Claims

[Claim 1] A pharmaceutical composition comprising:

(a) about 1 mg/mL to about 100 mg/mL granulocyte colony-stimulating factor (G-CSF) dimer;

(b) about 1 mM to about 50 mM buffering agent;

(c) about 0.1 mM to about 20 mM EDTA;

(d) about 1% (w/v) to about 15% (w/v) sorbitol; and

(e) about 0.001% (w/v) to about 0.1% (w/v) surfactant; and

wherein the pH of the pharmaceutical composition is about 4.2 to about 6.2.

[Claim 2] The pharmaceutical composition of claim 1, wherein the G-CSF dimer comprises two monomeric subunits, and wherein each monomeric subunit comprises a G-CSF monomer and a dimerization domain.

[Claim 3] The pharmaceutical composition of claim 2, wherein:

(a) the G-CSF monomer comprises the amino acid sequence of SEQ ID NO: 1;

(b) the G-CSF monomer is connected to the dimerization domain via an optional linker;

(c) the dimerization domain comprises at least two cysteines capable of forming intermolecular disulfide bonds;

(d) the dimerization domain comprises at least a portion of an Fc fragment; and/or

(e) the G-CSF monomer is N-terminal to the dimerization domain within each monomeric subunit.

[Claim 4] The pharmaceutical composition of claim 3,

(a) wherein the G-CSF monomer is connected to the dimerization domain via a linker, and wherein the linker:

(i) is about 6 to about 30 amino acids in length; and/or
(ii) comprises the amino acid sequence of SEQ ID NO: 12; and/or
(b) wherein the dimerization domain comprises an Fc fragment, and wherein the Fc fragment comprises an amino acid sequence of any of SEQ ID NOs: 2-5.

[Claim 5] The pharmaceutical composition of claim 3 or 4, wherein each monomeric subunit comprises an amino acid sequence of any of SEQ ID NOs: 6-10, or a variant thereof having at least about 90% sequence identity to the amino acid sequence of any of SEQ ID NOs: 6-10.

[Claim 6] The pharmaceutical composition of claim 5, wherein each monomeric subunit comprises the amino acid sequence of SEQ ID NO: 6.

[Claim 7] The pharmaceutical composition of any one of claims 1-6, wherein the G-CSF dimer is efbemalenograstim alfa.

[Claim 8] The pharmaceutical composition of any one of claims 1-7, wherein the concentration of the G-CSF dimer is about 5 mg/mL to about 50 mg/mL.

[Claim 9] The pharmaceutical composition of claim 8, wherein the concentration of the G-CSF dimer is about 20 mg/mL.

[Claim 10] The pharmaceutical composition of any one of claims 1-9, wherein the buffering agent is sodium acetate.

[Claim 11] The pharmaceutical composition of claim 10, wherein the concentration of the sodium acetate is about 1 mM to about 30 mM.

[Claim 12] The pharmaceutical composition of claim 11, wherein the concentration of the sodium acetate is about 10 mM.

[Claim 13] The pharmaceutical composition of any one of claims 1-12, wherein the concentration of the EDTA is about 0.1 mM to about 10 mM.

[Claim 14] The pharmaceutical composition of claim 13, wherein the concentration of the EDTA is about 1 mM.

[Claim 15] The pharmaceutical composition of any one of claims 1-14, wherein said pharmaceutical composition comprises about 1% (w/v) to about 8% (w/v) sorbitol.

[Claim 16] The pharmaceutical composition of claim 15, wherein said pharmaceutical composition comprises about 5% (w/v) sorbitol.

[Claim 17] The pharmaceutical composition of any one of claims 1-16, wherein the surfactant is polysorbate 20 (PS20) or polysorbate 80 (PS80).

[Claim 18] The pharmaceutical composition of claim 17, wherein the surfactant is PS20, and wherein said pharmaceutical composition comprises about 0.005% (w/v) to about 0.05% (w/v) PS20.

[Claim 19] The pharmaceutical composition of claim 18, wherein said pharmaceutical composition comprises about 0.01% (w/v) PS20.

[Claim 20] The pharmaceutical composition of any one of claims 1-19, wherein the pH of the pharmaceutical composition is about 5.0 to about 5.4.

[Claim 21] The pharmaceutical composition of claim 20, wherein the pH of the pharmaceutical composition is about 5.2.

[Claim 22] The pharmaceutical composition of any one of claims 1-21, wherein the pharmaceutical composition comprises:

(a) about 20 mg/mL of the G-CSF dimer;

(b) about 10 mM sodium acetate;

(c) about 1 mM EDTA;

(d) about 5% (w/v) sorbitol; and

(e) about 0.01% (w/v) PS20; and

wherein the pharmaceutical composition has a pH of about 5.2.

[Claim 23] The pharmaceutical composition of any one of claims 1-22, wherein the pharmaceutical composition is contained in a syringe.

[Claim 24] The pharmaceutical composition of claim 23, wherein:

(a) the volume of the pharmaceutical composition within the syringe is about 1 mL;

(b) the syringe is for single use; and/or

(c) the syringe is sterile.

[Claim 25] Use of an effective amount of the pharmaceutical composition of any one of claims 1-24 in the manufacture of a medicament for treating or preventing a disease or condition in an individual.

[Claim 26] The use of claim 25, wherein the disease or condition is chemotherapy-induced neutropenia or radiotherapy-induced neutropenia.

[Claim 27] The use of claim 26, wherein the disease or condition is chemotherapy-induced neutropenia, and wherein the medicament is for administration after the administration of a chemotherapeutic agent to the individual.

[Claim 28] The use of claim 27, wherein the chemotherapeutic agent is a myelosuppressive chemotherapeutic agent.

[Claim 29] The use of claim 27 or 28, wherein:
(a) the chemotherapeutic agent is for administration to the individual at least 4 cycles, and wherein the medicament is for administration after the administration of the chemotherapeutic agent in each cycle of the at least 4 cycles;
(b) the medicament is for administration at about 5 mg to about 25 mg of the G-CSF dimer for each administration;
(c) the medicament is for subcutaneous administration; and/or
(d) the individual is a human.

[Claim 30] A method of manufacturing the pharmaceutical composition of any one of claims 1-24, comprising:
(i) culturing a host cell under a condition suitable for expressing the G-CSF dimer;
(ii) isolating the expressed G-CSF dimer from the cell culture;
(iii) purifying the expressed G-CSF dimer; and
(iv) formulating the purified G-CSF dimer with the buffering agent, EDTA, sorbitol, and the surfactant.