PREMERA | BLUE CROSS

PHARMACY POLICY – 5.01.548

Pharmacotherapy of Cushing's Disease and Acromegaly

Effective Date:	Dec. 1, 2018	RELATED POLICIES:
Last Revised:	Nov. 21, 2018	None
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
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Introduction

The pituitary gland is about the size of a pea. It's just behind the bridge of the nose and is attached to the brain with nerve fibers. Despite its small size, it plays a very large role in controlling other glands throughout the body. For this reason, the pituitary is often called the master gland. The pituitary gland also produces other hormones, including ACTH and growth hormone. In Cushing's disease, a pituitary tumor causes the pituitary gland produce too much ACTH. The ACTH then signals the adrenal glands to produce cortisol. Removing the tumor often allows the pituitary gland to return to producing normal levels of ACTH, which then lowers the cortisol levels. Acromegaly is a condition that results in enlargement of the hands, feet, and face. It's caused by the pituitary gland producing too much growth hormone. A noncancerous tumor on the pituitary gland is the most common cause of acromegaly. Specific drugs may be used to treat Cushing's disease or acromegaly when surgery or other medications didn't work or can't be used. This policy describes when specific drugs to treat these conditions 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.

Policy Coverage Criteria

Drug	Medical Necessity
Signifor® (pasireotide) and Korlym® (mifepristone)	**Signifor® (pasireotide) and Korlym® (mifepristone) may be considered medically necessary for treatment of Cushing's disease when ALL of the following conditions are true:** • Patient has failed transsphenoidal surgery (TSS), is not a surgical candidate or has failed surgery **AND** • Patient has failed a trial of bromocriptine or cabergoline, unless contraindicated or otherwise medically inappropriate **AND** • Patient has failed a trial of metopirone or mitotane, unless contraindicated or otherwise medically inappropriate **All other uses of Signifor®, Signifor® LAR (pasireotide) and Korlym® (mifepristone) are considered investigational.**
Signifor® LAR (pasireotide)	**Signifor® LAR (pasireotide) may be considered medically necessary for the treatment of acromegaly when the following condition(s) is/are met:** • Patient has had an inadequate response to surgery **AND/OR** • Surgery is not an option

Coding

Code	Description
HCPCS	
J2502	Injection, pasireotide (Signifor®) long acting, 1 mg

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

Benefit Application

This policy is managed through the Pharmacy benefit.

Evidence Review

Description

Cushing's syndrome is a classic constellation of symptoms caused by long-term exposure to excessively high levels of circulating corticosteroid hormones. The most common cause of Cushing's syndrome is exogenous glucocorticoid administration. However, symptoms may result from endogenous causes including ACTH-dependent and ACTH-independent Cushing's. ACTH-dependent disease makes up 80% of endogenous cases and is due to pituitary adenoma in 85% of cases and ectopic tumor secretion in 15% of cases. Cushing's disease refers to pituitary tumors that secrete ACTH.

Cushing's syndrome occurs in 1-3 patients/million persons yearly with a prevalence of 40 cases/million persons, more frequently in females (3:1). Cushing's disease occurs more rarely than Cushing's syndrome and incidence peaks in the third to fourth decade.

The pituitary produces many hormones including TSH, growth hormone, ACTH, luteinizing hormone, follicle stimulating hormone, prolactin, and vasopressin. Pituitary adenomas can result in overproduction of ACTH, resulting in excess cortisol production from the adrenal glands. The hypothalamic-pituitary-adrenal (HPA) axis no longer retains its circadian rhythm and hypercortisolism occurs. Excess cortisol results in a wide constellation of symptoms including truncal obesity, hypertension, impaired glucose tolerance, dyslipidemia, increased risk of arterial thrombosis, psychiatric and cognitive disorders, osteoporosis, muscle and skin atrophy, impaired immune function, and hyperandrogenism. Quality of life (QOL) is frequently impaired. Morbidity and mortality is increased due to increased infections as well as cardiovascular disease resulting from increased cardiovascular risk factors such as hypertension, DM, and dyslipidemia. Estimated 5-year survival in untreated patients is 50%. With treatment, chances of death remain 2-4 times greater than the average population.

