Introduction

Imlygic® is a drug that uses a genetically altered virus to treat melanoma. This type of treatment is known as oncolytic viral therapy. This drug uses the herpes simplex 1 virus—the virus that can cause cold sores around the mouth—that has been changed to include a specific gene. This gene stimulates the immune system to create certain other cells that attack cancer. The modified virus can enter normal cells but normal cells are able to kill the virus. Cancer cells can’t. When the modified virus enters a cancer cell, it begins to grow and reproduce. The growing virus causes the cancer cells to burst and die. The dying cells then release a number of substances which then stimulate the body’s immune system to further attack the cancer cells. This policy describes when Imlygic may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
**Drug** | **Medical Necessity**
---|---
Imlygic® (talimogene laherparepvec) | Imlygic® (talimogene laherparepvec) may be considered medically necessary for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

**Drug** | **Investigational**
---|---
Imlygic® (talimogene laherparepvec) | Use of Imlygic® (talimogene laherparepvec) for all other indications is considered investigational.

**Length of Approval**

<table>
<thead>
<tr>
<th>Approval</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial authorization</td>
<td>Imlygic® (talimogene laherparepvec) may be approved up to 6 months.</td>
</tr>
<tr>
<td>Re-authorization criteria</td>
<td>Future re-authorization of Imlygic® (talimogene laherparepvec) may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the patient continues to show a positive clinical response to therapy.</td>
</tr>
</tbody>
</table>

**Documentation Requirements**

The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:

- Office visit notes that contain the diagnosis, relevant history and physical evaluation

**Coding**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS</td>
<td></td>
</tr>
<tr>
<td>J9325</td>
<td>Injection, talimogene laherparepvec (Imlygic®), per 1 million plaque forming units</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).
Evidence Review

Description

Imlygic® (talimogene laherparepvec) is a first-in-class oncolytic viral therapy. It is a herpes simplex 1 virus genetically modified to express human GM-CSF, indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

Melanoma

Melanoma accounts for a small (<5%) proportion of all skin cancers but, because it is more likely to metastasize than squamous cell or basal cell cancers, it causes a disproportionately high amount of skin cancer mortality. If recognized and treated early, it is almost always curable. Approximately 84% of melanomas are diagnosed at a localized stage with 5-year survival of 98%. However, the 5-year survival for the 4% of patients with metastatic disease at diagnosis is 15%.

Incidence rates for melanoma have been rising for at least 30 years. The age-adjusted incidence rate of melanoma was 20.8 per 100,000 men and women per year for the years 2004 to 2008. The American Cancer Society estimates that approximately 76,380 new cases of invasive melanoma will be diagnosed in the U.S. in 2016. An estimated 10,130 people will die of melanoma in 2016. The lifetime risk of melanoma is about 2% for Caucasians, 0.5% for Hispanics, and 0.1% for African Americans. Major risk factors for melanoma include atypical nevi (moles), more than 50 benign or atypical nevi, giant congenital nevus, and a personal or family history of melanoma. Other risk factors for all skin cancer types include: sun sensitivity, defined as easily sun burning, freckling, tanning with difficulty, or having naturally blond or red hair, history of excessive sun exposure, including sunburns, use of tanning booths and immune-deficiency states (eg, immunosuppressive chemotherapy, post-transplant immunosuppression, HIV/AIDS).
Rationale

One open-label, phase 3 Randomized Controlled Trial (RCT) has been published: The OPTiM study showed a significantly higher durable response rate in the talimogene laherparepvec (T-VEC) arm: (16.3% vs. 2.1% for GM-CSF, P<0.001). Overall, response rate was 26.4% for T-VEC vs. 5.7% for GM-CSF (p<0.001); 10.8% in the T-VEC arm had a Complete Remission (CR) compared to <1% in the GM-CSF arm, while 15.6% of the T-VEC arm achieved a Partial Response (PR) compared to 5.0% of the GM-CSF arm. T-VEC has not been shown to improve overall survival over GM-CSF.

Most common adverse events with T-VEC were fatigue (50% vs. 36% with GM-CSF), chills (49% vs. 9% with GM-CSF), pyrexia (43% vs. 9% with GM-CSF), nausea (36% vs. 20% with GM-CSF), flu-like illness (30% vs. 15% with GM-CSF), and injection-site pain (28% vs. 6% with GM-CSF). Long-term safety is currently unavailable. Further studies are underway.

Subgroup analyses found that differences in Durable Response Rate (DRR) between the T-VEC and GM-CSF arms were more pronounced in patients with stage IIIb or IIIC and IVM1a disease than in patients with stage IVM1b and IVM1c disease. Differences in DRR were also more pronounced in patients with treatment-naïve metastatic melanoma than in those receiving second-line or greater therapy. Similar patterns were seen for Overall Response Rate (ORR) and Overall Survival (OS).

Several trials are currently underway for stage IIIb to IV surgically unresectable melanoma, sarcoma, squamous cell carcinoma of the head and neck, and hepatocellular carcinoma and metastatic liver tumors.

2017 Update

Search of recent literature found no new information that would modify this policy.

