Algorithm for the Management of Bleeding in Hemophilia

**Hemophilia A with History of Inhibitor**

- **Mild hemorrhage***
  - Inhibitor titer BU>5
    - Switch to factor VIIa or FEIBA
  - Inhibitor titer BU<5
    - Continue factor VIII
  - Factor VIII ≥ target*
    - Continue to monitor factor VIII
  - Factor VIII < target*
    - Adjust dose or consider factor VIIa or FEIBA

- **Severe or life/limb threatening hemorrhage***
  - Initiate factor VIIa or FEIBA
  - Undetectable Inhibitor
    - Switch to factor VIII
  - Detectable inhibitor
    - Continue factor VIIa or FEIBA
  - Factor VIII ≥ target*
    - Adjust dose or consider factor VIIa or FEIBA
  - Factor VIII < target*
    - Continue to monitor factor VIII

- **Elective Surgery**
  - Wait for inhibitor results to initiate therapy
  - Undetectable inhibitor
    - Initiate Factor VIII
  - Detectable inhibitor
    - Initiate Factor VIIa or FEIBA

*^Initial laboratory tests include aPTT, factor VIII activity, and factor VIII inhibitor titer
*See Table 1 to determine severity of bleed, appropriate factor VIII target levels, and Table 2 for suggested dosages
Hemophilia A without History of Inhibitor

Consult hematology
Contact pathology
Contact pharmacy for factor product availability 8-8416
Order baseline laboratory tests^*  

Mild hemorrhage*
Initiate factor VIII and/or vasopressin and/or AMICAR

Factor VIII ≥ target*
Continue to monitor factor VIII

Factor VIII < target*
Adjust dose and/or consider obtaining factor VIII inhibitor level

Severe or life/limb threatening hemorrhage*
Initiate factor VIII  

Factor VIII ≥ target*
Continue to monitor factor VIII

Factor VIII < target*
Adjust dose and/or consider obtaining factor VIII inhibitor level

Elective Surgery
Initiate factor VIII  

Factor VIII < target*
Adjust dose and/or consider obtaining factor VIII inhibitor level

^Initial laboratory tests include aPTT, factor VIII activity, and aPTT mixing studies
*See Table 1 to determine severity of bleed, appropriate factor VIII target levels, and Table 2 for suggested dosages
Hemophilia B with History of Inhibitor

Consult hematology
Contact pathology
Contact pharmacy for factor product availability 8-8416
Order baseline laboratory tests^*

Mild hemorrhage*
Initiate factor IX

- Inhibitor titer BU>5
  - Switch to factor VIIa or FEIBA

- Factor IX ≥ target*
  - Continue to monitor factor IX q 1hr x 8-12hrs

- Factor IX < target*
  - Adjust dose or consider factor VIIa or FEIBA

Severe or life/limb threatening hemorrhage*
Initiate factor VIIa or FEIBA

- Undetectable Inhibitor
  - Switch to factor IX

  - Factor IX ≥ target*
    - Continue to monitor factor IX
  
  - Factor IX < target*
    - Adjust dose or consider factor VIIa or FEIBA

- Detectable inhibitor
  - Continue factor VIIa or FEIBA

  - Factor IX ≥ target*
    - Continue to monitor factor IX
  
  - Factor IX < target*
    - Adjust dose or consider factor VIIa or FEIBA

Elective Surgery
Wait for inhibitor results to initiate therapy

- Undetectable inhibitor
  - Initiate Factor IX

- Detectable inhibitor
  - Initiate Factor VIIa or FEIBA

^Initial laboratory tests include aPTT, factor IX activity, and factor IX inhibitor titer
*See Table 1 to determine severity of bleed, appropriate factor IX target levels, and Table 2 for suggested dosages
Hemophilia B without History of Inhibitor

Consult hematology
Contact pathology
Contact pharmacy for factor product availability 8-8416
Order baseline laboratory tests^ (Initial laboratory tests include aPTT, factor VIII activity, and aPTT mixing studies)

Mild hemorrhage*
  Initiate factor IX

  Factor IX ≥ target*
    Continue to monitor factor IX

  Factor IX < target*
    Adjust dose and/or consider obtaining factor IX inhibitor level

Severe or life/limb threatening hemorrhage*
  Initiate factor IX

  Factor IX ≥ target*
    Continue to monitor factor IX

  Factor IX < target*
    Adjust dose and/or consider obtaining factor IX inhibitor level

Elective Surgery
  Initiate factor IX

  Factor IX ≥ target*
    Continue to monitor factor IX

  Factor IX < target*
    Adjust dose and/or consider obtaining factor IX inhibitor level

*See Table 1 to determine severity of bleed, appropriate factor VIII target levels, and Table 2 for suggested dosages
Table 1: Target Factor Level and Duration of Administration

