TREATMENTS FOR GAUCHER DISEASE

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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TREATMENTS FOR GAUCHER DISEASE (cont.)

**Description:**

Gaucher’s disease is an inherited lysosomal storage disorder that results from the inability to produce the enzyme beta-glucocerebrosidase (also known as acid beta-glucosidase). The enzyme catalyzes the conversion of the glycosphingolipid glucocerebroside (also known as glucosylceramide, a glycolipid) into glucose and ceramide. Deficiency of the enzyme results in the accumulation of glucosylceramide in lysosomes of macrophages giving rise to foam cells (Gaucher cells) in the spleen, liver, kidneys, lungs, brain, bone marrow, and other organs.

Gaucher disease has three common clinical subtypes. Type 1 (non-neuropathic Gaucher disease) is the most common form of the disease. Type 2 (acute infantile neuropathic Gaucher disease) typically begins within 6 months of age. Type 3 (chronic neuropathic Gaucher disease) can begin at any time in childhood or even in adulthood; this type has three subtypes. Treatment may consist of enzyme replacement therapy (ERT) or substrate replacement therapy (SRT).

There are three recombinant glucocerebrosidases used as drugs for ERT: Cerezyme (imiglucerase) Elelyso (Taliglucerase alfa) or VPRIV (velaglucerase). All three are based on the human gene sequence for the native enzyme but are differentiated from each other according to the cell type used in production.

Cerezyme (imiglucerase) is an analogue of the human enzyme B-glucocerebrosidase, produced by recombinant DNA technology. Cerezyme is indicated for long-term enzyme replacement therapy for pediatric and adult individuals with a confirmed diagnosis of Type 1 Gaucher disease.

Elelyso (taliglucerase alfa) is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for the treatment of individuals with a confirmed diagnosis of Type 1 Gaucher disease.

Vpriv (velaglucerase alfa) is a hydrolytic lysosomal glucocerebroside-specific enzyme indicated for long-term enzyme replacement therapy (ERT) for individuals with type 1 Gaucher disease.
TREATMENTS FOR GAUCHER DISEASE (cont.)

Criteria:

See Resources section for FDA-approved dosage.

- FDA-approved dosage of Cerezyme for the treatment of long-term enzyme replacement therapy in Type 1 Gaucher disease for individuals 2 years of age and older is considered **medically necessary** with documentation of **ANY** of the following:
  1. Anemia
  2. Bone disease
  3. Hepatomegaly or splenomegaly
  4. Thrombocytopenia

- Cerezyme for all other indications not previously listed or if above criteria not met is considered **experimental or investigational** based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, but are not limited to:

- Combination SRT and ERT
- Gaucher disease type 2 and type 3
TREATMENTS FOR GAUCHER DISEASE (cont.)

Criteria: (cont.)

- FDA-approved dosage of Elelyso for individuals 4 years of age and older is considered *medically necessary* with documentation of a confirmed diagnosis of Type 1 Gaucher disease.

- Elelyso for all other indications not previously listed is considered *experimental or investigational* based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to*:

- Combination SRT and ERT
- Gaucher disease type 2 and type 3

- FDA-approved dosage of Vpriv for individuals 4 years of age and older is considered *medically necessary* for long-term enzyme replacement therapy with documentation of a confirmed diagnosis of Type 1 Gaucher disease.

- Vpriv for all other indications not previously listed is considered *experimental or investigational* based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to*:

- Combination SRT and ERT
- Gaucher disease type 2 and type 3
TREATMENTS FOR GAUCHER DISEASE (cont.)

Resources:

Literature reviewed 10/25/16. We do not include marketing materials, poster boards and non-published literature in our review.