Treatment Alternatives for Cushing's disease

The preferred treatment for Cushing's disease transsphenoidal surgery (TSS), which results in long-term remission rates of 60-90% with a recurrence risk of 26% within 10-years. Poor outcomes are seen with larger tumor size and repeat surgeries. Patients with persistent disease after surgery can be treated with pituitary irradiation; however, months to years of treatment may be required before an effect is seen. Bilateral adrenalectomy may also be performed; however, the pituitary adenoma remains in situ, negative feedback effects of cortisol are lost, and replacement gluco- and mineralocorticoids are required.

Medical therapy is used with unsuccessful surgery, patients without an adenoma image on MRI, those undergoing radiotherapy which is not yet effective, patients with severe complications of Cushing's, and with those ineligible for surgery. Cushing's disease can be treated with drugs that target the adenoma, adrenal ACTH receptors or glucocorticoid receptors. Drugs which target the pituitary include somatostatin analogs and dopamine agonists bromocriptine and cabergoline. Cabergoline is a dopamine agonist that targets dopamine receptor subtype 2 (D2R), which is expressed in 80% of ACTH-secreting pituitary adenomas.

Adrenal-targeting drugs include ketoconazole, metopirone, and mitotane. These agents act by inhibiting steroid formation. Ketoconazole's actions are linked to inhibition of CYP 450 enzymes. Mitotane is typically effective in >50% of cases while ketoconazole and metopirone are effective in approximately 50% of patients. Mifepristone is the only agent available which blocks glucocorticoid receptors, more specifically the cortisol and progesterone receptors. Mifepristone is FDA indicated for patients with Cushing's syndrome with diabetes or glucose intolerance that require glycemic control. Each of these agents, with the exception of pasireotide, has been evaluated in a small number of patients. All except pasireotide and mifepristone are not FDA indicated for Cushing's disease or syndrome. (NOTE: FDA has issued a warning against ketoconazole use because of case reports of potentially fatal liver injury. For this reason, its use in Cushing's disease is no longer recommended.)

Although several different guidelines address the diagnosis of Cushing's disease, few address medical treatment. The European Neuroendocrine Association and the Pituitary Society last published a consensus statement in 2008 which discussed therapy options as described above. The guidelines emphasized the importance of surgery as a first line option, but did not recommend any particular medical therapy above another.

Treatment Alternatives for Acromegaly

The goals of therapy are to lower the serum insulin-like growth factor 1 (IGF-1), and serum growth hormone (GH) concentrations. For a patient who has microadenoma/macroadenoma, which is resectable, transsphenoidal surgery is preferred. If adenoma is not resectable (or patient is not a candidate for surgery), then the preferred treatment would be a long-acting somatostatin analog, such as octreotide or lanreotide. If somatostatin analog treatment with or without cabergoline is not effective, adding pegvisomant may be necessary (note this approach has NOT been approved by the FDA). If adenoma size keeps increasing despite the use of somatostatin analog with pegvisomant, radiotherapy or repeat surgery may be warranted.

Signifor® LAR (pasireotide)

Signifor® LAR (pasireotide) is a cyclohexapeptide somatostatin analogue. Pasireotide binds to and activates somatostatin receptors. This results in the inhibition of ACTH, leading to decreased cortisol secretion. Of the five somatostatin receptors (hsst1-5), the somatostatin receptor hsst5 is overexpressed on corticotroph adenomas in patients with Cushing's disease. Pasireotide preferentially binds to hsst1,2,3,5 and has 40-fold higher affinity for hsst5 than octreotide. The dose of pasireotide is titrated based on response and tolerability. Treatment response is defined as a clinically meaningful decrease in 24-hour UFC and/or improved signs and symptoms of Cushing's disease. The maximum decrease in UFC typically occurs after 2 months of therapy. If dose reductions are necessary due to AEs, reductions of 0.3 mg are recommended. Caution is recommended with drugs which prolong the QT interval. Cyclosporine levels may decrease with pasireotide and a dose increase of cyclosporine may be required to maintain cyclosporine levels. Bromocriptine levels may increase with pasireotide and a dose reduction of bromocriptine may be necessary.

