Neupogen ®
Safety Data Sheet

Revision Number: 3 **Date Issued** 18-Feb-2013

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERSTANDING

1.1 Product identifier

Product Name: Neupogen
Common Name: Filgrastim
Chemical Name: Not Applicable
Synonyms: Filgrastim, Recombinant granulocyte colony stimulating factor, G-CSF, rHuG-CSF

1.2 Relevant identified uses of the substance or mixture and uses advised against

Recommended Use: Pharmaceutical
Uses advised against: No information available

Manufacturer:

Amgen Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799
1-805-447-7233
1-805-447-1000

Emergency Telephone Number:

Chemtrec
NORTH AMERICA 1-800-424-9300,
INTERNATIONAL 1-703-527-3887

2. HAZARDS IDENTIFICATION

Emergency Overview

Pharmaceutical product intended for research and development, clinical and manufacturing purposes only. Product contains filgrastim, a recombinant form of human granulocyte colony-stimulating factor. Dosage form contents may pose a health hazard only if exposure occurs to contents, e.g., after spill or leak. Repeated overexposure in manufacturing or from a significant spill may potentially cause effects seen in patients administered the drug such as increased neutrophil count, increased lactic dehydrogenase (LDH) and alkaline phosphatase (AP) levels. Filgrastim is listed by the State of California as a developmental toxicant; rabbits and rats treated during organogenesis had increased abortion and embryolethality. Avoid inhalation, skin contact, eye contact, and ingestion. Does not meet GHS classification criteria and therefore is not classified.

2.1 - Classification of the drug substance or mixture (drug product in final form, not applicable)

REGULATION (EC) No 1272/2008

Not classified

Classification according to EU Directives 67/548/EEC or 1999/45/EC
For the full text of the R phrases mentioned in this Section, see Section 16

2.2 Label elements

Not classified

2.3 Other Hazards No information available

3. COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Ingredients: Proprietary information

Chemical Name: Not Applicable
CAS-No: 121181-53-1

Syringes containing 300 mcg/0.5 mL syringe

	CAS Number:	Amount
Filgrastim	121181-53-1	300 µg
Acetate	12345	0.295 mg
Sorbitol	26566-34-7	25.0 mg
Polysorbate 80	9005-64-6	0.02 mg
Sodium	7647-14-5	0.0175 mg
Water for Injection, USP	7732-18-5	0.5 mL

Syringes containing 480 mcg/0.8 mL

	CAS Number:	Amount
Filgrastim	121181-53-1	480 µg
Acetate	12345	0.47 mg
Sorbitol	26566-34-7	40.0 mg
Polysorbate 80	9005-64-6	0.03 mg
Sodium	7647-14-5	0.03 mg
Water for Injection, USP	7732-18-5	0.8 mL

Vials containing 300 mcg/1.0 mL vial

	CAS Number:	Amount
Filgrastim	121181-53-1	300 µg
Acetate	12345	0.59 mg
Sorbitol	50-70-4	50.0 mg
Polysorbate 80	9005-65-6	0.04 mg
Sodium	7647-14-5	0.035 mg
Water for Injection, USP	7732-18-5	1.0 mL

Vials containing 480 mcg/1.6 mL vial

	CAS Number:	Amount
Filgrastim	121181-53-1	480 µg
Acetate	12345	0.94 mg
Sorbitol	50-70-4	80.0 mg
Polysorbate 80	9005-65-6	0.064 mg
Sodium	7647-14-5	0.056 mg
Water for Injection, USP	7732-18-5	1.6 mL

4. FIRST AID MEASURES

4.1 Description of first-aid measures

Eye Contact: In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

Skin Contact: Wash off immediately with soap and plenty of water removing all contaminated clothes and shoes. Consult a physician if necessary.

Inhalation: Move to fresh air. If symptoms persist, call a physician.

Ingestion: If symptoms persist, call a physician. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.

Notes to Physician: Treat symptomatically.

