ADULT AND PEDIATRIC BLOOD AND MARROW TRANSPLANT PROGRAM

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<th>APBMT-COMM-015</th>
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<tr>
<td>DOCUMENT TITLE:</td>
<td>Veno-Occlusive Disease (VOD)/Sinusoidal Obstruction Syndrome (SOS) Prophylaxis, Diagnosis and Treatment</td>
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<td>DOCUMENT NOTES:</td>
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APBMT-COMM-015
VENO-OCCULSIVE DISEASE (VOD)/SINUSOIDAL OBSTRUCTION SYNDROME (SOS) PROPHYLAXIS, DIAGNOSIS AND TREATMENT

1 PURPOSE
1.1 To provide a consistent approach to the prevention of hepatic veno-occlusive disease (VOD) / sinusoidal obstruction syndrome (SOS) in autologous and allogeneic hematopoietic stem cell transplant recipients. Guidelines for diagnosis and treatment of VOD/SOS are also reviewed.
1.2 To provide a consistent approach to the treatment of veno-occlusive disease/sinusoidal obstruction syndrome in autologous and allogeneic transplant recipients.

2 INTRODUCTION
2.1 Supportive Data:
2.1.1 Recipients of hematopoietic stem cell transplantation (HSCT) receiving myeloablative therapy are at risk of developing VOD/SOS.
2.1.2 Risk is associated with the preparative regimen, such as busulfan, prior treatment and other patient/disease-specific factors.
2.1.3 Patient’s with lower than normal levels of protein C in the 2 weeks prior to initiation of the preparative regimen are also at increased risk.

3 SCOPE AND RESPONSIBILITIES
3.1 The Adult and Pediatric Blood and Marrow Transplant (APBMT) medical team will provide medical management of the patient.
3.2 The nursing staff will provide supportive care and administer any treatment ordered by the medical team.

4 DEFINITIONS/ACRONYMS
4.1 ANC Absolute Neutrophil Count
4.2 APBMT Adult and Pediatric Blood and Marrow Transplant
4.3 HSCT Hematopoietic Stem Cell Transplantation
4.4 SOS Sinusoidal Obstruction Syndrome
4.5 VOD Veno-occlusive Disease

5 MATERIALS
5.1 NA
6  EQUIPMENT
6.1  NA

7  SAFETY
7.1  NA

8  PROCEDURE
8.1  Adult Program:
  8.1.1  Patients will begin taking Ursodiol 300 mg PO BID or 300 mg PO TID if weight is greater than (>) 90 kg beginning with the conditioning regimen or up to 3 weeks prior to starting the conditioning regimen.
  8.1.2  Ursodiol will continue through day +30 for autologous patients and day +90 for allogeneic patients.
  8.1.3  Patients receiving melphalan alone will not receive VOD/SOS prophylaxis unless otherwise directed.
  8.1.4  Alternative regimen: Heparin 100 units/kg/day will be administered as a continuous infusion beginning prior to initiation of the preparative regimen and continuing until 28 days or the time of engraftment defined as absolute neutrophil count (ANC) greater than or equal to 500 cells/mm³; monitoring of the aPTT is not required; patients should be monitored for signs and symptoms of bleeding.

8.2  Pediatric Program:
  8.2.1  Ursodiol 10 mg/kg by mouth three times a day (maximum dose: 300 mg by mouth 3 times a day).
  8.2.2  Alternative regimen: Heparin 100 units/kg/day will be administered as a continuous infusion beginning prior to initiation of the preparative regimen and continuing until 28 days or the time of engraftment defined as ANC greater than or equal to 500 cells/mm³; monitoring of the aPTT is not required; patients should be monitored for signs and symptoms of bleeding.
    8.2.2.1  Heparin therapy in infants weighing less than (<) 10kg may be reduced to 10 units/kg/hour.

8.3  Signs or symptoms of VOD/SOS:
  8.3.1  Weight gain (greater than 5% of initial body weight)
  8.3.2  Right upper quadrant pain
  8.3.3  Hyperbilirubinemia
  8.3.4  Ascites
  8.3.5  Coagulopathy (low ATIII, low factor VII)
  8.3.6  Reversal of flow on hepatic doppler ultrasound
8.3.7 Renal insufficiency

8.4 Treatment of VOD/SOS:
8.4.1 Defibrotide
8.4.2 Fluid restriction
8.4.3 Diuretics such as furosemide or spironolactone
8.4.4 ATIII
8.4.5 Plasmapheresis
8.4.6 Intrahepatic shunting
8.4.7 Draining of ascites if they cause respiratory compromise
8.4.8 Factor VII replacement therapy
8.4.9 Ursodiol

8.5 Reportable conditions:
8.5.1 Intolerance or allergy to prophylactic regimen; active bleeding.

8.6 Veno-occlusive Disease/Sinusoidal Obstruction Syndrome Treatment:
8.6.1 Maintain fluid balance by using aggressive diuretic therapy (e.g. furosemide and/or spironolactone to keep intake/output even and weight stable).
8.6.2 Initiate additional supportive measures as clinically indicated (e.g. FFP, Factor VII concentrate, ATIII concentrate, draining of ascites, ursodiol).
8.6.3 Additional therapeutic intervention is at the discretion of the attending physician.
8.6.4 If VOD/SOS is suspected, defibrotide should be strongly considered.

9 RELATED DOCUMENTS/FORMS
9.1 NA

10 REFERENCES
11 REVISION HISTORY

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<th>Description of Change(s)</th>
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| 05           | S. McCollum | - Low dose heparin changed to “alternative regimen” instead of 1st line treatment.  
- Ursodiol move to first line treatment.  
- Defibrotide updated to no longer be an investigational therapy.  
- The following sentence added to section 8.6: If VOD/SOS is suspected, defibrotide should be strongly considered. |
# Signature Manifest

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All dates and times are in Eastern Time.

## APBMT-COMM-015 Veno-Occlusive Disease, Sinusoidal Obstruction Syndrome, Prophylaxis, Diagnosis

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### Management

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