup>1</sup> The resulting practice guideline reports are convenient and up-to-date sources of the best available evidence on clinical topics, developed through systematic reviews, evidence synthesis and input from a broad community of practitioners. They are intended to promote evidence-based practice.

This practice guideline report has been formally approved by the Practice Guidelines Coordinating Committee, whose membership includes oncologists, other health providers, community representatives and Cancer Care Ontario executives. Formal approval of a practice guideline by the Coordinating Committee does not necessarily mean that the practice guideline has been adopted as a practice policy of CCO. The decision to adopt a practice guideline as a practice policy rests with each regional cancer network that is expected to consult with relevant stakeholders, including CCO.

### Reference:

<sup>1</sup> Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. *J Clin Oncol* 1995;13(2):502-12.

**For the most current versions of the guideline reports and information about the CCOPGI and the Program, please visit our Internet site at:**  
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**For more information, contact our office at:**  
**Phone: 905-525-9140, ext. 22055**  
**Fax: 905-522-7681**

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