5. FIRE-FIGHTING MEASURES

5.1 Extinguishing media

Flammable Properties: Not applicable/aqueous solution.

Extinguishing Media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No information available.

5.3 Advice for firefighters

Protective Equipment and Precautions for Firefighters: As in any fire, wear self-contained breathing apparatus pressure-demand, NIOSH (approved) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

Spill Procedures: If material is released or spilled, cordon off spill area. Take proper precautions to minimize exposure by using appropriate personal protective equipment in cleaning up a spill. If in powder form, wet down spilled material to minimize airborne dispersion. Soak up material with absorbent e.g., paper towels, and wash spill area thoroughly with appropriate cleaning materials. Dispose of collected material in accordance with applicable waste disposal regulations. Avoid release to the environment.

7. HANDLING AND STORAGE

7.1 Precautions for Safe Handling

Handling and Storage: Avoid contact with skin, eyes or clothing. Do not eat, drink or smoke in work areas. Use adequate ventilation to minimize exposure. Wash hands, face and other potentially exposed areas immediately after handling this material. Remove contaminated clothing prior to entering eating areas. Clean protective equipment thoroughly after each use. Store in a well ventilated area.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1 Control parameters

Occupational Exposure Limit: No exposure guidelines established by ACGIH, NIOSH or OSHA. Amgen recommends an occupational exposure limit (OEL) of 6 µg/m^3 as an 8-hour time weighted average over a 40-hour work week. The OEL is designed as an acceptable airborne concentration of a substance for which it is believed that workers may be repeatedly exposed day after day without adverse health effects. Neupogen® has been classified per Amgen's Hazard Classification System as an Occupational Exposure Band 4 compound (5 µg/m^3 - 20 µg/m^3).

Engineering Controls: When practicable, handle material in enclosed processes or in processes with effective local exhaust ventilation or within a chemical hood.

8.2 Exposure controls

Personal Protective Equipment

Eye/face Protection: Wear safety glasses with side shields, chemical splash goggles, or safety glasses with side shields and a full-face shield to prevent contact with eyes. The choice of protection should be based on the job activity and potential for exposure to the eyes and face.

Skin Protection: Use gloves or other appropriate personal protective equipment if skin contact with formulation is possible. Wear lab coat or other protective over garment if splashing is possible. The choice of protection should be based on the job activity and potential for skin contact.

Respiratory Protection: When possible, handle material in enclosed processes or containers. If it is properly handled with effective local exhaust ventilation or containment, respiratory protection may not be needed. For procedures involving larger quantities or dust/aerosol generating procedures such as weighing or a large transfer of liquids, an air-purifying respirator with NIOSH approval for dusts and mists may be needed.

Other: Wash hands, face and other potentially exposed areas after handling material (especially before eating, drinking or smoking). Clean protective equipment thoroughly after each use.

8.3 Environmental exposure controls

Environmental Exposure Controls Avoid release to the environment.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Clear Colorless
Physical State:	Liquid
Molecular Weight:	Approximately 18,800 Daltons
Odor:	No information available
Odor Threshold:	No information available
pH:	4.0
Melting Point:	Not applicable
Boiling point	Approx. 100 °C
Flash Point:	Not applicable
Evaporation Rate:	No information available
Lower explosive limit:	No information available
Upper explosive limit:	No information available
Vapor Pressure:	No information available
Vapor Density (air = 1):	Not applicable
Relative density:	No information available
Water Solubility:	Soluble
Partition Coefficient (log Kow):	No information available
Viscosity:	No information available

10. STABILITY AND REACTIVITY

10.1 Reactivity	No information available
10.2 Chemical stability	Stable
10.3 Possibility of hazardous reactions	No information available
10.4 Conditions to avoid	No Information available
10.5 Incompatible materials	No information available
10.6 Hazardous decomposition products	No information available
10.7 Other information	None

11. TOXICOLOGICAL INFORMATION

11.1 Information on toxicological effects

Acute Toxicity: No information available
Skin corrosion/irritation: No information available
Serious eye damage/eye irritation: No information available
Respiratory or skin sensitization: No information available
Germ cell mutagenicity: Even though this does not meet GHS classification, the following data is available: Not genotoxic based on a battery of in vitro and in vivo studies.
Carcinogenicity: No information available
Reproductive toxicity: Even though this does not meet GHS classification, the following data is available: Neupogen® has been shown to have adverse fetal effects to pregnant rabbits following intravenous exposure. In addition, preganant rats administered Neupogen® during late gestation and after delivery were associated with growth retardation and a delay in external differentiation.
STOT - single exposure: Even though this does not meet GHS classification, the following data is available: Neupogen® single-dose administration by the oral, intravenous (IV), subcutaneous (SC), or intraperitoneal (IP) routes resulted in no significant toxicity in mice, rats, hamsters, or monkeys.
STOT - repeated exposure: Even though this does not meet GHS classification, the following data is available: Neupogen® has been administered parenterally for up to 52 weeks in animals. In the 52-week chronic, repeated-dose studies performed in rats (IP injection up to 57.5 mcg/kg/day), and cynomolgus monkeys (IV injection of up to 115 mcg/kg/day). Effects included expected pharmacological actions such as dose-dependent increases in white cell counts, increased circulating segmented neutrophils and alkaline phosphatase levels, and increased myeloid:erythroid ratios in the bone marrow. Decreases in platelet counts were also noted in primates. In no animals tested were hemorrhagic complications observed. Rats displayed dose-related swelling of the hind limb, accompanied by some degree of hind limb dysfunction; osteopathy was noted microscopically. Enlarged spleens (both species) and livers (monkeys), reflective of ongoing extramedullary granulopoiesis, as well as myeloid hyperplasia of the bone marrow, were observed in a dose-dependent manner. In patients administered Neupogen® , rare but serious adverse events (e.g., allergic-type reactions, splenic rupture, acute respiratory distress syndrome (ARDS) alveolar hemorrhage and hemoptysis, and severe sickle cell crises) have been reported.
Aspiration Hazard: No information available

12. ECOLOGICAL INFORMATION

12.1 Toxicity

Ecotoxicity effects: No information available

12.2 Persistence and degradability

Persistence/Degradability: No information available

12.3 Bioaccumulative potential

Bioaccumulation/ Accumulation: No information available

12.4 Mobility in soil

Mobility in Environmental Media: No information available

12.5 Results of PBT and vPvB assessment

Results of PBT and vPvB assessment: No information available

12.6 Other adverse effects

Other Adverse Effects: No information available

13. DISPOSAL CONSIDERATIONS

13.1 Waste treatment methods

Waste Disposal Method: Dispose of any waste according to prescribed federal, state, local and competent authority guidelines.

14. TRANSPORT INFORMATION

DOT Not regulated by U.S. DOT or IATA

15. REGULATORY INFORMATION

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

International Inventories

TSCA:	-
EINECS/ELINCS	-
DSL/NDSL	-
PICCS:	-
ENCS:	-
CHINA:	-
AICS:	-
KECL:	-

Legend
TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
EINECS/ELINCS - European Inventory of Existing Commercial Chemical Substances/EU List of Notified Chemical Substances
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
PICCS - Philippines Inventory of Chemicals and Chemical Substances
ENCS - Japan Existing and New Chemical Substances
IECSC - China Inventory of Existing Chemical Substances
AICS - Australian Inventory of Chemical Substances
KECL - Korean Existing and Evaluated Chemical Substances

State Regulations

California Proposition 65: The active ingredient, filgrastim is listed as a developmental toxicant.

15.2 Chemical safety assessment

No CSA has been conducted.

16. OTHER INFORMATION

Text of R phrases mentioned in Section 2
No information available

Revision Number: 3

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections, which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it may be biologically active.