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MEDICAL POLICY – 5.01.530

Egrifta® (tesamorelin)

Effective Date:	July 1, 2018	RELATED MEDICAL POLICIES:
Last Revised:	June 22, 2018	None
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Lipodystrophy is a condition that affects how the body processes and stores fat. It can cause either a buildup or a loss of fat. Up to one half of people with HIV experience lipodystrophy. It's not known whether it's the virus or the drugs used to treat the virus that causes lipodystrophy. Egrifta is a drug that can be used to reduce the excess fat in the belly area in people with HIV. There have been no studies looking at whether Egrifta improves long-term heart health. Because of this and the lack of other scientific evidence about how it affects overall health, the use of Egrifta in those with HIV is considered cosmetic. All other uses are investigational (unproven).

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.

Policy Coverage Criteria

Drug	Cosmetic
Egrifta® (tesamorelin)	**Use of Egrifta® (tesamorelin) for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy is considered cosmetic.**

Drug	Investigational
Egrifta® (tesamorelin)	**All other uses of Egrifta® (tesamorelin) not outlined above are considered investigational at this time.**

Coding

Code	Description
HCPCS	
J3590	Unclassified biologics

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).

Related Information

N/A

Evidence Review

Description

Egrifta® (tesamorelin) is a growth hormone releasing factor (GRF) analog FDA-approved on November 10, 2010, for the reduction of excess abdominal fat in human immunodeficiency (HIV)–infected patients with lipodystrophy. Growth hormone-releasing factor (GRF), also known as growth hormone-releasing hormone (GHRH), is a 44-amino acid peptide that is released from the hypothalamus and binds to receptors on pituitary cells (somatotropes) that release growth hormone (GH). The interaction of GRF with its somatotrope receptors stimulates GH release. Tesamorelin is a synthetic growth GRF analogue consisting of the 44 amino acid sequence of human GRF with a hexenoyl moiety (a 6-carbon chain with a double bond at position 3) attached at the N-terminal. The hexenoyl moiety slows degradation of Egrifta® (tesamorelin), increasing its half-life. Tesamorelin is self-administered as a daily subcutaneous injection.

Disease Characteristics

The human immunodeficiency virus (HIV) lipodystrophy syndrome is characterized by fat loss (lipoatrophy) in the limbs, buttocks and face; localized fat accumulation (lipohypertrophy) at the back of the neck ("buffalo hump"), the upper trunk and breasts, around the abdominal viscera, and in lipomata; hyperlipidemia; insulin resistance; and hyperglycemia. Before the availability of antiretroviral therapy, severe wasting and decreased cholesterol levels were common metabolic abnormalities in advanced acquired immunodeficiency syndrome (AIDS). With the introduction of effective antiretroviral therapy, central lipohypertrophy with peripheral lipoatrophy was seen more commonly. Patients can have pure lipoatrophy, pure lipohypertrophy, or a mixture of both morphologic features.

Epidemiology and Risk Factors

A 2005 cohort study in the United States followed 452 HIV-infected patients for 1 year to assess risk factors for progression of morphologic abnormalities. Baseline prevalence rates were 35% for lipoatrophy, 44% for lipohypertrophy, and 14% for mixed morphology. Risk factors for lipohypertrophy included female sex and higher levels of body fat and serum triglyceride at baseline. Additional risk factors include use of protease inhibitors (eg, ritonavir and indinavir), increasing age, longer duration of antiretroviral therapy (ART), which may be a surrogate for longer duration of HIV infection, and a low-fiber diet. In contrast, risk factors for lipoatrophy include low baseline triceps skin-fold values, smaller hips, higher HIV ribonucleic acid (RNA) levels, and use of the nucleoside reverse transcriptase inhibitors (NRTIs), abacavir or stavudine. The findings suggest that lipoatrophy and lipohypertrophy are different syndromes.

