EXIPOGEN®

Filgrastim
300mcg/0.5 ml - Prefilled syringe

Pharmaceutical and packaging forms:
Each pre-filled syringe (0.5 ml) contains 300 mcg filgrastim produced by the Exir pharmaceutical company, supplied in 2- pre-filled syringe in 1 packages.

Category:
Colony stimulating factor; hematopoietic agent [1]

Indication:
Myelosuppressive chemotherapy recipients with non-myeloid malignancies.
Acute myeloid leukemia (ALM) following induction or consolidation chemotherapy
Bone marrow transplantation
Hematopoietic radiation injury syndrome, acute
peripheral blood progenitor cell collection and therapy
Sever chronic neutropenia. [1]

General tips:
This medicine is prescribed to treat your current condition. So avoid using it in the same way or recommend it to others.
Consults with physician or pharmacist in following cases:
Patients with sickle cell anemia.
During pregnancy and lactation or decision for pregnancy
If you have a history of drug allergy
Take this medicine with caution in the following cases:
Regularly monitoring serum plathates and platelets.
CBC and blood globules' count tests before chemotherapy.
Investigate and monitoring of sign and symptoms such as fever, respiratory infiltration, abdominal and shoulder pain, splenomegaly. Sickle cell cries Monitoring in sickle cell anemia patients. [3,1]

Contraindication:
History of serious allergic reaction to human granulocyte colony-stimulating factors, such as filgrastim or pegfilgrastim, or any component of the formulation.
Known hypersensitivity to *E.coli* – derived products. [1]

Consumption during pregnancy and lactation:
During Pregnancy considered in category C , and should be prescribed and monitored by physicians.
filgrastim has been shown to cross the placenta in humans. It can be detected in breast milk. One review suggests waiting until 3 days after the last dose to resume breast feeding until additional data is available. It's recommended that caution be exercised when administering filgrastim products to breast-feeding women. [1]

Warnings and Precautions:
Due to the increased sensitivity of myeloid cells to cytotoxic chemotherapy, avoid filigrastim from 14 days prior to 24 hours after administration of cytotoxic drugs.
The benefits of taking medication with less than two weeks have not been proven.
Drug administration on the day of chemotherapy is not recommended.
filigrastim can be a factor in the growth of any type of tumor, especially malignant tumors of the myeloid, so the use of the drug should be done with caution.
The use of this drug in patients who are under radiotherapy is not evaluated.
The use of this drug in patients whose chemotherapy is delayed by myelosuperacia (such as nitrates urea and mitomycin) has not been evaluated.
Serious allergic reactions have reported, usually with the initial exposure; may be managed symptomatically with administration of antihistamines; steroids, bronchodilators, and/or epinephrine.
Safety and efficacy of this drug on stem cell mobilization Peripheral Blood Progenitor Cell (PBPC) have not been evaluated.
Allergic reactions (anaphylaxis, angioedema, erythema, rash, and hives) may occur with the onset of treatment and the first dose and can be eliminated by discontinuation of therapy (delayed). In case of severe reactions, it is recommended to monitor the patient for several days and permanently discontinue the drug.
Few cases of spleen rupture have been reported. Patients should be advised to report pain in the upper and lower abdominal pain and shoulder pain.
There have been reports of acute respiratory syndrome (ARDS) in association with the use of this drug. People with pulmonary symptoms such as fever, pulmonary infiltration or respiratory distress should be excluded and should not be allowed to take medication if ARDS occurs. Or disconnect it.
In patients with tuberculosis, chills may occur (crises) in the cell cycle, in which case the benefits and disadvantages of drug use should be carefully considered.
The safety and efficacy of this drug in children have not been proven. A constant dose of 6 mg should not be used in infants, children and adolescents weighing less than 45 kg
History of serious allergic reaction to filgrastim or pegifilgrastim. Moderate or severe cutaneous vasculitis has been reported, generally. Withhold treatment if cutaneous vasculitis occurs; may be restarted with a dose reduction once syndromes resolve and the absolute netrophil count (ANC) has decreased. Capillary leak syndrome (CLS), characterized by hypotension, hypoalbuminemia, edema, and hemoconcentration, may occur in patients receiving human granulocyte colony-stimulating factor (G-CSF). If CLS develops, monitor closely and manage symptomatically. CLS may be life-threatening if treatment is delayed. White blood cell counts of ≥ 100,000 /mm³ have been reported with filgrastim dose > 5 mcg/kg/ day. Monitor complete blood cell count (CBC) twice weekly during therapy. Avoid simultaneous use of filgrastim products with chemotherapy and radiation therapy. Avoid concurrent radiation therapy with filgrastim. In patients with sickle cell disorders carefully evaluate potential risks and benefits. Discontinue in patients undergoing sickle cell crisis. Acute respiratory distress syndrome has been reported. [2,1]

