

BIOCON FORMULATIONS
MASTER PROOF OF APPROVED PRINTED PFS PIL ART WORK
FULPHILA, 6 mg FOR COLOUR COPY
(FOR MYLAN GENERAL EXPORT) ANNEXURE-4 [Ref. No. : BF/QA/SOP/006]
ARTWORK CODE: BF1517/01

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Fulphila™

6 mg (pegfilgrastim)

Pegylated Granulocyte Colony Stimulating Factor Injection (PEG-GCSF injection) 6 mg/0.6 mL

For Subcutaneous Use Only
Sterile Solution - No Preservative

COMPOSITION

Each pre-filled syringe contains 6 mg of pegfilgrastim in 0.6 mL sodium chloride injection. The concentration is 10 mg/mL based on protein only.

¹Product Details: Chemical and safety information including description by conjugation with polyethylene glycol (PEG).
The concentration is 20 mg/mL of the PEG moiety is included.

The potency of the product should not be compared to the potency of another pegylated or non-pegylated protein of the same therapeutic class.

For a full list of excipients, see Section 6.1 of Fulphila.

PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution for injection.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: immunostimulants, colony stimulating factor, ATC Code L03AA13.
Fulphila™ is a biosimilar medicinal product.

Human granulocyte colony stimulating factor (G-CSF) is a glycoprotein, which regulates the production and release of neutrophils from the bone marrow. Pegfilgrastim is a dimeric conjugate of recombinant human G-CSF (recombinant G-CSF) with a single 20 kDa polyethylene glycol (PEG) moiety.

Pegfilgrastim is a sustained duration form of filgrastim due to its prolonged elimination. Pegfilgrastim and filgrastim have been shown to have identical modes of action, causing a marked increase in peripheral blood neutrophil counts within 24 hours, with minor increases in recovery and length of hospital stay in filgrastim, respectively and no increase in pegfilgrastim. Also normal or enhanced function as demonstrated by tests of chemotactic and phagocytic function. As with other haematopoietic growth factors, G-CSF has been shown to induce the release of neutrophils from bone marrow. G-CSF can promote growth of myeloid cells, including myeloid cells, *in vitro* and similar effects may be seen in some non-myeloid cells *in vivo*.

In two randomized, double-blind, pivotal studies in patients with high-risk solid-tumor III-IV breast cancer undergoing myelosuppressive chemotherapy consisting of docetaxel and doxorubicin, use of pegfilgrastim, as a single once per cycle dose, reduced the duration of neutropenia and the incidence of febrile neutropenia in patients who observed their daily administration of filgrastim as a means of comparison. In the absence of growth factor support, this regimen has been reported to result in a mean duration of leukopenia of 16 days, and a 30% of incidence of febrile neutropenia.

In one study (n = 137), which used a 6 mg fixed dose of pegfilgrastim, the mean duration of grade 4 neutropenia for pegfilgrastim group was 14 days compared with 16 days in the filgrastim group difference 0.22 days. 95% CI (1.3, 0.3). Over the study, the rate of febrile neutropenia was 13% of pegfilgrastim-treated patients compared with 24% of filgrastim-treated patients (difference 7%, 95% CI (0.4, 13.5)). In a second study (n = 133), which used a weight-adjusted dose of 100 µg/kg, the mean duration of grade 4 neutropenia for the pegfilgrastim group was 17 days, compared with 18 days in the filgrastim group difference 1.03 days, 95% CI (1.6, 0.56). The overall rate of febrile neutropenia for patients treated with pegfilgrastim and 13% of patients treated with filgrastim (difference 3%, 95% CI (1.8, 1.1)).

In a phase-III, randomized, double-blind study in patients with breast cancer the effect of pegfilgrastim on the incidence of febrile neutropenia was evaluated following administration of a chemotherapy regimen associated with a febrile neutropenia rate of 10.2% (doxorubicin 100 mg/m² every 3 weeks for 4 cycles, fluo-rubicin 40 mg/m² every 4th patient week, recombinant human G-CSF 4.8 mg/kg every 24 hours, and pegfilgrastim 100 µg/kg subcutaneous on days 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 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3688, 3690, 3692, 3694, 3696, 3698,