Granulocyte Colony Stimulating Factor - Adult/Pediatric - Inpatient/Ambulatory Clinical Practice Guideline

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Executive Summary
Guideline Overview
These clinical practice guidelines are intended to guide clinicians in the use of granulocyte colony stimulating factor (GCSF) in adult and pediatric patients. Graded recommendations for indications, dosing, administration, and precautions for use are included.

Key Practice Recommendations
1. Prevention of febrile neutropenia in cancer patients receiving myelosuppressive chemotherapy
   1.1. GCSF should be used as primary prevention in patients receiving chemotherapy with a 20% or greater risk of neutropenic fever (Class I, Level of Evidence A)
   1.1.1. Secondary prevention can be considered in patients with previous dose modifications, delays in therapy, or neutropenic fever
   1.2. GCSF should be given at least 24 hours after the last dose of chemotherapy (Class I, Level of Evidence A)
   1.3. Dosing: (Class I, Level of Evidence A)
      1.3.1. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (Class I, Level of Evidence A)
      1.3.2. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (Class I, Level of Evidence A)
      1.3.3. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (Class I, Level of Evidence A)
   1.4. Duration of Therapy:
      1.4.1. Adult and pediatric patients will continue with daily GCSF administration until the ANC is 500 cells/mm$^3$ on two consecutive days (Class I, Level of Evidence A)
      1.4.2. Pediatric patients who remain on Children’s Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol. Pediatric patients who are NOT ON study should follow ANC targets as specified above.
2. Treatment of febrile neutropenia in patients with greater risk of mortality
   2.1. No improvement in overall survival has been shown for the use of GCSF in the treatment of neutropenic fever. GCSF should only be considered for the treatment of febrile neutropenia in patients with risk factors for greater mortality. (Class IIa, Level of Evidence A)
   2.2. Risk Factors: age > 65 years, sepsis syndrome, ANC < 100, anticipated prolonged neutropenia (greater than 10 days) (Class IIa, Level of Evidence A)
   2.3. Dosing:
      2.3.1. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (Class I, Level of Evidence A)
      2.3.2. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (Class I, Level of Evidence A)
2.3.3. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (Class I, Level of Evidence A)

2.4. Duration of Therapy:
2.4.1. Patients will continue with daily GCSF administration until the ANC is 500 cells/mm³ on two consecutive days (Class I, Level of Evidence A)

3. Mobilization in patients undergoing stem cell collection
3.1. Patients will receive twice daily GCSF to assist in promoting stem cell production and release from the bone marrow prior to stem cell collection for autologous peripheral stem cell transplants (Class I, Level of Evidence A)

3.2. Dosing:
3.2.1. All adult patients who weigh less than 60 kg should receive GCSF 300 mcg subcutaneously twice daily (Class I, Level of Evidence A)
3.2.2. All adult patients who weigh between 60 and 78 kg should receive GCSF 300 mcg subcutaneously in the morning and 480 mcg subcutaneously in the evening (Class I, Level of Evidence A)
3.2.3. All adult patients who weigh greater than 78 kg should receive GCSF 480 mcg subcutaneously twice daily (Class I, Level of Evidence A)
3.2.4. Pediatric patients will receive GCSF 10 mcg/kg daily subcutaneously (Class I, Level of Evidence A)

3.3. Duration of therapy:
3.3.1. Patients will continue on GCSF until an adequate amount of stem cells for autologous transplant have been collected. (Class I, Level of Evidence A)

4. In patients undergoing autologous peripheral blood or bone marrow transplant exception: multiple myeloma patients
4.1. Patients undergoing autologous peripheral blood or bone marrow transplant can receive GCSF to assist with engraftment and shorten the length of hospital stay. (Class I, Level of Evidence A)
4.2. Multiple myeloma patients will not receive GCSF as part of their autologous peripheral blood or bone marrow transplant. (Class I, Level of Evidence A)

4.3. Dosing:
4.3.1. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (Class I, Level of Evidence A)
4.3.2. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (Class I, Level of Evidence A)
4.3.3. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (Class I, Level of Evidence A)

4.4. Duration of Therapy:
4.4.1. Adult and pediatric patients will continue with daily GCSF administration until the ANC is 500 cells/mm³ on two consecutive days (Class I, Level of Evidence A)
4.4.2. Pediatric patients who remain on Children’s Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol. Pediatric patients who are NOT ON study should follow ANC targets as specified above.