Dosing:
The amount and method of taking the drug for each patient is documented by the doctor, but the usual dose is as follows:

Adults and geriatric note:
Do not administer in the periods 24 hours before to 24 hours after cytotoxic chemotherapy. May round the dose to the nearest vial size for convenience and cost minimization.
International consideration:
Dosage below expressed as microgram; 1mcg = 100,000 units

Myelosuppressive chemotherapy recipients with non-myeloid malignancies.
SubQ,IV: 5 mcg/kg/day: doses may be increased by 5 mcg/kg. According to the duration and severity of the neutropenia; continue for up to 14 days until the absolute neutrophil count (ANC) reaches 10,000/mm³. Discontinue if the ANC surpasses 10,000/mm³ after the expected chemotherapy –induced neutrophil nadir.

Acute myeloid leukemia (ALM) following induction or consolidation chemotherapy
SubQ, IV: 5 mcg/kg/day; doses may be increased by 5 mcg/kg. According to the duration and severity of the neutropenia; continue for up to 14 days until
the absolute neutrophil count (ANC) reaches 10,000/mm³. Discontinue if the ANC surpasses 10,000/mm³ after the expected chemotherapy –induced neutrophil nadir.

Bone marrow transplantation
IV infusion: 10 mcg/kg/day; Adjust the dose according to the duration and severity of the neutropenia.
Recommended steps based on neutrophil response:
When ANC remains > 1,000/mm³ for 3 consecutive days: Reduce the dose to 5 mcg/kg/day
When ANC remains > 1,000/mm³ for 3 more consecutive days: discontinue
When ANC decreases to < 1,000/mm³: Resume at 5 mcg/kg/day
When ANC decreases to < 1,000/mm³ during the 5 mcg/kg/day: increase dose to 10 mcg/kg/day and follow the above steps

Hematopoietic radiation injury syndrome, acute peripheral blood
10 mcg/kg once daily; begin as soon as possible after suspected or confirmed radiation dose >2 gray (Gy) and continue filgrastim until ANC remains > 1,000/mm³ for 3 consecutive CBCS or ANC exceed 10,000/ mm³ after the radiation – induced nadir.

Peripheral blood progenitor (PBPC) cell collection and therapy
SubQ, IV: 10 mcg/kg daily, usually for 6 to 7 days. begin at least 4 days before the first apheresis and continue until the last apheresis; discontinue for WBC > 100,000 mm³.

Sever chronic neutropenia.
SubQ:
Congenital: initial: 6 mcg/kg/day in 2 divided doses; adjust the dose based on ANC and clinical response; mean dose: 6 mcg/kg/day.
Idiopathic: initial: 5 mcg/kg/day once daily; adjust the dose based on ANC and clinical response. Total daily dose may be administered in 1 to 2 divided dose; mean dose: 1.2 mcg/kg/day.
Cyclic: initial: 5 mcg/kg once daily: adjust the dose based on ANC and clinical response; total daily dose may be administered in 1 or 2 divided dose; mean dose: 2.1mcg/kg/day. [1]

Pediatric note:
Do not administer in the periods 24 hours before to 24 hours after cytotoxic chemotherapy.
International consideration:
Dosage below expressed as microgram; 1mcg =100,000 units

Myelosuppressive chemotherapy recipients with non-myeloid malignancies.
SubQ,IV: 5 mcg/kg/day: doses may be increased by 5 mcg/kg. according to the duration and severity of the neutropenia; continue for up to 14 days until the absolute neutrophil count (ANC) reaches 10,000/mm³ . Discontinue if the ANC surpasses 10,000/mm³ after the expected chemotherapy –induced neutrophil nadir

Bone marrow transplantation
IV infusion: 10 mcg/kg/day; Adjust the dose according to the duration severity of the neutropenia.

