

# ASK A PHARMACIST



PUNCHSTOCK

High-fiber foods prevent constipation.

## Timing of Neulasta and preventing opioid-induced constipation

### What is the danger of giving Neulasta on the day of chemotherapy instead of 24 hours later?

—Shirley Harvey, RN, BNS, OCN

Pegfilgrastim (Neulasta) is a granulocyte-colony stimulating factor (G-CSF) that is used to prevent neutropenia in patients receiving myelosuppressive chemotherapy. G-CSF stimulates white blood cell precursors (myeloid cells) to grow and differentiate. The concern with administering G-CSF on the day of chemotherapy is that increasing growth of myeloid cells may increase their sensitivity to cytotoxic chemotherapy agents. Since cytotoxic chemotherapy causes the most damage to rapidly growing cells, giving an agent that causes myeloid cells to grow faster while chemotherapy is present may cause more toxicity.

As next-day administration can be a significant patient burden, especially in rural areas, some researchers have questioned

this assumption. Some retrospective trials of selected chemotherapy regimens have not noted increased neutropenia with same-day administration of G-CSF compared to next-day administration. However, same-day administration is not widely used in clinical practice because of insufficient evidence with many myelosuppressive chemotherapy regimens. The package insert for pegfilgrastim notes that it should not be administered between 14 days before and 24 hours after administration of cytotoxic chemotherapy. Optimal timing is considered to be within 24 to 72 hours after chemotherapy administration.

### What are the best methods for preventing opioid-induced constipation?

Opioids cause constipation by stimulating opioid receptors in the central nervous system and gut, causing decreased GI motility, prolonged transit time, decreased defecatory reflex, and increased sphincter tone. These effects are noted even with parenteral opioid administration. Nearly all patients receiving opioids will develop constipation if they are not receiving preventive treatment. While patients may become tolerant to other opioid adverse effects such as sedation, tolerance to constipation does not occur. Therefore, patients receiving opioid therapy require continued use of a bowel regimen.

Stimulant laxatives such as senna and bisacodyl are the agents of choice in pre-

vention of opioid-induced constipation, and they should be taken scheduled rather than as needed. Stool softeners such as docusate may also be helpful but should be used in combination with a stimulant laxative rather than as monotherapy. Osmotic laxatives such as lactulose, sorbitol, magnesium citrate, or polyethylene glycol 3350 (MiraLax) may be added to the above therapies if they are not effective. Bowel regimens should be titrated to a goal of one nonforced bowel movement every 1 to 2 days.

Other means of preventing constipation, such as optimizing fluid intake, participating in regular physical activity, minimizing use of other medications that may be constipating, and optimizing dietary fiber intake, should be employed in addition to a bowel regimen as described above. Of note, fiber supplements (for example, Metamucil) are not recommended for opioid-induced constipation because they lack efficacy and have a potential for increased adverse events in this setting.

The opioid-antagonist methylnaltrexone (Relistor) is approved for palliative care patients with constipation refractory to laxative therapy. Because of its high cost and the need for subcutaneous administration, methylnaltrexone should be used only in these patients. The National Comprehensive Cancer Network Adult Cancer Pain guidelines (available online at [www.nccn.org](http://www.nccn.org)) are an excellent resource for managing this and other opioid adverse effects. ■



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