<table>
<thead>
<tr>
<th>Hemorrhage Type</th>
<th>Hemophilia A</th>
<th>Hemophilia B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Desired Level</td>
<td>Duration (days)</td>
</tr>
<tr>
<td><strong>Joint</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemophilia A</td>
<td>40-60%</td>
<td>1-2; sometimes longer if response is inadequate</td>
</tr>
<tr>
<td>Hemophilia B</td>
<td>40-60%</td>
<td>1-2; sometimes longer if response is inadequate</td>
</tr>
<tr>
<td><strong>Muscle (except iliopsoas)</strong></td>
<td>40-60%</td>
<td>2-3; sometimes longer if response is inadequate</td>
</tr>
<tr>
<td><strong>Iliopsoas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Initial</td>
<td>80-100%</td>
<td>1-2</td>
</tr>
<tr>
<td>-Maintenance</td>
<td>30-60%</td>
<td>3-5 (sometimes longer as secondary prophylaxis during physiotherapy)</td>
</tr>
<tr>
<td><strong>CNS/Head</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Initial</td>
<td>80-100%</td>
<td>1-7</td>
</tr>
<tr>
<td>-Maintenance</td>
<td>50%</td>
<td>8-21</td>
</tr>
<tr>
<td><strong>Throat and neck</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Initial</td>
<td>80-100%</td>
<td>1-7</td>
</tr>
<tr>
<td>-Maintenance</td>
<td>50%</td>
<td>8-14</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Initial</td>
<td>80-100%</td>
<td>1-6</td>
</tr>
<tr>
<td>-Maintenance</td>
<td>50%</td>
<td>7-14</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td>50%</td>
<td>3-5</td>
</tr>
<tr>
<td><strong>Deep laceration</strong></td>
<td>50%</td>
<td>5-7</td>
</tr>
<tr>
<td><strong>Surgery (major)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Pre-op</td>
<td>80-100%</td>
<td>1-3</td>
</tr>
<tr>
<td>-Post-op</td>
<td>60-80%</td>
<td>4-6</td>
</tr>
<tr>
<td></td>
<td>40-60%</td>
<td>7-14</td>
</tr>
<tr>
<td></td>
<td>30-50%</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from: Guidelines for the Management of Hemophilia. World Federation of Hemophilia 2005
### Table 2: Product Information

<table>
<thead>
<tr>
<th>Product</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vasopressin (DDAVP)</strong></td>
<td>IV: 0.3mcg/kg diluted in 50-100 mL NS infused over 20-30 minutes</td>
<td>-Boosts plasma levels of FVIII by 3-6 fold</td>
</tr>
<tr>
<td></td>
<td>-Peak response is seen 90 minutes after infusion</td>
<td>-Does not effect FIX levels, so not effective in hemophilia B</td>
</tr>
<tr>
<td><strong>Aminocaproic Acid (AMICAR)</strong></td>
<td>5g in 250mL NS infused over 1 hours followed by 1g every hour x 8 hrs or until bleeding stops</td>
<td>-Should not be used in combination with FIX products</td>
</tr>
<tr>
<td><strong>Factor VIII</strong></td>
<td><strong>Factor VIII Dose (int. units) = weight (kg) x (desired factor % increase) x (0.5 int. unit/kg)</strong></td>
<td>-See table 1 for desired factor activity %</td>
</tr>
<tr>
<td></td>
<td>-Administer IV over 5-10 minutes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-May repeat dose every 6-24 hours according to bleed severity and continued factor activity monitoring</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Administration by continuous infusion has been studied</td>
<td></td>
</tr>
<tr>
<td><strong>Factor IX</strong></td>
<td><strong>Factor IX Dose (int. units) = weight (kg) x (desired factor % increase) x (1 int. unit/kg)</strong></td>
<td>-See table 1 for desired factor activity %</td>
</tr>
<tr>
<td></td>
<td>-Administer IV at rate not to exceed 10 mL/minute</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-May repeat dose every 12-24 hours according to continued factor activity monitoring</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Administration by continuous infusion has been studied</td>
<td></td>
</tr>
<tr>
<td><strong>Factor VIIa</strong></td>
<td>90mcg/kg IV every 2-3 hours. Successful control of bleeding has been reported using doses that range between 35-120 mcg/kg.</td>
<td>-Bypassing agent</td>
</tr>
<tr>
<td></td>
<td>-Treatment can be tapered by increasing the time interval between doses</td>
<td>-Reserved for patients with inhibitors to factors VIII or IX</td>
</tr>
<tr>
<td></td>
<td>-Administration by continuous infusion has been studied</td>
<td></td>
</tr>
<tr>
<td><strong>FEIBA</strong></td>
<td><strong>Joint or mucous membrane bleed:</strong> Initial 50 units/kg every 6-12 hrs (May increase to 100 units/kg if hemorrhage does not stop)**</td>
<td>-Bypassing agent</td>
</tr>
<tr>
<td></td>
<td><strong>Soft Tissue Hemorrhage:</strong> 100 units/kg every 12 hrs</td>
<td>-Reserved for patients with inhibitors to factors VIII or IX</td>
</tr>
<tr>
<td></td>
<td><strong>Other Severe Hemorrhage:</strong> 100 units/kg every 6-12 hours</td>
<td>-Made from human plasma</td>
</tr>
<tr>
<td></td>
<td>Due to the risk of thromboembolic events, single doses &gt; 100 units/kg and daily dose of &gt; 200 units/kg should not be exceeded unless absolutely necessary to stop bleeding.</td>
<td></td>
</tr>
</tbody>
</table>
References


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