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NCCN Clinical Practice Guidelines in Oncology™

Antiemesis

V.3.2008

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MYLAN - EXHIBIT 1045
Mylan Laboratories Limited v. Aventis Pharma S.A.

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Clinical Trials: The NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

To find clinical trials online at NCCN member institutions, [click here: nccn.org/clinical_trials/physician.html](#)

NCCN Categories of Evidence and Consensus: All recommendations are Category 2A unless otherwise specified.

See [NCCN Categories of Evidence and Consensus](#)

These guidelines are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. The clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no representations nor warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way. These guidelines are copyrighted by National Comprehensive Cancer Network. All rights reserved. These guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2008.

SUMMARY OF GUIDELINES UPDATES

Change in the 3.2008 version of the NCCN Antiemesis Guidelines from the 2.2008 version is the addition of fosaprepitant dimeglumine on pages [AE-2](#) and [AE-3](#) for prevention of emesis in chemotherapy with high and moderate emetic risk. Also added was the following footnote: Fosaprepitant dimeglumine (115 mg) may be substituted for aprepitant (125 mg) 30 minutes prior to chemotherapy, on Day 1 of the CINV regimen as an infusion administered over 15 minutes.

Change in the 2.2008 version of the NCCN Antiemesis Guidelines from the 1.2008 version is the addition of the 2008 manuscript.

Summary of changes in the 1.2008 version of the NCCN Antiemesis Guidelines from the 1.2007 version include:

General

Deleted recommendation prochlorperazine for 15 mg Spansule PO every 8 or every 12 h throughout the guidelines.

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Added footnote g: "Monitor for dystonic reactions; use diphenhydramine for dystonic reactions."

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Added Vorinostat to the list of agents with low emetic risk.

Added Cetuximab, Lapatinib, Panitumumab, and Temsirolimus to the list of agents with minimal emetic risk.

B Principles for Managing Breakthrough Emesis

The general principle of breakthrough treatment is to give an additional agent from a different drug class. Added the following statement: No one treatment is better than the other for managing breakthrough emesis.

Multiple concurrent agents, perhaps in alternating schedules or by alternating routes, may be necessary. Added the following statement: Dopamine antagonists (eg, metoclopramide), haloperidol, corticosteroids and agents such as lorazepam may be required.

All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

PRINCIPLES OF EMESIS CONTROL IN THE CANCER PATIENT

- Prevention of nausea/vomiting is the goal.
- The risk of emesis and nausea for persons receiving chemotherapy of high and moderate emetic risk lasts for at least 4 days. Patients need to be protected throughout the full period of risk.
- Oral and IV antiemetic formulations have equivalent efficacy.
- Consider the toxicity of the specific antiemetic(s) .
- Choice of antiemetic(s) used should be based on the emetic risk of the therapy, prior experience with antiemetics, as well as patient factors.
- There are other potential causes of emesis in cancer patients.
These may include:
 - ▶ Partial or complete bowel obstruction
 - ▶ Vestibular dysfunction
 - ▶ Brain metastases
 - ▶ Electrolyte imbalance: hypercalcemia, hyperglycemia, hyponatremia
 - ▶ Uremia
 - ▶ Concomitant drug treatments including opiates
 - ▶ Gastroparesis, tumor or chemotherapy (vincristine etc) induced.
 - ▶ Psychophysiologic:
 - * Anxiety
 - * Anticipatory nausea and vomiting
- For use of antiemetics for nausea and vomiting that is not related to radiation and/or chemotherapy, [See NCCN Palliative Care Guidelines](#)

All recommendations are category 2A unless otherwise indicated.

Randomized Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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