SOMATULINE® DEPOT (lanreotide acetate)

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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SOMATULINE DEPOT (lanreotide acetate) (cont.)

Description:

Somatuline Depot (lanreotide acetate is indicated for 1) the long-term treatment of individuals with acromegaly who have had an inadequate response to surgery and/or radiotherapy or for whom surgery and/or radiotherapy is not an option; 2) the treatment of individuals with unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival; and 3) the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

Somatuline Depot is a synthetic cyclical octapeptide analog of the natural hormone somatostatin. The mechanism of action of lanreotide is believed to be similar to that of natural somatostatin. Like somatostatin, lanreotide acetate is an inhibitor of various endocrine, neuroendocrine, exocrine, and paracrine functions.

In acromegaly, lanreotide acetate reduces insulin growth factor-1 (IGF-1) and growth hormone (GH) levels. After a single injection, plasma GH levels fall rapidly and are maintained for at least 28 days. The goal of treatment in acromegaly is to reduce IGF-1 to within the normal range and reduce GH levels to less than 1 mcg/L (or 1 mg/dL).

Definitions:

Adult: Age 18 years and older

Acromegaly:
Acromegaly is a disease characterized by excessive release of growth hormone (GH). Increased levels of GH stimulate an increase in hepatic production of insulin-like growth factor-1 (IGF-1). Excess IGF-1 causes increased growth of bones and soft-tissues while excess GH can cause other conditions such as diabetes mellitus and hypertension which can increase cardiovascular risk.

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs):
GEP-NETs are cancers that come from endocrine cells that are found anywhere along the gastrointestinal tract and include a diverse group of neoplasms that have the ability to produce, store and secrete a large number of hormones and other biologic compounds that can lead to the development of distinct clinical syndromes. Based on hormone type, they are grouped as follows: carcinoid, gastrinoma, insulinoma, glucagonoma, and VIPoma.

Carcinoid syndrome:
Carcinoid syndrome are tumors of the gastrointestinal tract that produce and secrete certain hormones into the blood stream causing a variety of symptoms. Symptoms include facial flushing, diarrhea, abdominal pain, asthma, rash, heart disease, and intestinal bleeding.
SOMATULINE DEPOT (lanreotide acetate) (cont.)

Criteria:

See Resources section for FDA-approved dosage.

- Somatuline Depot is considered medically necessary for adults with documentation of no previous hypersensitivity reaction to lanreotide and ANY of the following:
  
  1. For the long-term treatment of individuals with acromegaly who have had an inadequate response to surgery and/or radiotherapy or for whom surgery and/or radiotherapy is not an option
  2. For the treatment of individuals with unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival
  3. For the treatment of individuals with carcinoid syndrome

- Continuation of Somatuline Depot is considered medically necessary for adults with documentation of ANY of the following:
  
  1. For the treatment of individuals with acromegaly with documentation of ALL of the following:
      - The age- and gender-adjusted IGF-1 level using the same assay and same laboratory has decreased or is within the normal range
      - The GH level has decreased or is within the normal range
      - There are no unacceptable drug toxicities while on therapy
  2. For the treatment of individuals with GEP-NETs with documentation of ALL of the following:
      - There has been no disease progression while on therapy
      - There are no unacceptable drug toxicities while on therapy
  3. For the treatment of individuals with carcinoid syndrome with documentation of ALL of the following:
      - There has been a reduction in the severity and frequency of flushing and/or diarrhea
      - There is a reduced need for short-acting somatostatin rescue therapy
      - There are no unacceptable drug toxicities while on therapy
SOMATULINE DEPOT (lanreotide acetate) (cont.)

Criteria: (cont.)

- Somatuline Depot 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:

- Treatment with dosing or frequency outside the FDA-approved dosing and frequency
SOMATULINE DEPOT (lanreotide acetate) (cont.)

Resources:

Literature reviewed 02/20/18. We do not include marketing materials, poster boards and non-published literature in our review.