5. In patients undergoing allogeneic cord-blood transplants
5.1. Patients undergoing allogeneic cord-blood transplants can receive GCSF to assist with engraftment and shorten the length of neutropenia. (Class IIb, Level of Evidence C)

5.2. Patients receiving other allogeneic peripheral blood stem cell transplants should not receive GCSF as it increases the risk of severe graft versus host disease. (Class I, Level of Evidence A)

5.3. Dosing:
   5.3.1. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (Class I, Level of Evidence A)
   5.3.2. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (Class I, Level of Evidence A)
   5.3.3. Pediatric patients will receive GCSF 10 mcg/kg/day intravenously (Class I, Level of Evidence A)

5.4. Duration of Therapy:
   5.4.1. Adult and pediatric patients will continue with daily GCSF administration until the ANC is 500 cells/mm³ on two consecutive days (Class I, Level of Evidence A)
   5.4.2. Pediatric patients who remain on Children’s Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol. Pediatric patients who are NOT ON study should follow ANC targets as specified above.

6. Drug-induced neutropenia (Class IIb, Level of Evidence C)
   6.1. GCSF should not be used as the primary treatment of drug-induced neutropenia, other than in the populations specified in this guideline. Dose reduction, discontinuation, or temporary cessation of the offending medication(s) should be the primary treatment for these patients. (Class IIb, Level of Evidence C)
   6.2. GCSF can only be considered in certain situations where patients who remain neutropenic despite dose reduction, discontinuation, or temporary cessation of the offending medication(s). (Class IIb, Level of Evidence C)

7. Drug-induced leukopenia in solid organ transplant patients on chronic immunosuppression or antiviral agents (i.e. ganciclovir, valganciclovir, mycophenolate, azathioprine)
   7.1. GCSF should only be considered in conjunction with dose reduction, discontinuation, or temporary cessation of the offending medication(s). (Class IIb, Level of Evidence B)

7.2. Dosing:
   7.2.1. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (Class I, Level of Evidence A)
   7.2.2. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (Class I, Level of Evidence A)
   7.2.3. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (Class I, Level of Evidence A)

7.3. Duration of Therapy:
   7.3.1. Adult and pediatric patients may initiate therapy at ANC values of less than 1000 cells/mm³. Patients may continue daily administration until
the ANC is greater than 1000 cells/mm$^3$ for one day. *(Class IIb, Level of Evidence C)*

8. **Drug-induced leukopenia in HIV patients on anti-retroviral therapy** (i.e. zidovudine) or immune suppressive antiviral agents (i.e. ganciclovir, valganciclovir)

8.1. In patients who are on anti-retroviral therapy for the treatment of HIV or antiviral medications with bone marrow suppressive side effects, GCSF could be considered in conjunction with dose reduction, discontinuation, or temporary cessation of the offending medication(s). *(Class IIb, Level of Evidence B)*

8.2. Neutropenia associated with the AIDS disease process is considered an inappropriate use by the University Health-system Consortium Colony Stimulating Factors expert panel. *(Class IIb, Level of Evidence B)*

8.3. **Dosing:**

8.3.1. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily *(Class I, Level of Evidence A)*

8.3.2. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily *(Class I, Level of Evidence A)*

8.3.3. Pediatric patients will receive GCSF 5 mcg/kg once daily intravenously or subcutaneously *(Class I, Level of Evidence A)*