Pathophysiology

Lipodystrophy is thought to result from mitochondrial toxicity and derangements in adipocytokines (adipose derived proteins) that regulate energy homeostasis, including those that regulate growth hormone (GH). In HIV seropositive or seronegative obese patients, the amount of GH secreted per burst is decreased, and the response to growth hormone-releasing factor (GF) and arginine stimulation testing is blunted. Additionally, deficiency of adiponectin and elevation of leptin are seen in HIV lipohypertrophy. Adiponectin is an adipocyte-derived hormone that functions as an insulin sensitizer by reducing triglyceride levels and inhibiting

gluconeogenesis in the liver. Leptin is a hormone involved in the central regulation of energy homeostasis and insulin resistance. In HIV-infected individuals, leptin levels seem to correlate with body fat phenotype, with the lowest levels seen in patients with lipoatrophy, and the highest levels, consistent with a state of leptin resistance, in patients with lipohypertrophy.

Clinical Presentation

Abdominal lipohypertrophy reflects an excess of visceral adipose tissue (VAT) that results in an increased abdominal girth. "Buffalo hump" results from an accumulation of fat in the dorsocervical area. Both men and women may develop accumulation of extra breast fat or symmetrical deposits of subcutaneous fat nodules on their trunk and extremities (lipomata). In many cases, it may be difficult to distinguish the syndrome from simple obesity, in which visceral fat is also accompanied by increased amounts of subcutaneous fat in the abdominal wall. The distinguishing feature of HIV-associated lipodystrophy is that visceral fat deposition is accompanied by normal or decreased (but not increased) amounts of subcutaneous fat. These body changes are distressing and can be stigmatizing for sufferers.

To assess 10-year coronary heart disease (CHD) risk estimates in patients with HIV lipodystrophy, 91 HIV-infected patients were compared with 273 HIV-seronegative controls from the Framingham Offspring Study who were matched for age, gender and body mass index.

Ten-year risk estimates were significantly higher in HIV-infected patients with evidence of fat redistribution compared to matched controls (7.4% ± 0.6% vs. 5.3% ± 0.3%, p=0.002). When these patients were matched to controls for waist-to-hip ratio measurements, the CHD risk was similar (7.6% ± 0.6% vs. 7.6% ± 0.4%; p=0.9). The CHD risk estimate was greatest in HIV-infected patients who had primary lipoatrophy (9.2% ± 1.8%) compared with those who had either abdominal lipohypertrophy (4.3% ± 0.7%, p<0.05) or mixed fat redistribution (7.6% ± 0.8%, p-value not reported). HIV-infected patients without fat redistribution did not have a greater CHD risk estimate than did controls (4.1% ± 0.7% vs. 3.3% ± 0.3%, p=0.27). The authors conclude that "although CHD risk is increased in HIV-infected patients with fat redistribution, the pattern of fat distribution is a potential important component in determining the risk in this population."

Diagnosis

There are a wide range of screening techniques for abdominal obesity. A simple measure is the waist circumference, which is considered more accurate than the waist circumference: hip circumference ratio. An abdominal circumference >102 cm for men and >88 cm for women is

considered abnormal. Quantitative measurements of visceral adipose tissue by computed tomography (CT) or magnetic resonance imaging (MRI) are usually done in research trials only. Dual-energy x-ray absorptiometry (DEXA) cannot distinguish between visceral and subcutaneous adipose tissue and is not recommended.

Principal Therapeutic Options

Potential interventions for lipohypertrophy include exercise, surgical interventions, and medical therapy. Both aerobic and resistance exercise should be encouraged for HIV-infected individuals with central or generalized fat accumulation. Moderate exercise is well tolerated by HIV-infected patients and does not increase viral load. In a small study of resistance exercise training in HIV-infected patients who complained of increased abdominal girth, there was a significant decline in total fat, measured by dual-energy x-ray absorptiometry (DEXA), and the majority of fat loss occurred in the truncal region.

Medical therapies for lipohypertrophy, predominantly abdominal, include metformin, somatropin and pioglitazone. Each of these alternatives is associated with significant and potentially serious side effects.