Somatuline Depot Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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| Acromegaly                        | Dose range is 60 mg to 120 mg every 4 weeks. Recommended starting dose is 90 mg every 4 weeks for 3 months. Adjust thereafter based on GH and/or IGF-1 levels. Moderate and Severe Renal and Hepatic Impairment: Initial dose is 60 mg every 4 weeks for 3 months. Adjust thereafter based on GH and/or IGF-1 levels. Patients should begin treatment with Somatuline Depot 90 mg given via the deep subcutaneous route, at 4-week intervals for 3 months. After 3 months, dosage may be adjusted as follows:  
  - GH greater than 1 ng/mL to less than or equal to 2.5 ng/mL, IGF-1 normal, and clinical symptoms controlled: maintain dose at 90 mg every 4 weeks  
  - GH greater than 2.5 ng/mL, IGF-1 elevated, and/or clinical symptoms uncontrolled: increase dose to 120 mg every 4 weeks  
  - GH less than or equal to 1 ng/mL, IGF-1 normal, and clinical symptoms controlled: reduce dose to 60 mg every 4 weeks.  
  - Thereafter, the dose should be adjusted according to the response of the patient as judged by a reduction in serum GH and/or IGF-1 levels; and/or changes in symptoms of acromegaly. Patients who are controlled on Somatuline Depot 60 mg or 90 mg may be considered for an extended dosing interval of 120 mg every 6 or 8 weeks. GH and IGF-1 levels should be obtained 6 weeks after this change in dosing regimen to evaluate persistence of patient response. Continued monitoring of patient response with dose adjustments for biochemical and clinical symptom control, as necessary, is recommended. The starting dose in patients with moderate or severe renal impairment or moderate or severe hepatic impairment should be 60 mg via the deep subcutaneous route at 4-week intervals for 3 months followed by dose adjustment as described above. |
SOMATULINE DEPOT (lanreotide acetate) (cont.)

Resources: (cont.)

Somatuline Depot Package Insert: (cont.)

- FDA-approved indication and dosage: (cont.)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<tr>
<td>Unresectable, well- or moderately differentiated, locally advanced or</td>
<td>The recommended dose of Somatuline Depot is 120 mg administered every 4 weeks by</td>
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<tr>
<td>metabolic gastroenteropancreatic neuroendocrine tumors</td>
<td>deep subcutaneous injection. There is no recommended dose adjustment for mild or</td>
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<tr>
<td>Advise women not to breastfeed during treatment with Somatuline Depot and</td>
<td>moderate renal impairment. There is insufficient information to recommend a dose for</td>
</tr>
<tr>
<td>for 6 months after the last dose.</td>
<td>patients with severe renal impairment or with hepatic impairment of any severity.</td>
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</tbody>
</table>

| Adults with carcinoid syndrome; when used, it reduces the frequency of     | The recommended dosage of Somatuline Depot is 120 mg administered every 4 weeks   |
| short-acting somatostatin analog rescue therapy                           | by deep subcutaneous injection. If patients are already being treated with       |
| Advise women not to breastfeed during treatment with Somatuline Depot    | Somatuline Depot for GEP-NETs, do not administer an additional dose for the       |
| and for 6 months after the last dose.                                     | treatment of carcinoid syndrome.                                                |

Initial Approval Duration:
12 months

Renewal Approval Duration:
12 months
SOMATULINE DEPOT (lanreotide acetate) (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/file/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 nilínii Blue Cross Blue Shield of Arizona haada yit’eegí bíná’díl’kidgo éí doodago Háida biýání aniyeedígíí t’áadoo le’é yína’idíl’kidgo beehaz’áanii hólo díí t’áa hazaad’ehí háká a’dooowolgo bee haz’a doo báąh ilínígóó. Ata’ halné’ígíí kojí’ bích’yí hodiihíí 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 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 thể thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ dịch viễn, xin gọi 877-475-4799.

Arabic: إن كان لديك أو لدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona الضرورية بلغتك من دون دفع كلفة للتحدث مع مترجم يصل إلى 877-475-4799.
SOMATULINE DEPOT (lanreotide acetate) (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulungan, ay mga maya-maya kananugnang tungkol sa Blue Cross Blue Shield of Arizona, may karapatang na mag-uulat ng tulong at impormasyon sa iyong wika at walang gastos. Upang maging ang iisang tagsalamin, 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 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 동역사와 매기기 위해서는 877-475-4799로 전화해주시요.

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まで電話ください。

Farsi:

انگلیسی: ما به شما یا کسی که شما به آن کمک می‌کنید، سوال‌های مربوط به Blue Cross Blue Shield of Arizona را در مورد کمک و خدمات آموزشی به شما می‌دهیم و به شما بهترین راه حل‌ها را می‌آوریم.

Assyrian:

Blue Cross Blue Shield of Arizona یک شرکت جهانی است که به مردم کمک می‌کند، مثلاً به مردم که به مردم کمک می‌کنند.

Serbo-Croatian: Ukoliko Vi ili neko kom Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodocem, nazovite 877-475-4799.

Thai: หากคุณ หรือคนที่คุณช่วยเหลือตามกฎหมายของ Blue Cross Blue Shield of Arizona คุณมีสิทธิ์ได้รับความช่วยเหลือและข้อมูลภาษาของคุณได้โดยไม่เสียค่าใช้จ่าย ติดต่อเราที่ 877-475-4799.