

## Post Transplant Neutropenia – Filgrastim (G-CSF) Protocol October 2017

### Background:

Solid organ transplant recipients commonly experience low white blood cell counts (neutropenia) post-transplant. The cause of neutropenia is usually due to bone marrow suppression effects of anti-rejection and antiviral transplant medications or infections such as cytomegalovirus (CMV) related to transplantation. Patients with very low neutrophil counts are at very high risk for severe infections which require hospital admission, antibiotics and therapy with filgrastim. The addition of filgrastim to BC Transplant's drug formulary would enable transplant clinicians the ability to treat patients with severe neutropenia as outpatients, decreasing the risk of infection and rejection, and the costs associated with inpatient admission. The management of neutropenia post-transplant involves a careful assessment of the cause(s) of neutropenia and adjustments in immunosuppressive regimens and/or anti-viral therapies if CMV is suspected as the cause of the neutropenia. The most common medication adjustment includes reduction in the anti-metabolite (mycophenolate/azathioprine) dose to allow for neutrophil count recovery. However, there are many cases where a reduction in anti-metabolite dose is not the optimal choice as it can pose an increased risk of graft rejection. Clinicians are challenged with balancing neutropenia and the risk of infection versus immunosuppression reduction and risk of graft rejection. In some clinical situations where the risk of rejection and the consequences of rejection are extreme, the use of filgrastim will allow the continuation of anti-rejection treatment.

### Evidence for filgrastim use in solid organ transplants:

Although not extensively studied, filgrastim has been used to increase neutrophil counts in solid organ transplant patients. Schmaldienst et al studied 19 renal transplant patients that experienced leukopenia in the 2 weeks to 24 months after transplantation (1). In comparison to an age-matched historical control group, patients receiving filgrastim had shorter duration of leukopenia (1.29 versus 7 days), with fewer infections; in addition, there were no episodes of rejection 2 weeks following administration. Turgeon et al retrospectively reviewed 50 renal or liver transplant patients (2). Of the 50 patients, 43 patients had a rise in the leukocyte count to greater than  $5.0 \times 10^9/L$  following filgrastim. In 81.6% of cases, filgrastim therapy allowed for recommended dosing of ganciclovir or valganciclovir for treatment of CMV-induced neutropenia. Most recently, an abstract presented by Poon et al at the American Transplant Congress 2016 demonstrated effective reversal of neutropenia in kidney transplant recipients without increasing the risk of rejection (3).

### Protocol:

The BC Transplant Drug Strategy Advisory Committee, and PHSA leadership and Finance have approved the addition of filgrastim to the BC Transplant Drug Formulary. With the support of the various organ group specialists/clinicians, BC Transplant has established the proposed protocol as outlined on page 3 (also on **page 37** of current BC Transplant Clinical Guidelines for Transplant Medications).

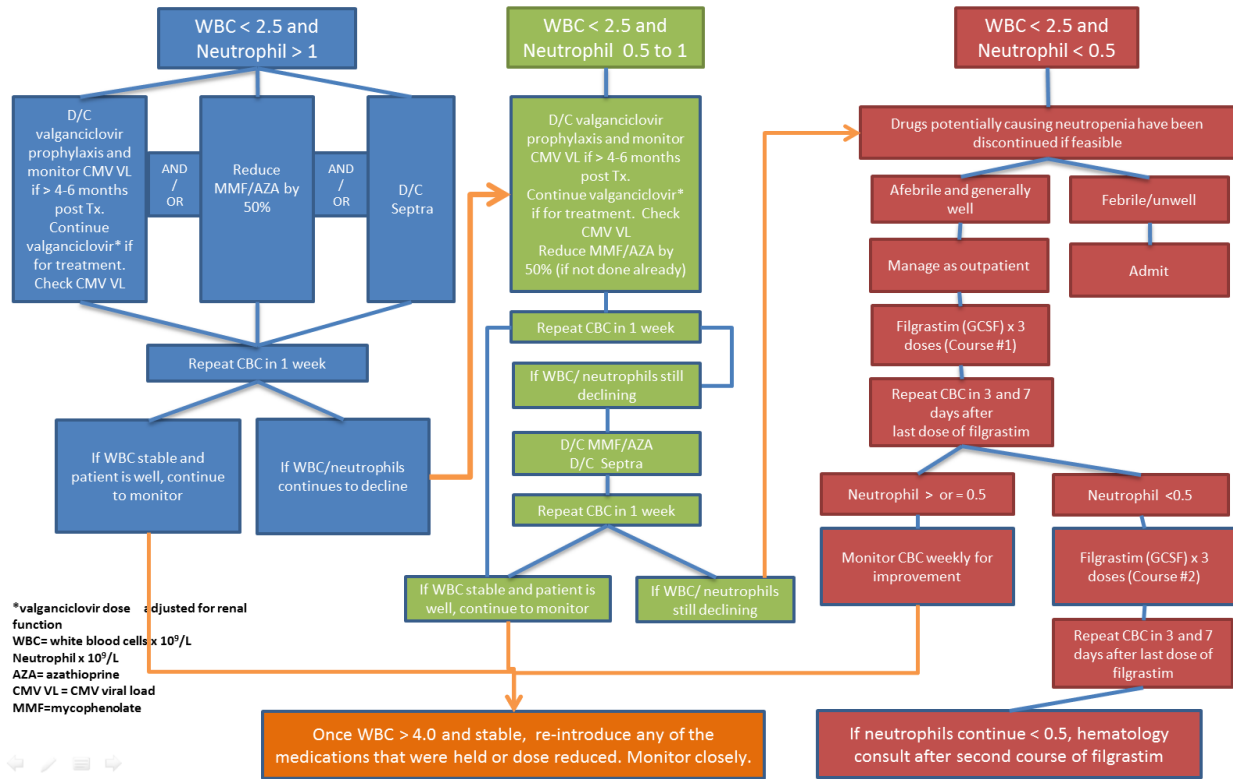
**Updated Sept 2023:** Clinicians are no longer required to complete the **data collection-prescription** form. Please fax a prescription (or use the revised form on page 4) to a BC Transplant Pharmacy Partner to dispense the filgrastim. Usage and cost data will be monitored monthly by BC Transplant. If a patient requires more than 2 courses in a 12 month period, please consult with Hematology and contact the pharmacist at BC Transplant.