Rationale

Efficacy

The clinical development program of Egrifta® (tesamorelin) included 2 randomized, placebo-controlled, double-blind, Phase III pivotal trials conducted in the US, Canada, and Europe. The design of the trials was similar. Each consisted of a 26-week Main Phase followed by a 26-week Extension Phase. A total of 816 HIV-infected adults with clinically-defined lipodystrophy receiving antiretroviral therapy for at least 8 weeks were enrolled. Patients with diabetes mellitus requiring medication were excluded. Patients self-administered tesamorelin (Egrifta®) 2 mg or placebo subcutaneously daily. The primary efficacy outcome was percent reduction in visceral adipose tissue (VAT) as measured by single-slice CT scan at the L4-L5 level. The minimum clinically meaningful reduction was defined a priori as 8%. Secondary endpoints included effects on lipid profile and patient-reported outcomes related to belly image. The FDA questioned the content validity of the scale used to assess the patient-reported outcomes. Patients who completed the Main Phase trials were invited to enroll in the Extension Phases (total n=578).

Patients in the tesamorelin group were randomized to continue tesamorelin (Egrifta®) or switch to placebo. Patients in the placebo group were switched to tesamorelin (Egrifta®).

In one main phase trial, Trial 10, VAT in the Egrifta® (tesamorelin) group decreased by 18% compared to an increase of 2% in the placebo group (mean treatment difference [95% confidence interval (CI)] -20% [-24% to -15%]). In the other Main Phase trial, Trial 11, VAT in the Egrifta® (tesamorelin) group decreased by 14% compared to a decrease of 2% in the placebo group (mean treatment difference [95% CI] -12% [-16% to -7%]). In the Extension Phase trials, reductions in VAT were maintained in patients that continued Egrifta® (tesamorelin) for an additional 26 weeks and reverted back toward baseline in patients that switched to placebo.

In Trial 10, mean triglyceride level decreased by 48 mg/dL in the Egrifta® (tesamorelin) group and increased by 5 mg/dL in the placebo group, a statistically significant difference ($p<0.001$). In Trial 11, mean triglyceride level decreased by 19 mg/dL in the Egrifta® (tesamorelin) group and increased by 1 mg/dL in the placebo group, a difference that was not statistically significant ($p=0.10$). Similarly, reductions in total cholesterol: high-density lipoprotein (HDL) cholesterol ratio and non-HDL cholesterol were statistically significant in Trial 10 but not in Trial 11. In the Extension Phase trials, Egrifta® (tesamorelin) effects on triglyceride levels were variable and of similar magnitude to the Main Phase trial effects.

Patient-reported outcomes related to belly image were inconsistent across trials. The mean between-group difference in improvement from baseline belly size evaluation to week 26 was 1.5 points in Trial 10 ($p=0.75$) and 2.9 points in Trial 11 ($p=0.21$). Responder criteria required an improvement of 50 points. For belly appearance distress, the mean between-group difference in improvement was 5.4 points in Trial 10 ($p=0.08$) and 3.1 points in Trial 11 ($p=0.02$). Responder criteria required an improvement of 25 points.

The effect of VAT reduction on cardiovascular (CV) risk reduction was not a requirement for FDA-approval of Egrifta® (tesamorelin). Instead, clinical correlations with secondary supportive efficacy measures of improved patient-reported body image and lipid abnormalities were expected. FDA did not consider the observed changes in these measures to be robust and concludes that the clinical benefit of the observed reductions in VAT is uncertain.

Safety

The most common adverse events seen with Egrifta® (tesamorelin) treatment in clinical trials were:

- Hypersensitivity reactions (eg, rash, urticaria);

- Adverse events associated with the use of growth hormone (eg, arthralgia, peripheral edema, hyperglycemia, carpal tunnel syndrome) which occurred in 25.6% of Egrifta® (tesamorelin) patients and 13.7% of placebo patients during the Main Phase trials; and
- Injection site reactions (erythema, pruritis, pain, urticaria, irritation, swelling, hemorrhage) which occurred in 24.5% of Egrifta® (tesamorelin) patients and 14.4% of placebo patients overall.

