Granulocytes

NOT available at all Versiti sites. Contact your Hospital Relations Specialist before ordering.

How Supplied:

Granulocytes are collected from stimulated donors (G-CSF or corticosteroids depending on Versiti site) to improve the amount of granulocytes in each product. Each unit collected contains >1x10^{10} granulocytes (4 x10^{10} on average with G-CSF stimulation) with a final volume of 200-300mL. A typical course consists of 3-5 daily collections (if pediatric patient every other day may be an option).

- All requests for granulocytes are referred to a Versiti physician (at the applicable site) for consultation with the ordering provider prior to initiation of collection.

Utilization Review Guidelines:

Granulocytes can be administered for the treatment of severe neutropenia with the indications below. Documentation of the indication(s) for a transfusion episode and special circumstances for transfusion that take place outside these guidelines is recommended.

Indications:

1. Severe neutropenia (absolute neutrophil count or ANC <500/µL) with reversible marrow hypoplasia and documented bacterial or fungal infection unresponsive to appropriate antibiotic therapy[1]
2. Patients with severe neutrophil dysfunction and bacterial or fungal infection[1]

Dosing Recommendations:

- 1 unit daily or every other day is recommended until evidence of recovery indicated by:
  - Clinical resolution of infection
  - Neutrophil count >500/µL

Comments:

- Granulocyte transfusion therapy remains controversial. There is clear evidence of no harm of transfusing granulocytes to the neutropenic patient.[2-6] However, there is insufficient and conflicting evidence if granulocyte transfusion therapy affects the risk of death or number of patients who recover from an infection.[5-6] Therefore, the risks and benefits for granulocyte transfusion must be weighed on a case-by-case basis.

- Granulocytes are generally not indicated for patients in whom marrow recovery is not anticipated.

- A target dose of at least 1.5-3x10^{8} granulocytes per kg is recommended. Apheresis granulocyte containing at least 1x10^{10} is sufficient to achieve this dose in an average adult (70 kg).[7] While it is generally agreed that lower doses could be ineffective, higher doses have shown no clear

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advantage for improved infection control or reduced mortality.[8] In a retrospective study[9] of 491 granulocyte transfusions to 96 patients where the authors investigated whether the dose of granulocytes impacted infection-related mortality, patients with bacterial infections who received doses higher than $3x10^8$ cell/kg had similar poor outcomes as those patients receiving insufficient doses (<1.5 x 10^8 cells/kg).[9] In the same study, patients receiving median doses of 1.5–$3.0x10^8$ cell/kg had a reduced infection-related mortality and lower ICU admission rate in comparison with patients receiving both lower or higher doses of granulocytes.

- While CMV IgG seronegative donors are preferentially selected for collection, there may be insufficient donors to meet the request. In patients who are CMV IgG seropositive, CMV unscreened donors may be an option. The low risk of CMV transmission may need to be balanced against the risk of an inadequate supply of granulocyte products and morbidity/mortality from bacterial or fungal infection.[10]

- The safety of granulocyte transfusions in patients with HLA antibodies is unclear. In a sub analysis of patients in the RING study[11] who had HLA antibodies at baseline, there was no apparent correlation between alloimmunization and severe reactions or poorer ANC increments. Thus, the authors suggested that HLA matching is not routinely required. However, case reports of acute pulmonary reactions have been reported in granulocyte recipients with HLA alloimmunization.[12] In addition, while no increase in adverse events was seen in a small cohort of autologous peripheral blood stem cell transplant patients who had HLA antibodies and received prophylactic granulocytes, a trend toward lower absolute neutrophil count increments later in the treatment was noted.[13] Generally granulocyte transfusions can be given without regard to HLA antibody testing and subsequent matching. However, in highly sensitized recipients known to be refractory to platelet transfusions it is important to discuss the selection and availability of product with the Versiti physicians.

- **Granulocytes must be irradiated before use.**

- Granulocytes have a 24 hour shelf life but have best efficacy when transfused as soon as possible after collection.

- Granulocytes contain on average 20-60 mL of red cells and ideally should be ABO compatible. In view of this residual amount of red cells, granulocytes must be crossmatched prior to issue for administration.

- Bedside **leukoreduction filter** should ***NOT*** be used during administration; use blood administration tubing with 170-260 micron filter.

- Patients are more likely to experience a transfusion reaction with granulocyte transfusion. Premedication with diphenhydramine and acetaminophen and/or corticosteroids as well as slow infusion is suggested to mitigate adverse events.

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- Increased risk for alloimmunization to HLA antigens are to be expected after course of granulocyte transfusions and may complicate future transfusion therapies.[7,14]

References:

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14. Gea-Banacloche J. Granulocyte transfusions: a concise review for practitioners. *Cytotherapy* 2017 Nov;19(11):1256-1269.

Additional Resources:

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