Cerezyme Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term enzyme replacement therapy for individuals 4 years of age and</td>
<td>For intravenous use only. Infusion over 1-2 hrs. There is no well-established maximum dose for the approved indication. Dosage should be individualized to each individual.</td>
</tr>
<tr>
<td>older with Type 1 Gaucher disease that results in 1 or more of the</td>
<td>Adult: Initial dose 2.5U/kg 3 times weekly, up to 60 units/kg every 2 weeks. Dosage adjustments are made based on assessment and therapeutic goals.</td>
</tr>
<tr>
<td>following conditions: anemia, bone disease, hepatomegaly or splenomegaly,</td>
<td>Pediatric: 30 to 60 units/kg/dose every 2 weeks based on risk for complications. Failure to respond to treatment within 6 months may indicate the need for a higher dose.</td>
</tr>
<tr>
<td>and thrombocytopenia</td>
<td></td>
</tr>
</tbody>
</table>

Eleyso Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>For the treatment of individuals 4 years and older with a confirmed</td>
<td>For long term treatment 60 units/kg of body weight administered every other week as a 1-2 hr. intravenous infusion.</td>
</tr>
<tr>
<td>diagnosis of Type 1 Gaucher disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For individuals switching from imiglucerase, begin treatment at the same unit/kg dose as the individual’s previous imiglucerase dose.</td>
</tr>
<tr>
<td></td>
<td>Dosage adjustments can be based on achievement and maintenance of each individual’s therapeutic goals.</td>
</tr>
</tbody>
</table>
**TREATMENTS FOR GAUCHER DISEASE** (cont.)

**Resources:** (cont.)

Vpriv Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
</table>
| For the treatment of individuals 4 years and older with a confirmed diagnosis of Type 1 Gaucher disease | For long term treatment 60 units/kg of body weight administered every other week as a 1hr. intravenous infusion.  
For individuals switching from imiglucerase, begin treatment at the same unit/kg dose as the individual’s previous imiglucerase dose.  
Dosage adjustments can be based on achievement and maintenance of each individual’s therapeutic goals. |
TREATMENTS FOR GAUCHER DISEASE (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ’s Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe’é atah niilíngií Blue Cross Blue Shield of Arizona haada yít’éego bíná’idilkidgo éí doodago Háida bijá aniyeedííjí t’áadoo le’é yina’idilkidgo bee hazaaz’áaní hólo díí t’áá hazaadke’éhi’ háká a’dowolgo bee haza’ doo báásh iliingóó. Atá’ halne’ígíí kojí bichi’’ y hodíílnííí 877-475-4799.

Chinese: 如果您，或是您正在协助的对象，有关于插入项目的名称 Blue Cross Blue Shield of Arizona 方面的问题，您有权利免费以您的母语得到帮助和讯息。洽询一位翻译员，请拨打电话 在此插入数字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Đề nghị chuyển với một thống dịch viên, xin gọi 877-475-4799.

Arabic:
إن كان لديك أو لدى شخص تساعدته أسئلة بخصوص Blue Cross Blue Shield of Arizona، فللذك الحق في الحصول على المساعدة والمعلومات الضرورية بغض النظر عن دولة تكلفة. للتحدث مع مترجم يصلب 877-475-4799.
TREATMENTS FOR GAUCHER DISEASE (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ika, o ang iyong tinutuangan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuya ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makeasap ang isang tagsalog, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그러한 도움과 정보 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역사와 매기기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu’un que vous êtes en train d’aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d’obtenir de l’aide et l’information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi: اگر شما یا کسی که شما به آن کمک می‌کنید، سوال در مورد اطلاعات به زبان خود را به مرور رایگان در 877-475-4799 دریافت نمایید.

Assyrian: Blue Cross Blue Shield of Arizona ئاسمە، ئاشەکەیەکانی ئەوە کە شییەکەیەکانی ئەکەکانی ئەوە کە نەکاتبەکەیەکانی ئەمەکەیەکانی نەکاتبەکەیەکانی 877-475-4799.


Thai: หากคุณ หรือคนที่คุณช่วยเหลือมีคำถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณมีสิทธิได้รับความช่วยเหลือและข้อมูลภาษาอื่น ๆ ของคุณได้โดยไม่เสียเงิน ติดต่อที่หมายเลขโทรศัพท์ 877-475-4799.