Hypersensitivity

Hypersensitivity reactions occurred in 27 of 740 Egrifta® (tesamorelin)-treated patients (3.6%) compared with 1 of 263 placebo-treated patients (0.4%). These reactions included pruritus, erythema, flushing, urticaria, and other rash. Anaphylaxis was not observed. Of these 27 patients, 23 (85%) tested positive for anti- Egrifta® (tesamorelin) antibodies, compared to a seropositive rate of approximately 50% for the pivotal trial population as a whole. The presence or titer of anti- Egrifta® (tesamorelin) antibodies did not appear to correlate with the clinical severity of the hypersensitivity reaction.

Glucose Intolerance

During the Main Phase trials and their extensions, there were no clinically significant changes in mean values for fasting blood glucose, fasting serum insulin, homeostasis model assessment of insulin resistance (HOMA-IR), or glycosylated hemoglobin (HbA1c). However, during the Main Phase trials, the proportion of patients with HbA1c in the diabetic range (≥6.5%) increased from 2.1% at baseline to 6.6% at week 26 in the Egrifta® (tesamorelin) group and from 1.2% to 2.5% in the placebo group, a statistically significant difference (odds ratio [95% confidence interval] 3.6 [1.5, 12.0]).1, 2 In the Extension Phase trials, the proportion of patients with HbA1c in the diabetic range decreased from 4.9% at week 26 to 1.5% at week 52 in the T-T group, and from 5.2% to 4.3% in the T-P group.

Increased IGF-1 and Cancer Risk

In Phase III trials, 15 patients developed cancer, including 8 patients during the Main Phase trials and 7 patients during the Extension Phase trials. No specific pattern of cancers differentiated Egrifta® (tesamorelin) from placebo. Because of the suspected link between high insulin-like

growth factor (IGF)-1 levels and the risk of tumorigenesis, IGF-1 values for all patients who developed cancer during clinical trials were reviewed. Twelve of 15 IGF-1 values (80%) fell within the normal range (not more than 2 standard deviations [SDs] from mean normal). Three patients had IGF-1 levels above the upper limit of normal. Basal cell carcinoma developed in 2 of these patients and lung cancer in the third.

Off-Label Use

No published trials of Egrifta® (tesamorelin) for use in other clinical conditions were identified. The clinical trials database of the National Institutes of Health currently lists 4 active trials of Egrifta® (tesamorelin):

- 2 trials of HIV-infected patients with lipodystrophy,
- 1 phase 2 trial of VAT reduction in obesity, and
- 1 phase 2 trial of mild cognitive impairment in adults ≥ 55 years of age.

Conclusion

The primary efficacy outcome was percent reduction in VAT as determined by abdominal computed tomography (CT) scan. Significant reductions in VAT that exceeded the agreed-upon minimum clinically meaningful threshold (8% reduction) were demonstrated with Egrifta® (tesamorelin) in both phase 3 trials. The effect of VAT reduction on cardiovascular (CV) risk reduction was not a requirement for FDA-approval of Egrifta® (tesamorelin). Instead, clinical correlations with secondary supportive efficacy measures of improved patient-reported body image and lipid abnormalities were expected. The changes in these measures were not robust or consistent. Therefore, the clinical benefit of the observed reductions in VAT is uncertain.

The assumed efficacy of tesamorelin in reducing risk of CV events is therefore based on population-based risk analyses that assume that reducing VAT in HIV lipodystrophy patients will produce risk profiles comparable to those of non-HIV infected individuals with similar VAT. The available evidence does not adequately demonstrate that this assumption is warranted.

Although Egrifta® (tesamorelin) is FDA-approved for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy, an improvement in net health outcome has not been demonstrated. Specifically:

- Long-term cardiovascular benefit has not been studied.
- Long-term risks of elevated IGF-1 levels are unknown.
- There are no data to support improved compliance with antiretroviral therapies.
- Effects on quality of life measures were not assessed.
- Patient-reported outcomes related to belly image were inconsistent across trials.

Given the relatively low prevalence of HIV-lipodystrophy and of CV event rates, FDA considers a randomized trial to assess CV outcomes infeasible. Instead, post-marketing requirements include a long-term observational study to assess long-term risks associated with Egrifta® (tesamorelin) including major adverse cardiac events (MACE), cancer risk, and hypersensitivity reactions and a double-blind, randomized, placebo-controlled clinical trial of HIV-infected patients with lipodystrophy and type 2 diabetes mellitus to assess the risk of retinopathy.