2018 Update

Search of recent literature from October 1, 2017, to October 31, 2018, found no new information that would modify this policy. Updated references.
2019 Update

Reviewed Imlygic® (talimogene laherparepvec) prescribing information and conducted a literature search from November 1, 2018, through November 30, 2019. No new information was identified that would require changes to this policy.

References


History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/01/16</td>
<td>New Policy, approved April 12, 2016. Add to Prescription Drug section. Imlygic may be considered medically necessary for labeled indication. Reviewed by Pharmacy and Therapeutics Committee, February 25, 2016.</td>
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<tr>
<td>01/01/17</td>
<td>Coding update; added new HCPCS code J9325 effective 1/1/17.</td>
</tr>
<tr>
<td>06/01/17</td>
<td>Coding update; removed HCPCS codes J3490, J3590, and J9999.</td>
</tr>
<tr>
<td>10/01/17</td>
<td>Annual Review, approved September 5, 2017. A literature search was conducted from 04/13/16 to 8/18/17. No new studies were found that would require changes to this policy.</td>
</tr>
<tr>
<td>12/01/18</td>
<td>Annual Review, approved November 21, 2018. Literature search found no new information that would modify this policy. Updated references.</td>
</tr>
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</table>
**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2020 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera 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:
Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the 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, D.C. 20201, 1-800-368-1019, 800-537-7697 (TTY)
Complaint forms are available at

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.
Call 800-722-1471 (TTY: 800-842-5357).

Arabic (Arabic):
يُوصى هذا الإشعار باللغة العربية للأشخاص الذين يتحدثون العربية. قد يكون هناك ترجمة متاحة للأشخاص الذين يتحدثون العربية.

Chinese (Chinese):

Iloklo (Ilocano):
Daytoy a Pakdaar ket naglaon iti Napatge nga Impormasion. Daytoy a pakdaar mabalih nga adda ket naglaon iti napagte nga impormasion mainpanggepi a aplikasyonno wenyong coverage babaen iti Premera Blue Cross. Daytoy ket mabalih dagiti importante a pelta iti daytoy a pakdaar. Mabalih nga adda rumbang nga aramidenyo nga addang sambay dagiti partikular a naituding nga aildaw tapno mapapatgalinday ni ti coverage ti salun-atyo wenyong coverage. Adda karbenganyo a mangala ti daytoy nga impormasion ken tungul iti bukoday nga pagsasao nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potresto essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.
Chiama 800-722-1471 (TTY: 800-842-5357).

Fŏsish (Frisian):
Daytoy a Pakdaar ket naglaon iti Napatge nga Impormasion. Daytoy a pakdaar mabalih nga adda ket naglaon iti napagte nga impormasion mainpanggepi a aplikasyonno wenyong coverage babaen iti Premera Blue Cross. Daytoy ket mabalih dagiti importante a pelta iti daytoy a pakdaar. Mabalih nga adda rumbang nga aramidenyo nga addang sambay dagiti partikular a naituding nga aildaw tapno mapapatgalinday ni ti coverage ti salun-atyo wenyong coverage. Adda karbenganyo a mangala ti daytoy nga impormasion ken tungul iti bukoday nga pagsasao nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).
Thông báo này có thông tin quan trọng. Thông báo này có thông tin quan trọng và dựa trên việc xác minh thông tin của Premera Blue Cross. Thông báo này không bao gồm các thông tin cụ thể về việc chăm sóc sức khỏe của bạn. Bạn nên hỏi bác sĩ hoặc chuyên gia y tế của bạn về các câu hỏi liên quan đến sức khỏe của bạn. Thông báo này không phải là một sự thay thế cho việc tham gia các cuộc họp với bác sĩ hoặc chuyên gia y tế.

Panele Ochrany: Premera Blue Cross

Los Angeles: 800-722-1471 (TTY: 800-842-5357)

Panama: 800-722-1471 (TTY: 800-842-5357)

Tagalog (Tagalog):
Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang paunawa na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaring may mga mahalagang petsa dito sa paunawa. Maaring ito ay maaaring naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Es posible que haya fechas claras en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):
ประกาศนี้มีข้อมูลสำคัญเกี่ยวกับการรับรู้สิทธิ์และการบริการของคุณตามการจัดการสุขภาพของคุณ Premera Blue Cross และที่มีกำหนดไว้ในประกาศนี้ คุณควรตรวจสอบด้วยตนเองในกำหนดเวลาที่แน่นอนเพื่อจะทราบการบริการสุขภาพของคุณที่มีการจัดการ คุณมีสิทธิ์ที่จะได้รับคำชี้แจงและข้อมูลเกี่ยวกับการจัดการสุขภาพของคุณได้.

Polskie (Polish):

Português (Portuguese):
Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir dados importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação a ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Русский (Russian):
Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В этом уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Español (ES):
Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas claras en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Український (Ukrainian):
Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страхувального покриття через Premera Blue Cross. Зверніться узвід на ключові дати, які можуть бути вказані у цьому повідомленні. Існує ймовірність того, що Вам треба буде здійснити деякі кроки у конкретні кінцеві строки для того, щоб забезпечити Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дозвоніться за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):