Pasireotide has been studied in a phase II and a phase III trial for Cushing's disease. Both trials assessed changes in urinary free cortisol (UFC) level, a biomarker, rather than clinical symptoms of Cushing's disease. The phase III trial randomized 162 patients to pasireotide 600 mcg or 900 mcg subcutaneously twice daily for 6 months. No comparator arm was included. Pasireotide was considered efficacious based on the predefined study efficacy criteria of >15% responder rate which was achieved with both doses of pasireotide (15% 600 mcg, 26% 900 mcg); however, the study was not powered to compare study arms. Changes in clinical symptoms of Cushing's disease were considered secondary endpoints. Significant changes were noted in weight (-6.7 kg, $p<0.001$) as well as systolic (-6 mm Hg, $p=0.03$) and diastolic blood pressure (-3.7 mm Hg, $p=0.03$). However, changes in antihypertensive medications were allowed during the trial and

may have influenced the latter results. Lastly, the open-label, 15-day, phase II trial in 29 patients found 17% of patients normalized UFC with pasireotide 600 mcg. None of the pasireotide trials were of long enough duration to assess changes in mortality. Trial sizes are small due to the limited number of patients with Cushing's disease. Lastly, none of the trials included a comparator arm. Use of a placebo arm was considered unethical and, at the time of trial design, no other medications were FDA approved for Cushing's. Since that time, mifepristone (Korlym) has received approval for the control of hyperglycemia due to hypercortisolism in patients with Cushing's syndrome with diabetes mellitus (DM) or glucose intolerance that failed or are not eligible for surgery.

Pasireotide (Signifor® LAR) in the setting of acromegaly was approved based on two multicenter Phase III studies, C2305 and C2402, which respectively examined medically naïve patients, who have had prior surgery, or for whom surgery was not an option, and patients with acromegaly inadequately controlled on first generation somatostatin analogs. In both studies, higher rates of full biochemical control (defined as mean GH level <2.5mcg/L and normal IGF-1 levels) were achieved with Signifor LAR compared to a first generation somatostatin analog. A crossover extension to C2305 showed 17.3% (14/81) of patients that did not reach biochemical control (GH still ≥ 2.5 mcg/L and IGF-1 still above normal) were able to achieve control of both GH and IGF-1 after switching to pasireotide. Zero out of thirty-eight patients switching to octreotide achieved control. Pasireotide patients had more hyperglycemic adverse effects (27.2% vs. 13.2%)

A 12 month, multicenter, double-blind RCT superiority study (n=358) determined that pasireotide was superior to octreotide in acromegaly patients. Patients studied were medically naïve. Patients could have had a prior pituitary surgery, or otherwise refused surgery or had surgery contraindicated. The primary outcome was growth hormone falling under 2.5 µg/L as well as normal IGF-1 at month 12. Significantly more pasireotide LAR patients achieved control than octreotide LAR patients (31.3% vs 19.2%, p value = 0.007). Pasireotide patients had a significantly higher rate of hyperglycemia (57.3% vs. 21.7). Acromegaly guidelines available at this time do not recommend pasireotide as a first line option due to a shorter history of efficacy and safety vs. other somatostatin analogs.

An open-label, multicenter, single-arm, expanded-treatment study (2017) evaluated the safety profile of Signifor® LAR administered intramuscularly every 28 days in 44 adult patients with active acromegaly for an average of 37.6 weeks. There were 25 grade ≥3 treatment-emergent adverse events reported in 11 patients (25%), with 27.3% of those experiencing grade ≥3 hyperglycemia. There were 21 patients (48%) who needed to initiate antidiabetic medications. Overall, hyperglycemia-related adverse events were most common, but they were generally manageable.