8.4. **Duration of Therapy**

8.4.1. Adult and pediatric patients will initiate therapy at ANC values of less than 1000 cells/mm$^3$. Patients will continue daily administration until the ANC is greater than 1000 cells/mm$^3$ for one day. *(Class IIb, Level of Evidence C)*

9. **Severe Chronic Neutropenia**

9.1. Patients with symptomatic congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia will receive chronic GCSF to reduce the incidence and duration of sequelae of neutropenia (i.e. fever, infection, oropharyngreal ulcers) *(3,4) (Class I, Level of Evidence B)*

9.2. **Dosing:**

9.2.1. Patients receiving GCSF for severe chronic neutropenia will receive a daily dose titrated to an ANC goal of 1500 cells/mm$^3$ *(3,4) (Class I, Level of Evidence B)*

9.2.2. It is appropriate to use the patient’s home dose of GCSF in these situations *(Class I, Level of Evidence B)*

9.3. **Duration of therapy**

9.3.1. Patients will continue daily GCSF indefinitely. The dose will be titrated to maintain an ANC target of 1500 cells/mm$^3$ *(3,4) (Class I, Level of Evidence B)*
Scope

Disease/Condition(s):
All adult and pediatric patients with neutropenia including the following:
1. Prevention and treatment of febrile neutropenia in patients receiving myelosuppressive therapy
2. Patients undergoing mobilization for stem cell collection
3. Patients undergoing autologous peripheral blood or bone marrow transplant
4. Patients undergoing allogeneic cord blood transplant
5. Patients with drug-induced leukopenia secondary to chronic immunosuppression or antiviral agents following solid organ transplant
6. Patients with drug-induced leukopenia secondary to anti-retroviral therapy for the treatment of HIV
7. Patients with severe chronic neutropenia

Clinical Specialty:
Bone Marrow Transplant, Hematology, Oncology, Solid Organ Transplant, Infectious Diseases

Intended Users:
This guideline is intended to be used by physicians, advanced practice providers, pharmacists, and nurses.

Objective(s):
These clinical practice guidelines are intended to guide clinicians in the use of GCSF in adult and pediatric patients including recommendations for indications, dosing, administration, and precautions for use.

Target Population:
Patients with neutropenia

Interventions and Practices Considered:
1. Indications of appropriate GCSF use
2. ANC goals for all indications
3. Adult and pediatric dosing recommendations for all indications
4. Monitoring parameters

Major Outcomes Considered:
Successful management of patients with neutropenia
Cost savings from appropriate utilization of treatment strategies.

Guideline Metrics:
Successful management of patients with neutropenia.
Cost savings from appropriate utilization of treatment strategies
Methodology

Methods Used to Collect/Select the Evidence:
Review of the following:
1. National guideline recommendations including National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), Infectious Diseases Society of America (IDSA), and European Organization for the Research and Treatment of Cancer (EORTC)
2. FDA package inserts using Drugs@FDA website
3. Existing UW Health Clinical Practice Guidelines
4. PubMed database with the keywords: granulocyte colony stimulating factor, GCSF, filgrastim, neutropenia

Methods Used to Assess the Quality and Strength of the Evidence:
A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.(1)

Rating Scheme for the Strength of the Evidence:
Methods Used to Formulate the Recommendations:
Review of standard drug databases, pertinent guidelines and literature with treatment effect size and estimate of certainty of the treatment effect established according to the rating scheme.

