Grastim™

Filgrastim Concentrated Solution BP

Composition
Each 0.5 ml Pre-Filled Syringe contains sterile Filgrastim Concentrated Solution BP (G-CSF) 300 mcg (30 MU).

Description
Filgrastim is a recombinant methionyl human granulocyte colony stimulating factor (Filgrastim). Filgrastim is a 175 amino acid protein manufactured by recombinant DNA technology using E.coli as an expression host. The protein has an amino acid sequence similar to the natural sequence predicted from the human DNA sequence analysis, except for the addition of an N-terminal methionine.

Clinical Pharmacology
Filgrastim is a glycoprotein which regulates the production and release of functional neutrophils from the bone marrow. Filgrastim causes marked increases in peripheral blood neutrophil counts within 24 hours, with minor increases in monocytes. Elevations of neutrophil counts are dose-dependent at recommended doses. Following termination of Filgrastim therapy, circulating neutrophil counts decrease by 50% within 1 to 2 days, and to normal levels within 1 to 7 days.

Indications and usage
1. Cancer patients receiving myelosuppressive chemotherapy:
Filgrastim is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients with Acute Myeloid Leukemia, receiving induction or consolidation chemotherapy:
Filgrastim is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML.

3. Cancer patients receiving bone marrow transplant (BMT):
Filgrastim is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g. febrile neutropenia, in patients with non-myeloid malignancies undergoing myeloab lative chemotherapy followed by bone marrow transplantation (BMT).

4. Patients undergoing peripheral blood progenitor cell collection and therapy: Filgrastim is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients with severe chronic neutropenia:
Filgrastim is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g. fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia or idiopathic neutropenia.

Dosage and administration

Administration
Filgrastim should not be administered during 24 hours before or after chemotherapy, since antineoplastic agents target rapidly proliferating cells thus attenuating the effect of Filgrastim.
Filgrastim is administered by subcutaneous injection or IV infusion. When administered by IV infusion in patients with chemotherapy-induced neutropenia, Filgrastim is usually infused over 15–30 minutes, although infusion periods extending up to 24 hours may be used. In patients who have undergone bone marrow transplantation (BMT), Filgrastim is infused IV over 30 min. When administered by subcutaneous infusion for either use, Filgrastim usually is infused over 24 hours. For direct, rapid subcutaneous injection, Filgrastim injection is administered undiluted.

Dosage
1. Cancer Patients Receiving Myelosuppressive Chemotherapy:
The recommended starting dose of Filgrastim is 5 mcg/kg/day, administered as a single daily injection by SC bolus injection, by short IV infusion (15 to 30 minutes), or by continuous SC or continuous IV infusion. Doses may be increased in increments of 5 mcg/kg for each chemotherapy cycle, according to the duration and severity of the ANC (Absolute Neutrofil Count).

2. Cancer Patients Receiving Bone Marrow Transplant (BMT):
The recommended dose of Filgrastim following BMT is 10 mcg/kg/day given as an IV infusion of 4 or 24 hours, or as a continuous 24-hour SC infusion. For patients receiving BMT, the first dose of Filgrastim should be administered at least 24 hours after cytotoxic chemotherapy and at least 24 hours after bone marrow infusion.
During the period of neutrophil recovery, the daily dose of Filgrastim should be titrated against the neutrophil response as follows:

When ANC > 1000/mm^3 for 3 consecutive days	Reduce to 5 mcg/kg/day
then: If ANC remains > 1000/mm^3 for 3 more consecutive days	Discontinue filgrastim
then: If ANC decreases to < 1000/mm^3	Resume at 5 mcg/kg/day

If ANC decreases to < 1000/mm3 at anytime during the 5 mcg/kg/day administration, Filgrastim should be increased to 10 mcg/kg/day, and the above steps should then be followed.

3. Peripheral blood progenitor cell collection and therapy to mobilize hematopoietic progenitor cells into peripheral blood for collection by leukapheresis:
The recommended dosage of Filgrastim is 10 mcg/kg daily given by subcutaneous injection or continuous subcutaneous infusion once daily for at least 4 days prior to the first leukapheresis to collect peripheral blood progenitor cells (PBPC) and continued until the last leukapheresis is performed.