Korlym® (mifepristone)

Korlym® (mifepristone) is a glucocorticoid receptor-II (GR-II) antagonist that has high affinity for the GR-II receptor but little affinity for the GR-I (mineralocorticoid) receptor. It also blocks progesterone receptors. There appears to be little or no affinity for estrogen, muscarinic, histaminic, or monoamine receptors. The approval of mifepristone for the treatment of hyperglycemia due to hypercortisolism secondary to Cushing's syndrome was primarily based on results from one 24 week, phase III, multicenter, open-label, single arm study (Study of the Efficacy and Safety of Mifepristone in the treatment of Endogenous Cushing's Syndrome [SEISMIC]). Results showed significant clinical, metabolic, and health-related quality of life improvements in 50 patients, the majority of whom had failed multiple therapeutic modalities. While the strength of evidence of efficacy is weak, the authors and FDA approval suggests benefits outweigh risks for this orphan indication with unmet need. An extension study for SEISMIC participants examining long-term safety and efficacy is ongoing. Numerous case reports and small retrospective studies of mifepristone use for hypercortisolism are also available in the literature. The majority of patients in these reports had failed multiple therapeutic modalities, including surgery, prior to use of mifepristone. Doses of the agent ranged from 200 to 2000 mg/day for up to 2 years. Most publications reported improvements in the clinical manifestations of the condition. Mifepristone has a large potential for drug-drug interactions via the CYP3A4, CYP2C8 and CYP2C9 pathways. Its efficacy data remains limited, and long-term data is unavailable.

Summary

Interpretation of available data on the efficacy and safety of most drugs currently used in the treatment of Cushing's disease is difficult. Published study designs have varied considerably with only a few small prospective, randomized, controlled studies available. Furthermore, there is significant variation in clinical outcomes or biochemical parameters used as the primary endpoint (eg, urine free cortisol [UFC], serum and salivary cortisol, and plasma ACTH), and reference values derived from a sufficiently large population are largely lacking, especially for some of the more recently developed assays. Unfortunately, criteria for defining a clear and effective response to treatment, and for disease control, are insufficient at this time.

2014 Update

Updated per literature search from July 1, 2013, through October 31, 2014. No changes required.

2015 Update

Updated per the package insert on June 2, 2015. Purpose of the update is to include a recently added indication (12/14) for the use of pasireotide (Signifor® LAR) in the setting of acromegaly.

2016 Update

Updated the rationale section for pasireotide and mifepristone per the literature search conducted from July 1, 2016, through December 7, 2016. No policy criteria changes were made with this review. References updated.

2017 Update

A literature search was conducted from December 1, 2016 through November 2, 2017. No policy criteria changes were made with this review. References updated.

2018 Update

A literature search was conducted from November 1, 2017 through October 31, 2018. No policy criteria changes were made with this review. References updated.

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History

Date	Comments
10/14/13	New policy. Add to Prescription Drug section. *Pasireotide (Signifor)*® and *mifepristone (Korlym)*® considered medically necessary to treat Cushing's disease when criteria are met.
12/17/14	Annual Review. Policy updated with literature review; no change in policy statement.
06/09/15	Annual Review. Policy scope expanded to address acromegaly; title expanded to include acromegaly. Medically necessary policy statement added for acromegaly with criteria of inadequate response to surgery and/or not a surgical candidate.
01/19/16	Coding update. New HCPCS code J2502, effective 1/1/16, added to policy.
01/01/17	Annual Review, approved December 13, 2016. Policy updated with literature review.
12/01/17	Annual Review, approved November 21, 2017. Policy was updated with literature review. Reference added. No policy changes were made.
12/01/18	Annual Review, approved November 21, 2018. No changes; references update.

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

Tiếng Việt (Vietnamese):
Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hợp đồng bảo hiểm của quý vị qua chương trình Premera Blue Cross. Xin xem ngày quan trọng trong thông báo này. Quý vị có thể phải thực hiện theo thông báo đúng trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357).