Definitions
1. Absolute neutrophil count (ANC) – the total number of neutrophils in the peripheral blood
2. Allogeneic stem cell transplant – peripheral blood or bone marrow transplant where the recipient receives a donor’s cells
3. Autologous stem cell transplant – peripheral blood or bone marrow transplant where the recipient receives his/her own cells
4. Cord-blood transplant – peripheral blood transplant where the recipient receives progenitor cells harvested from an umbilical cord
5. Febrile neutropenia – a single oral or tympanic temperature of ≥38.3°C (101°F), or a temperature of ≥ 38.0°C (100.4°F) sustained over an hour AND an ANC of ≤ 500 cells/mm3. (2)
6. Granulocyte colony stimulating hormone (GCSF) – a hormone in the body that regulates the production of neutrophils within the bone marrow and affects neutrophil progenitor cell proliferation, differentiation, and end-cell functional activation.(3)
7. Mobilization – the use of GCSF with or without chemotherapy to stimulate the production of progenitor cells in the bone marrow and their release into the peripheral blood
8. Neutropenia – hematologic abnormality where the ANC is <1000 cells/mm3. Severe neutropenia is defined as ANC < 500 cells/mm3
9. Stem cell collection – the collection of peripheral blood progenitor cells by leukapheresis procedure

Introduction
Granulocyte colony stimulating factor (GCSF) is an analogue of the human GCSF produced by Escherichia coli (E. coli) bacteria through recombinant DNA technology. GCSF is FDA approved for the reduction of the duration and severity of febrile neutropenia in adult and pediatric cancer patients receiving chemotherapy, in patients undergoing stem cell collection, and in patients with severe chronic neutropenia. (3, 4) GCSF is an expensive medication with few available alternatives. The American Society of Clinical Oncology (ASCO), National Comprehensive Cancer Network (NCCN) and European Organization for Research and Treatment of Cancer (EORTC) clinical practice guidelines define appropriate indications for oncology patients to receive GCSF as well as the appropriate ANC goal.(5-7) Recent literature supports expanded indications for GCSF such as the treatment of drug-induced leukopenia in solid organ...
transplant patients and patients infected with human immunodeficiency virus (HIV); however, ANC goals and durations of therapy have not yet been established at this time.(8-13) This guideline was developed based on the available evidence in the literature to establish defined standards for GCSF use at the UWHC.

Recommendations

The following recommendations are separated into appropriate indications with dosing and duration of therapy of each. Monitoring parameters will apply to all indications.

1. Prevention of febrile neutropenia in cancer patients receiving myelosuppressive chemotherapy

   a. GCSF should be used as primary prevention in patients receiving chemotherapy with a 20% or greater risk of neutropenic fever (5-7) (Class I, Level of Evidence A)
      i. Secondary prevention can be considered in patients with previous dose modifications, delays in therapy, or previous incidence of neutropenic fever (5-7) (Class I, Level of Evidence A)

   b. GCSF should be given at least 24 hours after the last dose of chemotherapy (5-7) (Class I, Level of Evidence A)

   c. Dosing:
      i. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)
      ii. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)
      iii. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (5-7) (Class I, Level of Evidence A)

   d. Duration of Therapy:
      i. Adult and pediatric patients will continue with daily GCSF administration until the ANC is 500 cells/mm$^3$ on two consecutive days (5-7) (Class I, Level of Evidence A)
      ii. Pediatric patients who remain on Children’s Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol. Pediatric patients who are NOT ON study should follow ANC targets as specified above.

2. Treatment of febrile neutropenia in patients with greater risk of mortality

   a. No improvement in overall survival has been shown for the use of GCSF in the treatment of neutropenic fever. GCSF should only be considered for the treatment of febrile neutropenia in patients with risk factors for greater mortality. (5,6) (Class IIa, Level of Evidence A)

   b. Risk Factors: age > 65 years, sepsis syndrome, ANC < 100, anticipated prolonged neutropenia (greater than 10 days) (5,6) (Class IIa, Level of Evidence A)

   c. Dosing:
i. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)

ii. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)

iii. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (5-7) (Class I, Level of Evidence A)

d. Duration of Therapy

i. Patients will continue with daily GCSF administration until the ANC is 500 cells/mm$^3$ on two consecutive days (5-7) (Class I, Level of Evidence A)