2012 Update

A literature search of the MEDLINE database conducted from January 2011 through February 2012 did not identify any additional published studies that would prompt reconsideration of the policy statements.

2013 Update

A literature search of the MEDLINE database conducted from January through December 2012 did not identify any additional published studies that would prompt reconsideration of the policy statements.

2014 Update

A literature search conducted from January 2013 through February 2014 found no new evidence that would change this policy.

2015 Update

A literature search conducted from January 2014 through February 2015 found no new evidence that would change this policy.

2016 Update

A literature search conducted from June 1, 2015, through December 6, 2016, found no new evidence that would change this policy.

2017 Update

A literature search conducted from June 1, 2016, through August 11, 2017, found no new evidence that would change this policy.

2018 Update

A literature search conducted from July 1, 2017, through June 12, 2018, found no new evidence that would change this policy.

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History

Date	Comments
03/08/11	Add to Prescription Drug Section - New Policy. Reviewed and recommended by P&T January 2011.
04/25/12	Replace policy. Policy updated with literature review; no changes to policy statements.
04/16/13	Replace policy. Policy updated with literature review; no changes to policy statements. Reference 31 added.
04/14/14	Annual Review. Policy updated with literature review; no changes to policy statements. Reference 32 added.
04/24/15	Annual review. Policy updated with literature review; no changes to policy statements.

Date	Comments
01/01/17	Annual review, approved December 13, 2016. Policy updated with literature review; no changes to policy statements.
09/01/17	Annual Review, approved August 22, 2017. Title changed to Egrifta® (tesamorelin). Policy updated with literature review; no changes to policy statements.
07/01/18	Annual Review, approved June 22, 2018. Policy updated with literature review; no changes to policy statements.

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.

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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).

አማሪኛ (Amharic):
ይህ ማስታወቂያ አስፈላጊ መረጃ ይዟል። ይህ ማስታወቂያ ስለ ማመልከቻዎ ወይም የ Premera Blue Cross ሽፋን አስፈላጊ መረጃ ሊኖረው ይችላል። በዚህ ማስታወቂያ ውስጥ ቁልፍ ቀኖች ሊኖሩ ይችላሉ። የጤናን ሽፋንዎን ለመጠበቅና በአከፋፈል እርዳታ ለማግኘት በተውሰኑ የጊዜ ገደቦች እርምጃ መውሰድ ይገባዎት ይሆናል። ይህን መረጃ እንዲያገኙ እና ያለምንም ክፍያ በቋንቋዎ እርዳታ እንዲያገኙ መብት አለዎት።በስልክ ቁጥር 800-722-1471 (TTY: 800-842-5357) ይደውሉ።

العربية (Arabic):
يحوي هذا الإشعار معلومات هامة. قد يحوي هذا الإشعار معلومات مهمة بخصوص طلبك أو التغطية التي تريد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك تواريخ مهمة في هذا الإشعار. وقد تحتاج لاتخاذ إجراء في تواريخ معينة للحفاظ على تغطيتك الصحية أو للمساعدة في دفع التكاليف. يحق لك الحصول على هذه المعلومات والمساعدة بلغتك دون تكبد أية تكلفة. اتصل بـ800-722-1471 (TTY: 800-842-5357)

中文 (Chinese):
本通知有重要的訊息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知內可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或者費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357)。

Oromoo (Cushite):
Beeksisni kun odeeffannoo barbaachisaa qaba. Beeksisti kun sagantaa yookan karaa Premera Blue Cross tiin tajaajila keessan ilaalchisee odeeffannoo barbaachisaa qabaachuu danda'a. Guyyaawwan murteessaa ta'an beeksisa kana keessatti ilaalaa. Tarii kaffaltiidhaan deeggaramuuf yookan tajaajila fayyaa keessaniif guyyaa dhumaa irratti wanti raawwattan jiraachuu danda'a. Kaffaltii irraa bilisa haala ta'een afaan keessaniin odeeffannoo argachuu fi deeggarsa argachuuf mirga ni qabaattu. Lakkoofsa bilbilaa 800-722-1471 (TTY: 800-842-5357) tii bilbilaa.

Français (French):
Cet avis a d'importantes informations. Cet avis peut avoir d'importantes informations sur votre demande ou la couverture par l'intermédiaire de Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous devrez peut-être prendre des mesures par certains délais pour maintenir votre couverture de santé ou d'aide avec les coûts. Vous avez le droit d'obtenir cette information et de l'aide dans votre langue à aucun coût. Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):
Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konsènan kouvèti asirans lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kèk aksyon avan sèten dat limit pou ka kenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resevwa enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rele nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):
Diese Benachrichtigung enthält wichtige Informationen. Diese Benachrichtigung enthält unter Umständen wichtige Informationen bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Rufen Sie an unter 800-722-1471 (TTY: 800-842-5357).

Hmoob (Hmong):
Tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsab ntawv tshaj xo no muaj cov ntsiab lus tseem ceeb txog koj daim ntawv thov kev pab los yog koj qhov kev pab cuam los ntawm Premera Blue Cross. Tej zaum muaj cov hnub tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau ua qee yam uas peb kom koj ua tsis pub dhau cov caij nyoog uas teev tseg rau hauv daim ntawv no mas koj thiaj yuav tau txais kev pab cuam kho mob los yog kev pab them tej nqi kho mob ntawd. Koj muaj cai kom lawv muab cov ntshiab lus no uas tau muab sau ua koj hom lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Iloko (Ilocano):
Daytoy a Pakdaar ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaon iti napateg nga impormasion maipanggep iti apliksayonyo wenno coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petsa iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding nga aldaw tapno mapagtalinaedyo ti coverage ti salun-atyo wenno tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagsasao nga awan ti bayadanyo. Tumawag iti 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. Potrebbero esserci date chiave in questo avviso. Potrebbe 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).

日本語 (Japanese):
この通知には重要な情報が含まれています。この通知には、Premera Blue Cross の申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている可能性がある重要な日付をご確認ください。健康保険や有料サポートを維持するには、特定の期日までに行動を取らなければならない場合があります。ご希望の言語による情報とサポートが無料で提供されます。800-722-1471 (TTY: 800-842-5357)までお電話ください。

한국어 (Korean):
본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관하여 그리고 Premera Blue Cross 를 통한 커버리지에 관한 정보를 포함하고 있을 수 있습니다. 본 통지서에는 핵심이 되는 날짜들이 있을 수 있습니다. 귀하는 귀하의 건강 커버리지를 계속 유지하거나 비용을 절감하기 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하는 이러한 정보와 도움을 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357) 로 전화하십시오.

ລາວ (Lao):
ແຈ້ງການນີ້ມີຂໍ້ມູນສຳຄັນ. ແຈ້ງການນີ້ອາດຈະມີຂໍ້ມູນສຳຄັນກ່ຽວກັບຄຳຮ້ອງສະໝັກ ຫຼື ຄວາມຄຸ້ມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີສຳຄັນໃນແຈ້ງການນີ້. ທ່ານອາດຈະຈຳເປັນຕ້ອງດຳເນີນການຕາມກຳນົດເວລາສະເພາະເພື່ອຮັກສາຄວາມຄຸ້ມຄອງປະກັນສຸຂະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເລື່ອງຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄວ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໂທຫາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):
សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរ៉ាប់រងរបស់អ្នកតាមរយៈ Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ចេញសមត្ថភាព ដល់កំណត់ថ្ងៃជាក់ច្បាស់នានា ដើម្បីនឹងរក្សាទុកការជានាវ៉ាប់រងសុខភាពរបស់អ្នក ឬប្រាក់ជំនួយចេញផ្លែ។ អ្នកមានសិទ្ធិទទួលព័ត៌មាននេះ និងជំនួយនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ សូមទូរស័ព្ទ 800-722-1471 (TTY: 800-842-5357)។

ਪੰਜਾਬੀ (Punjabi):
ਇਸ ਨੋਟਿਸ ਵਿਚ ਖਾਸ ਜਾਣਕਾਰੀ ਹੈ. ਇਸ ਨੋਟਿਸ ਵਿਚ Premera Blue Cross ਵਲੋਂ ਤੁਹਾਡੀ ਕਵਰੇਜ ਅਤੇ ਅਰਜੀ ਬਾਰੇ ਮਹੱਤਵਪੂਰਨ ਜਾਣਕਾਰੀ ਹੋ ਸਕਦੀ ਹੈ . ਇਸ ਨੋਜਿਸ ਜਵਚ ਖਾਸ ਤਾਰੀਖਾ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀ ਜਸਹਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਛੁੱਕ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ਼ ਤੋਂ ਪਹਿਲਾਂ ਕੁੱਝ ਖਾਸ ਕਦਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫ਼ਤ ਵਿੱਚ ਤੇ ਆਪਣੀ ਭਾਸ਼ਾ ਵਿੱਚ ਜਾਣਕਾਰੀ ਅਤੇ ਮਦਦ ਪ੍ਰਾਪਤ ਕਰਨ ਦਾ ਅਧਿਕਾਰ ਹੈ ,ਕਾਲ 800-722-1471 (TTY: 800-842-5357).

فارسی (Farsi):
این اعلامیه حاوی اطلاعات مهم میباشد .این اعلامیه ممکن است حاوی اطلاعات مهم درباره فرم تقاضا و یا پوشش بیمه ای شما از طریق Premera Blue Cross باشد. به تاریخ های مهم در این اعلامیه توجه نمایید .شما ممکن است برای حفظ پوشش بیمه تان یا کمک در پرداخت هزینه های درمانی تان، به تاریخ های مشخصی برای انجام کارهای خاصی احتیاج داشته باشید .شما حق این را دارید که این اطلاعات و کمک را به زبان خود به طور رایگان دریافت نمایید. برای کسب اطلاعات با شماره 800-722-1471 (کاربران TTY تماس باشماره 800-842-5357) تماس برقرار نمایید.

Polskie (Polish):
To ogłoszenie może zawierać ważne informacje. To ogłoszenie może zawierać ważne informacje odnośnie Państwa wniosku lub zakresu świadczeń poprzez Premera Blue Cross. Prosimy zwrócic uwagę na kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej informacji we własnym języku. Zadzwońcie pod 800-722-1471 (TTY: 800-842-5357).

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 datas 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 e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Română (Romanian):
Prezenta notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării dumneavoastre de sănătate prin Premera Blue Cross. Pot exista date cheie în această notificare. Este posibil să fie nevoie să acționați până la anumite termene limită pentru a vă menține acoperirea asigurării de sănătate sau asistența privitoare la costuri. Aveți dreptul de a obține gratuit aceste informații și ajutor în limba dumneavoastră. Sunați la 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 настоящем 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).

Fa'asamoa (Samoan):
Atonu ua iai i lenei fa'asilasilaga ni fa'amatalaga e sili ona taua e tatau ona e malamalama i ai. O lenei fa'asilasilaga o se fesoasoani e fa'amatala atili i ai i le tulaga o le polokalame, Premera Blue Cross, ua e tau fia maua atu i ai. Fa'amolemole, ia e iloilo fa'alelei i aso fa'apitoa olo'o iai i lenei fa'asilasilaga taua. Masalo o le'a iai ni feau e tatau ona e faia ao le'i aulia le aso ua ta'ua i lenei fa'asilasilaga ina ia e iai pea ma maua fesoasoani mai ai i le polokalame a le Malo olo'o e iai i ai. Olo'o iai iate oe le aia tatau e maua atu i lenei fa'asilasilaga ma lenei fa'amatalaga i legagana e te malamalama i ai aunoa ma se togiga tupe. Vili atu i le telefoni 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):
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 clave 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).

Tagalog (Tagalog):
Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang paunawa na ito ay maaaring naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itinakdang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na walang gastos. May karapatan ka na makakuha ng ganitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):
ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับการการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือนี้ในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471 (TTY: 800-842-5357)

Український (Ukrainian):
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