Hematopoietic radiation injury syndrome, acute
SubQ: 10 mcg/kg once daily; begin as soon as possible after suspected or confirmed radiation dose >2 gray (Gy) and continue filgrastim until ANC remains > 1,000/mm³ for 3 consecutive CBCs or ANC exceed 10,000/ mm³ after the radiation – induced nadir

Peripheral blood progenitor cell collection and therapy
SubQ: 10 mcg/kg daily, usually for 6 to 7 days. begin at least 4 days before the first apheresis and continue until the last apheresis; discontinue for WBC > 100,000 mm³.

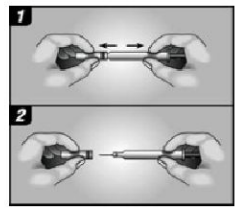
Sever chronic neutropenia.
SubQ:Congenital: initial: 6 mcg/kg/day in 2 divided doses; adjust the dose based on ANC and clinical response; mean dose: 6 mcg/kg/day.
Idiopathic: initial: 5 mcg/kg/day once daily; adjust the dose based on ANC and clinical response. Total daily dose may be administered in 1 to 2 divided dose; mean dose: 1.2 mcg/kg/day
Cyclic: initial: 5 mcg/kg once daily: adjust the dose based on ANC and clinical response; totally daily dose may be administered in 1 or 2 divided dose ; mean dose: 2.1mcg/kg/day

Drug Interactions:
No known interactions with this medication are known. Filgrastim may increase the effects of: Belotecan, Belomycin, Cyclophosphamide, Topotecan. [1]

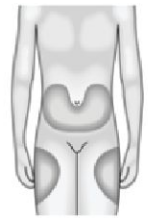
Adverse effects:
Along with therapeutic effects the drugs have side effects, which some of the side effects of filgrastim are listed blew:
Cardiac arrhythmia, chest pain, hypertension, myocardial infraction , peripheral edema, Dizziness, fatigue, headache, hypoesthesia, insomnia, malaise, mouth pain, pain, back pain muscle spasm , skin rash , increased lactate dehydrogenase, increased uric acid , constipation, decreased appetite, diarrhea, nausea, vomiting , urinary tract infection, anemia, leukocytosis, petechia, splenomegaly, thrombocytopenia , increased serum alkaline phosphatase hypersensitive reaction, transfusion reaction , antibody development , nose bleeding , sepsis [1,5]

Poisoning:
If you accidentally use more than recommended, go to the treatment center immediately.

Preparation and injection method:
Before subcutaneous injection, read the following:
- Remove the syringe from the refrigerator for about 30 minutes before injection. If the temperature of the product reaches room temperature, it will be easier to inject.
- Do not use any other method to warm EXIPOGEN®.
- Avoid shaking the product.
- Do not detach the needle until ready for injection.
- To prevent the needle tipping, remove the cap slowly in accordance with the shape and without twisting the cap.



Do not touch the needle.
Do not press the syringe piston.
The best areas for subcutaneous injection on the thigh and the lower and lower cuffs (with a minimum distance of 5 cm from the navel). If injected by someone else, the arm can also be suitable for injection.



Storage condition:
Store in 2 – 8°C protect from light and freezing.
Before injection the drug should reach to room temperature.
The drug Stable at room temperature up to 24 hour
Keep medicine out of the reach and sight of children.
Single use syringe-discharge unused portion.
Prescription-only medicine.
Look carefully at the appearance of the product before injection. Avoid using color in the event of discoloration or particles.
The product should be stored in the original medicine box before injection.
Preservative-free [1]

References:
1. Lexi comp Drug information handbook, 2019, 26th edition , Pages: 976-980
2. Drug facts and comparisons, 2010, Pages: 2204-2206
3. USP DI 2007, 27th edition, Drug information for the health care professional, Volume 1, Pages: 29-34
4. Handbook on INJECTABLE DRUGS, 16th edition, 2011, Page: 6

2205608/ 1

MANUFACTURED BY EXIR PHARMACEUTICAL CO. IRAN

EXIR 98.04.02
Black U
292 U
297*140 mm