3. Mobilization in patients undergoing stem cell collection

a. Patients will receive twice daily GCSF to assist in promoting stem cell production and release from the bone marrow prior to stem cell collection for autologous peripheral stem cell transplants (5-7) (Class I, Level of Evidence A)

b. Dosing:

i. All adult patients who weigh less than 60 kg should receive GCSF 300 mcg subcutaneously twice daily (5-7) (Class I, Level of Evidence A)

ii. All adult patients who weigh between 60 and 78 kg should receive GCSF 300 mcg subcutaneously in the morning and 480 mcg subcutaneously in the evening (5-7) (Class I, Level of Evidence A)

iii. All adult patients who weigh greater than 78 kg should receive GCSF 480 mcg subcutaneously twice daily (5-7) (Class I, Level of Evidence A)

iv. Pediatric patients will receive GCSF 10 mcg/kg daily subcutaneously (5-7) (Class I, Level of Evidence A)

c. Duration of therapy:

i. Patients will continue on GCSF until an adequate amount of stem cells for autologous transplant have been collected. (5-7) (Class I, Level of Evidence A)

4. In patients undergoing autologous peripheral blood or bone marrow transplant exception: multiple myeloma patients

a. Patients undergoing autologous peripheral blood or bone marrow transplant can receive GCSF to assist with engraftment and shorten the length of hospital stay. (5-7) (Class I, Level of Evidence A)

b. Multiple myeloma patients will not receive GCSF as part of their autologous peripheral blood or bone marrow transplant. (5-7) (Class I, Level of Evidence A)

c. Dosing:

i. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)
ii. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)

iii. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (5-7) (Class I, Level of Evidence A)

d. Duration of Therapy:
   i. Adult and pediatric patients will continue with daily GCSF administration until the ANC is 500 cells/mm$^3$ on two consecutive days (5-7) (Class I, Level of Evidence A)

   ii. Pediatric patients who remain on Children's Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol. Pediatric patients who are NOT ON study should follow ANC targets as specified above.

5. In patients undergoing allogeneic cord-blood transplants
   a. Patients undergoing allogeneic cord-blood transplants can receive GCSF to assist with engraftment and shorten the length of neutropenia. (5-7) (Class IIb, Level of Evidence C)

   b. Patients receiving other allogeneic peripheral blood stem cell transplants should not receive GCSF as it increases the risk of severe graft versus host disease.(5) (Class I, Level of Evidence A)

c. Dosing:
   i. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)

   ii. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (5-7) (Class I, Level of Evidence A)

   iii. Pediatric patients will receive GCSF 10 mcg/kg/day intravenously (5-7) (Class I, Level of Evidence A)

d. Duration of Therapy:
   i. Adult and pediatric patients will continue with daily GCSF administration until the ANC is 500 cells/mm$^3$ on two consecutive days (5-7) (Class I, Level of Evidence A)

   ii. Pediatric patients who remain on Children’s Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol. Pediatric patients who are NOT ON study should follow ANC targets as specified above.

6. Drug-induced neutropenia
   a. GCSF should not be used as the primary treatment of drug-induced neutropenia, other than in the populations specified in this guideline. Dose reduction, discontinuation, or temporary cessation of the offending medication(s) should be the primary treatment for these patients. (14) (Class IIb, Level of Evidence C)
b. GCSF can **only** be considered in certain situations where patients who remain neutropenic despite dose reduction, discontinuation, or temporary cessation of the offending medication(s). (14) *(Class IIb, Level of Evidence C)*

7. **Drug-induced leukopenia in solid organ transplant patients on chronic immunosuppression or antiviral agents (i.e. ganciclovir, valganciclovir, mycophenolate, azathioprine)**
   a. GCSF should **only** be considered in conjunction with dose reduction, discontinuation, or temporary cessation of the offending medication(s). (8-11) *(Class IIb, Level of Evidence B)*
   b. Dosing:
      i. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (5-7) *(Class I, Level of Evidence A)*
      ii. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (5-7) *(Class I, Level of Evidence A)*
      iii. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (5-7) *(Class I, Level of Evidence A)*
   c. Duration of Therapy:
      i. Adult and pediatric patients may initiate therapy at ANC values of less than 1000 cells/mm$^3$. Patients may continue daily administration until the ANC is greater than 1000 cells/mm$^3$ for one day. (8-11) *(Class IIb, Level of Evidence C)*

8. **Drug-induced leukopenia in HIV patients on anti-retroviral therapy (i.e. zidovudine) or immune suppressive antiviral agents (i.e. ganciclovir, valganciclovir)**
   a. In patients who are on anti-retroviral therapy for the treatment of HIV or anti-viral medications with bone marrow suppressive side effects, GCSF could be considered in conjunction with dose reduction, discontinuation, or temporary cessation of the offending medication(s). (12,13) *(Class IIb, Level of Evidence B)*
   b. Neutropenia associated with the AIDS disease process is considered an inappropriate use by the University Health-system Consortium Colony Stimulating Factors expert panel. (12,13) *(Class IIb, Level of Evidence B)*
   c. Dosing:
      i. All adult patients who weigh 80 kg or less should receive GCSF 300 mcg subcutaneously once daily (5-7) *(Class I, Level of Evidence A)*
      ii. All adult patients who weigh greater than 80 kg should receive GCSF 480 mcg subcutaneously once daily (5-7) *(Class I, Level of Evidence A)*
      iii. Pediatric patients will receive GCSF 5 mcg/kg/day intravenously or subcutaneously (5-7) *(Class I, Level of Evidence A)*
   d. Duration of Therapy
i. Adult and pediatric patients will initiate therapy at ANC values of less than 1000 cells/mm$^3$. Patients will continue daily administration until the ANC is greater than 1000 cells/mm$^3$ for one day. (12,13) (Class IIb, Level of Evidence C)

9. **Severe Chronic Neutropenia**
   a. Patients with symptomatic congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia will receive chronic GCSF to reduce the incidence and duration of sequelae of neutropenia (i.e. fever, infection, oropharyngeal ulcers) (4,15,16) (Class I, Level of Evidence B)
   b. Dosing:
      i. Patients receiving GCSF for severe chronic neutropenia will receive a daily dose titrated to an ANC goal of 1500 cells/mm$^3$ (3,4) (Class I, Level of Evidence B)
      ii. It is appropriate to use the patient's home dose of GCSF in these situations
   c. Duration of therapy
      i. Patients will continue daily GCSF indefinitely. The dose will be titrated to maintain an ANC target of 1500 cells/mm$^3$ (3,4) (Class I, Level of Evidence B)

10. Monitoring parameters
   a. Complete blood count (CBC) with differential daily (3, 4) (Class I, Level of Evidence A)
      i. Note: if the white blood cell count is < 0.5 cells/mm$^3$, a neutrophil level will not be reported
   b. Bone Pain (3, 4) (Class I, Level of Evidence A)
      i. Patients experiencing bone pain with GCSF administration can be treated with non-steroidal anti-inflammatory drugs (NSAIDS).
   c. Toxicity
      i. Hypersensitivity reactions (3, 4) (Class I, Level of Evidence A)
         1. Generally characterized by systemic symptoms involving at least two body systems (example reactions: rash, urticaria, facial edema, wheezing, dyspnea, hypotension, and tachycardia).
         2. Reactions tend to occur within the first 30 minutes after administration
         3. Reactions can be managed in most cases with the administration of antihistamines, steroids, bronchodilators, and/or epinephrine. Symptoms are likely to recur in patients that are rechallenged.
      ii. Splenic rupture (3, 4) (Class I, Level of Evidence A)
         1. Monitor left upper abdominal pain and/or shoulder tip pain.
      iii. Acute Respiratory Distress Syndrome (ARDS) (3, 4) (Class I, Level of Evidence A)
         1. Monitor patient temperature, respiratory status, breath sounds and chest X-ray as needed.
UW Health Implementation

Potential Benefits:
This guideline has been developed based on best evidence based recommendations. By implementing the parameters set forth in the guideline, patients will receive filgrastim appropriately and safely allowing for controlled cost of this medication.