4. Severe chronic neutropenia:
The recommended dose of Filgrastim for the treatment of cyclic/idiopathic/chronic neutropenia is 5 mcg/kg administered once daily by subcutaneous injection. Dosage in patients with congenital neutropenia is 6 mcg/kg daily by subcutaneous injection. ANC should be observed periodically to evaluate duration of therapy.

Adverse effects
Neutropenia, vomiting, leukopenia, anaemia, thrombocytopenia, pyrexia, back pain, abdominal pain, diarrhoea, cough, pain, nausea, pain in extremity, headache, constipation, stomatitis, asthenia, mucosal inflammation, alopecia.

Contraindications
Filgrastim is contraindicated in patients hypersensitive to the drug, any ingredient in the formulation, or proteins derived from *E. coli*.

Precautions
1. Complete blood cell counts (CBCs) and platelet counts should be performed prior to initiation of Filgrastim therapy and routinely during therapy to monitor myeloid recovery and avoid the potential complications of excessive leukocytosis and/or thrombo-cytopenia. It is recommended that these hematologic tests be performed twice weekly in patients receiving the drug for chemotherapy-induced neutropenia and 3 times weekly in patients receiving the drug following bone marrow transplantation (BMT).

2. In patients with congenital, cyclic or idiopathic neutropenia, CBCs and platelet counts should be performed twice weekly during the initial 4 weeks of Filgrastim therapy, twice weekly during the first 2 weeks following any dosage adjustment and once monthly after the patient is clinically stable.

3. Regular monitoring of leukocyte counts (especially at the time of recovery from the ANC nadir) is recommended to avoid excessive leukocytosis. It is recommended that Filgrastim be discontinued if the ANC exceeds 10,000/mm^3 after the ANC nadir has occurred; dosages that increase the ANC to such levels may not result in any additional clinical benefit but might be associated with an increased risk of toxicity (e.g., bone pain).

4. Because some malignant myeloid cells have receptors for G-CSF and because the clinical importance of these receptors has not been fully determined to date, extreme caution regarding the use of Filgrastim in patients with any malignancy having myeloid characteristics (e.g., acute myeloid leukemia [AML]) is advised. However, the drug currently is used in patients with AML receiving induction or consolidation chemotherapy without evidence of a negative effect on the disease (e.g., proliferation of the leukemic clone).

5. Because rapidly dividing myeloid cells may be particularly sensitive to cytotoxic chemotherapy, Filgrastim should not be administered during the 24 hours before or after administration of cytotoxic chemotherapy. Filgrastim should not be administered concomitantly with radiation therapy.

Pediatric precautions
Filgrastim has been used in children 3 months to 18 years of age without unusual adverse effect. However, safety and efficacy of the drug in neonates or patients with autoimmune neutropenia of infancy have not been established.

Pregnancy and lactation
Pregnancy category: C. Although there are no adequate and controlled studies to date in humans, Filgrastim has been shown to adversely affect pregnancy and the fetus in animals. Filgrastim should be used during pregnancy only when the potential benefits justify the possible risks to the fetus. It is not known whether Filgrastim is distributed into milk. Because many drugs are distributed into milk, Filgrastim should be used with caution in nursing women.

Drug Interaction
1. The safety and efficacy of concomitant administration of doses of Filgrastim with doses of myelosuppressive antineoplastic agents have not been established. Because Filgrastim stimulates proliferation of neutrophil precursors and because many antineoplastic agents target rapidly proliferating cells, Filgrastim doses should not be administered within 24 hours before or after a dose of one of these agents.

2. Because transient decreases in platelet counts have been reported in some patients receiving Filgrastim, it is recommended that the drug should be used with caution in patients receiving other drugs known to decrease the platelet count.

Overdose
Limited information is available on the acute toxicity of Filgrastim in humans. Overdosage of the drug would be expected to produce manifestations that are principally extensions of the pharmacologic and common adverse effects of the drug.

Storage
Grastim™ should be stored between 2°C- 8°C in a refrigerator. Do not freeze. Avoid shaking

Presentation
Grastim™ : Each box contains 1 Pre-filled Syringe of 300 mcg (30 MU) Filgrastim in Alu-PVC blister pack.

Manufactured by

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH