### Retrospective Drug Use Criteria

**Parenteral Enzyme or Protein Replacement Therapy**

- **Publication History**
  - Revised April 2015; March 2015; February 2013.
  - Developed December 2012.

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Note: Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. HHSC is not responsible for any errors in transmission or any errors or omissions in the document.
1. Dosage [*]

Enzyme replacement therapy is Food and Drug Administration (FDA)-approved for conditions characterized by enzyme deficiencies such as adenosine deaminase (ADA) deficiency in severe combined immunodeficiency (SCID) patients (pegademase bovine), Fabry disease (agalsidase beta), Gaucher disease (imiglucerase, taliglucerase alfa, velaglucerase alfa), hereditary angioedema (HAE) (C1 esterase inhibitor), mucopolysaccharidoses (MPS) [Maroteaux-Lamy syndrome (MPS VI) - galsulfase; Hunter syndrome (MPS II) – idursulfase; Hurler and Hurler-Scheie forms of MPS 1 – laronidase; Morquio A syndrome (MPS IVA) - elosulfase], Pompe disease (alglucosidase alfa) and severe congenital protein C deficiency (protein C concentrate).1-28

1.1. Adults

Recommended doses for enzyme replacement therapy FDA-approved for use in adults are summarized in Table 1. Patient profiles containing doses exceeding maximum recommendations will be reviewed.

Table 1 - Adult Parenteral Protein/Enzyme Replacement Therapy Maximum Dosages1-10,12-18

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Adult Maximum Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Replacement Enzyme</strong></td>
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<tr>
<td>Agalsidase beta (Fabrazyme®)</td>
<td>Fabry disease: 1 mg/kg by intravenous (IV) infusion every 2 weeks</td>
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<tr>
<td>Alglucosidase alfa (Lumizyme®, Myozyme®)</td>
<td>Late-onset (non-infantile) Pompe disease (Lumizyme®): 20 mg/kg as an IV infusion every 2 weeks</td>
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<tr>
<td></td>
<td>Infantile-onset Pompe disease (Myozyme®): 20 mg/kg as IV infusion every 2 weeks</td>
</tr>
<tr>
<td>C1 esterase inhibitor, human (Berinert®, Cinryze®)</td>
<td>HAE treatment (Berinert®): 20 IU/kg by IV injection as a single dose</td>
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<tr>
<td></td>
<td>Routine prevention of HAE attacks (Cinryze®): 1000 U by IV infusion every 3-4 days</td>
</tr>
<tr>
<td>C1 esterase inhibitor, recombinant (Ruconest®)</td>
<td>HAE treatment:</td>
</tr>
<tr>
<td></td>
<td>• &lt; 84 kg: 50 units/kg as single IV dose; may repeat x1 if attack symptoms persist</td>
</tr>
<tr>
<td></td>
<td>• ≥ 84 kg: 4200 units as a single IV dose; may repeat x1 if attack symptoms persist</td>
</tr>
<tr>
<td>Elosulfase (Vimizim®)</td>
<td>Morquio A syndrome: 2 mg/kg by IV infusion over a minimum of 3.5 to 4.5 hours once weekly</td>
</tr>
<tr>
<td>Galsulfase (Naglazyme®)</td>
<td>Maroteaux-Lamy syndrome: 1 mg/kg by IV infusion once weekly</td>
</tr>
<tr>
<td>Idursulfase (Elaprase®)</td>
<td>Hunter syndrome: 0.5 mg/kg as IV infusion once weekly</td>
</tr>
<tr>
<td>Imiglucerase (Cerezyme®)</td>
<td>Gaucher disease, type 1: 60 U/kg by IV infusion over 1-2 hours every 2 weeks</td>
</tr>
<tr>
<td>Laronidase (Aldurazyme®)</td>
<td>MPS 1 (Hurler and Hurler-Scheie forms): 0.58 mg/kg by IV infusion once weekly</td>
</tr>
<tr>
<td>Taliglucerase alfa (Elelyso™)</td>
<td>Gaucher disease, type 1: 60 U/kg by IV infusion once every other week</td>
</tr>
<tr>
<td>Velaglucerase alfa (Vpriv®)</td>
<td>Gaucher disease, type 1: 60 U/kg as an IV infusion every other week</td>
</tr>
</tbody>
</table>

**Replacement Protein**
Parenteral Enzyme or Protein Replacement Therapy

### Retrospective Drug Use Criteria

**Parenteral Enzyme or Protein Replacement Therapy**

**Drug Name** | **Adult Maximum Recommended Dosage**
---|---
Protein C concentrate (Ceprotin®) | - Protein C deficiency (acute episode*): 100-120 IU/kg initial dose by IV infusion, followed by 60-80 IU/kg every 6 hours for 3 doses by IV infusion
- Protein C deficiency (short-term prophylaxis/maintenance dose*): 45-60 IU/kg every 6 to 12 hours by IV infusion
- Protein C deficiency (long-term prophylaxis*): 45-60 IU/kg every 12 hours by IV infusion

**Table notes:**
- * Maximum protein C concentrate infusion rate: 2 ml/min

#### 1.2. Pediatrics

Pegademase bovine is FDA-approved for use in neonates, infants and children with ADA deficiency due to severe combined immunodeficiency who have failed or are not candidates for bone marrow transplantation; pegademase bovine safety and efficacy have not been established in adults. C1 esterase inhibitor safety and efficacy have not been determined in pediatric patients younger than 13 years of age. Maximum recommended dosages for protein/enzyme replacement therapies FDA-approved for use in pediatric patients are summarized in Table 2. Dosages exceeding these recommendations will be reviewed.