Potential Harms:
Some patients with neutropenia may be excluded based on guideline criteria despite possible benefit from GCSF.

Implementation Plan/Tools
1. Dosing guidelines will be built into Health Link to be visible upon order entry of GCSF
2. Education will be provided to health care providers
3. Guideline is attached to GCSF medication record
4. Guideline is available on UConnect
5. Education will be provided as necessary

Disclaimer
CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.
## Appendix A

### Table 1: Summary of Recommendations

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<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Duration of Therapy</th>
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<tbody>
<tr>
<td>Febrile neutropenia prevention in cancer patients receiving myelosuppressive chemotherapy</td>
<td>- Adults ≤ 80 kg should receive GCSF 300 mcg SC daily&lt;br&gt;- Adults &gt; 80 kg should receive GCSF 480 mcg SC daily&lt;br&gt;- Pediatric patients should receive GCSF 5 mcg/kg/day IV</td>
<td>Until the ANC is 500 cells/mm³ on two consecutive days&lt;br&gt;&lt;br&gt;Exception: Pediatric patients who remain on Children’s Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol.</td>
</tr>
<tr>
<td>Febrile neutropenia treatment</td>
<td>- Adults ≤ 80 kg should receive GCSF 300 mcg SC daily&lt;br&gt;- Adults &gt; 80 kg should receive GCSF 480 mcg SC daily&lt;br&gt;- Pediatric patients should receive GCSF 5 mcg/kg/day IV</td>
<td>Until ANC is 500 cells/mm³ on two consecutive days</td>
</tr>
<tr>
<td>Mobilization</td>
<td>- Adults &lt; 60 kg should receive GCSF 300 mcg SC BID&lt;br&gt;- Adults 60-78 kg should receive GCSF 300 mcg SC in the morning and 480 mcg SC in the evening&lt;br&gt;- Adults &gt; 78 kg should receive GCSF 480 mcg SC BID&lt;br&gt;- Pediatric patients should receive GCSF 10 mcg/kg/day IV</td>
<td>Until an adequate amount of stem cells for autologous transplant have been collected</td>
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<tr>
<td>Autologous peripheral blood or bone marrow transplant</td>
<td>- Adults ≤ 80 kg should receive GCSF 300 mcg SC daily&lt;br&gt;- Adults &gt; 80 kg should receive GCSF 480 mcg SC daily&lt;br&gt;- Pediatric patients should receive GCSF 5 mcg/kg/day IV</td>
<td>Until ANC is 500 cells/mm³ on two consecutive days&lt;br&gt;&lt;br&gt;Exception: Pediatric patients who remain on Children’s Oncology Group (COG) protocols and are ON study may continue GCSF as is specified by the ANC target of the COG protocol.</td>
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<td>Allogeneic cord-blood transplants</td>
<td>- Adults ≤ 80 kg should receive GCSF 300 mcg SC daily&lt;br&gt;- Adults &gt; 80 kg should receive GCSF 480 mcg SC daily&lt;br&gt;- Pediatric patients should receive GCSF 5 mcg/kg/day IV</td>
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<tr>
<td>Solid organ transplant patients: drug-associated neutropenia</td>
<td>- Adults ≤ 80 kg should receive GCSF 300 mcg SC daily&lt;br&gt;- Adults &gt; 80 kg should receive GCSF 480 mcg SC daily&lt;br&gt;- Pediatric patients should receive GCSF 5 mcg/kg/day IV</td>
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<tr>
<td>Severe Chronic Neutropenia</td>
<td>- Dose titrated to an ANC goal of 1500 cells/mm³</td>
<td>Indefinitely</td>
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References