## **References**

1. Schmaldienst S, Bekesi G, Deicher R, Franz M, Hörl WH, Pohanka E. Recombinant human granulocyte colony-stimulating factor after kidney transplantation: a retrospective analysis to evaluate the benefit or risk of immunostimulation. *Transplantation*. 2000 Feb 27;69(4):527-31.
2. Turgeon N, Hovingh GK, Fishman JA, Basgoz N, Tolkoff-Rubin NE, Doran M, Cosimi AB, Rubin RH. Safety and efficacy of granulocyte colony-stimulating factor in kidney and liver transplant recipients. *Transpl Infect Dis*. 2000 Mar;2(1):15-21.
3. Poon T, Guerra C. Evaluation of the Utilization of Filgrastim in Kidney Transplant Recipients. [abstract]. *Am J Transplant*. 2016; 16 (suppl 3). <http://www.atcmeetingabstracts.com/abstract/evaluation-of-the-utilization-of-filgrastim-in-kidney-transplant-recipients/>. Accessed February 7, 2017

## Management of Neutropenia Post Transplant v2.2

Post transplant neutropenia could be related to CMV, mycophenolate, azathioprine, valganciclovir\*, Septra (cotrimoxazole). The primary transplant specialists should be consulted regarding changes in immunosuppression and the re-introduction of antimetabolites, Septra when neutropenia has resolved. Decreasing or stopping anti-rejection medications in the "high risk" for rejection patient needs careful consideration.



## Filgrastim (G-CSF, Grastofil) Prescription/Worksheet (Optional – form revised Sept 2023)

1. Provider/Clinic to complete and fax to a BC Transplant contracted Pharmacy to dispense

2. Ensure patient is registered with BC Transplant and have BCT ID for coverage

Organ group:  Heart  Kidney  Liver  Lung  Pancreas/Islet Requesting clinic: \_\_\_\_\_

### Assessment:

(dd-mmm-yy)	Date:	Date:	Date:	Date:	Date
WBC: (10 <sup>9</sup> /L)					
Neutrophil: (10 <sup>9</sup> /L)					

Indication(s) for filgrastim:

- Neutrophil < 0.5  
 Febrile neutropenia  
 Other: \_\_\_\_\_

If transplant medication adjustments cannot be made, please indicate reason: \_\_\_\_\_

<b>Prescription:</b> <input type="checkbox"/> 1 <sup>st</sup> course – recommend 300 mcg dose for first course <input type="checkbox"/> 2 <sup>nd</sup> course *If neutrophils not responding after 2nd course in a 12 month period, please consult BCT and hematology *For pediatric patients at BC Children's – please supply Neupogen brand filgrastim
<input type="checkbox"/> filgrastim (Grastofil) 300 mcg SC daily X 3 days
<input type="checkbox"/> filgrastim (Grastofil) 480 mcg SC daily X 3 days

### Pharmacy:

- VGH  SPH  
 BCCH  RJH  
  
 Abb  Lang  
 Nan  
 Kam  
  
 Kel  Pen  
 PG  Trl  Sur

Prescriber signature

Print Name

College ID

Date