

# Pegfilgrastim for Chemotherapy-Induced Neutropenia

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Chemotherapy-induced neutropenia (CIN) is a frequent adverse event in patients treated with myelosuppressive chemotherapy. The depth and duration of the neutrophil nadir following chemotherapy correlates with the development of infectious complications. However, minimizing the duration and severity of neutropenia by stimulating the growth and development of neutrophils in the bone marrow is possible by using granulocyte-colony-stimulating factors, such as filgrastim (Welte, Gabrilove, Bronchud, Platzer, & Morstyn, 1996). The prophylactic administration of filgrastim can reduce the incidence of febrile neutropenia and decrease hospitalizations and IV antibiotic use, as well as facilitate the delivery of on-time chemotherapy doses (Crawford et al., 1991; Gabrilove et al., 1988; Morstyn et al., 1988; Trillet-Lenoir et al., 1993; Zinzani et al., 1997). Clinical data indicate that delivering the chemotherapy dose on time is important to treatment outcomes in certain tumor types (Bonadonna, Valagussa, Moliterni, Zambetti, & Brambilla, 1995; Kwak, Halpern, Olshen, & Horning, 1990).

One of the main drawbacks of filgrastim is that it is a small protein that is rapidly cleared from the body through the kidneys and requires daily IV or subcutaneous injections for up to two weeks (Welte et al., 1996). Daily dosing can necessitate frequent visits to the clinic for drug administration. This may be difficult for patients who have problems finding transportation or rely on caregivers to take them to the clinic.

Many chemotherapy regimens cause myelosuppression, which can result in febrile neutropenia and potentially lead to serious infections. The risk of neutropenia and its complications can be reduced with filgrastim, a granulocyte-colony-stimulating factor. Filgrastim is safe and effective, but it is cleared rapidly from the body (predominantly through the kidneys) and requires daily administration for up to 14 days. A pegylated form of filgrastim, pegfilgrastim, has been developed by attaching a polyethylene glycol molecule to filgrastim. Pegfilgrastim has an extended circulation half-life and self-regulating, patient-specific pharmacokinetics, making it possible to give the treatment as a single dose once per chemotherapy cycle. Clinical trials have shown that a single, subcutaneous dose of pegfilgrastim is as safe and effective as daily filgrastim injections in patients treated with myelosuppressive chemotherapy. In addition, a single, 6 mg fixed dose of pegfilgrastim per chemotherapy cycle is sufficient in adult patients, regardless of their body weight, making pegfilgrastim a simple, effective, and well-tolerated option for managing chemotherapy-induced neutropenia.

**Key Words:** neutropenia; granulocyte colony-stimulating factor, recombinant; filgrastim

To increase the duration of action, pegfilgrastim, a pegylated form of filgrastim, has been developed and can be administered subcutaneously once per chemotherapy cycle. Once-per-cycle dosing with pegfilgrastim can reduce the number of trips that patients and their caregivers must make to the clinic as well as decrease the number of injections that patients must endure as part of their treatment regimen.

Pegfilgrastim also may result in improvements with patient adherence because pa-

tients no longer have to rely on caregivers, healthcare providers, or themselves to administer their daily injections. The need to arrange for weekend administration and daily clinic visits is reduced because of the self-regulating nature of the drug.

## The Science of Pegylation

The term pegylation refers to the process of attaching a polyethylene glycol (PEG) molecule to another molecule, such as a protein. PEG molecules are pH-neutral, nontoxic, water-soluble polymers that consist of repeating ethylene oxide subunits, each with a molecular weight of 44 daltons (d) and two terminal hydroxyl groups (Bailon & Berthold, 1998). They can be either linear (5–30 kd) or branched (40–60 kd) chain structures. A protein can be pegylated by attaching a single large PEG chain at one site or by attaching several smaller PEG chains at many sites. In the case of pegfilgrastim, a 20 kd PEG chain is covalently attached directly to the N-terminal amino

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