**Table 2 - Pediatric Parenteral Maximum Dosages for Protein/Enzyme Replacement Therapy**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Pediatric Maximum Recommended Dosage</th>
</tr>
</thead>
</table>
| Agalsidase beta | Fabry disease:  
- 8-16 years of age: 1 mg/kg by intravenous (IV) infusion every 2 weeks |
| Alglucosidase alfa | infantile-onset Pompe disease (Myozyme®):  
- 1 month of age and older: 20 mg/kg as IV infusion every 2 weeks  
Late-onset (non-infantile) Pompe disease(Lumizyme®):  
- 8 years of age and older: 20 mg/kg as an IV infusion every 2 weeks |
| C1 esterase inhibitor, human | HAE treatment – acute abdominal, laryngeal, facial attacks (Berinert®):  
- adolescents (13-17 years of age): 20 IU/kg by IV injection as a single dose  
Routine prevention of HAE attacks (Cinryze®):  
- adolescents (13-17 years of age): 1000 U by IV infusion every 3-4 days |
| C1 esterase inhibitor, recombinant | HAE treatment – acute attacks (not laryngeal) (Ruconest®):  
- Adolescents (13-17 years of age):  
  - < 84 kg: 50 units/kg as a single IV dose; may repeat x1 if attack symptoms persist  
  - ≥ 84 kg: 4200 units as a single IV dose; may repeat x1 if attack symptoms persist |
| Elosulfase | Morquio A syndrome:  
- 5 years of age and older: 2 mg/kg by IV infusion over a minimum of 3.5-4.5 hours once weekly |
| Galsulfase | Maroteaux-Lamy syndrome:  
- 5 years of age and older*: 1 mg/kg by IV infusion once weekly |
| Idursulfase | Hunter syndrome:  
- 5 years of age and older: 0.5 mg/kg as IV infusion once weekly |
| Imiglucerase | Gaucher disease, type 1:  
- 2 years to 16 years of age: 60 U/kg by IV infusion over 1-2 hours every 2 weeks |
Parenteral Enzyme or Protein Replacement Therapy

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Pediatric Maximum Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laronidase</td>
<td>MPS 1 (Hurler and Hurler-Scheie forms):</td>
</tr>
<tr>
<td></td>
<td>• 6 months of age and older: 0.58 mg/kg by IV infusion once weekly</td>
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<tr>
<td>Pegademase bovine (Adagen®)</td>
<td>ADA deficiency in SCID:</td>
</tr>
<tr>
<td></td>
<td>• Birth to any age: 30 U/kg intramuscularly once weekly</td>
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<tr>
<td>Taliglucerase alfa</td>
<td>Gaucher disease, type I:</td>
</tr>
<tr>
<td></td>
<td>• 4 years of age and older: 60 U/kg by IV infusion once every other week</td>
</tr>
<tr>
<td>Velaglucerase alfa</td>
<td>Gaucher disease, type I:</td>
</tr>
<tr>
<td></td>
<td>• 4-17 years of age: 60 U/kg as an IV infusion every other week</td>
</tr>
</tbody>
</table>

Replacement Protein

| Protein C concentrate                    | Protein C deficiency (acute episode*):                                                                 |
|                                          | • Birth to any age: 100-120 IU/kg initial dose by IV infusion, followed by 60-80 IU/kg every 6 hours for 3 doses by IV infusion* |
|                                          | Protein C deficiency (short-term prophylaxis/maintenance dose*):                                       |
|                                          | • Birth to any age: 45-60 IU/kg every 6 to 12 hours by IV infusion                                     |
|                                          | Protein C deficiency (long-term prophylaxis*):                                                        |
|                                          | • Birth to any age: 45-60 IU/kg every 12 hours by IV infusion                                          |

Table notes:
- + Open-label studies showed safe use of galsulfase in 4 infants 3 months to 12.7 months of age
- * Maximum protein C concentrate infusion rate: 2 ml/min, except in children < 10 kg, where infusion rate should not exceed 0.2 ml/kg/min

Although not FDA-approved, some investigators have studied agalsidase use in children younger than 8 years of age to reduce or prevent complications associated with Fabry disease (e.g., kidney complications, cardiovascular disease, cerebrovascular dysfunction). Studies have included patients ranging in age from 2.5 to 8 years of age for boys and 4.4 to 8 years of age for girls. Results, based on small patient numbers, have shown improvements in disease manifestations, pain and quality of life without significant adverse effects in younger children. Further, long-term trials are necessary to confirm these results.26, 27

Although not FDA-approved, alglucosidase alfa has been evaluated for early use to treat Pompe disease. In a small study, investigators found that alglucosidase therapy initiated early after diagnosis in neonates < 1 month of age can improve clinical outcomes even before onset of clinical symptoms in infants with Pompe disease. Further, long-term trials are needed to corroborate these findings.28

2. Duration of Therapy

There is no basis for limiting the duration of enzyme replacement therapy as enzyme deficiencies represent chronic disorders and require sustained treatment.

3. Duplicative Therapy [*]

FDA-approved enzyme replacement therapies are indicated for specific enzyme deficiencies. Patients with multiple enzyme deficiencies may be prescribed multiple enzyme replacement therapies concurrently. Adjunctive administration of enzyme replacement therapies without multiple enzyme deficiency diagnoses is not clinically reasonable and will be evaluated.
4. References

20. Darras BT, Craigen WJ. Lysosomal acid maltase deficiency (glycogen storage disease II, Pompe disease). In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on March 10th, 2015.)