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.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| **Signifor® (pasireotide) SC** | **Signifor® (pasireotide) may be considered medically necessary for treatment of Cushing’s disease when ALL of the following conditions are true:**  
  • Patient has a documented diagnosis of Cushing’s disease established by any of the following tests:  
    o 24-hour urinary free-cortisol test  
    o Late-night salivary cortisol test  
    o Overnight low-dose dexamethasone suppression test  
    o Dexamethasone-corticotropin-releasing hormone (CRH) test  
  AND  
  • Patient is 18 years of age or older  
  AND  
  • Patient has failed pituitary surgery, or is not a surgical candidate  
  AND  
  • Patient has had a trial and treatment failure with **all** of the following, unless contraindicated or otherwise medically inappropriate:  
    o Ketoconazole  
    **AND**  
    o Cabergoline  
    **AND**  
    o Metopirone® (metyrapone) or Lysodren® (mitotane) |
| **Signifor® LAR (pasireotide) IM** | **Signifor® LAR (pasireotide) may be considered medically necessary for treatment of Cushing’s disease when ALL of the following conditions are true:**  
  • Patient has a documented diagnosis of Cushing’s disease established by any of the following tests:  
    o 24-hour urinary free-cortisol test  
    o Late-night salivary cortisol test  
    o Overnight low-dose dexamethasone suppression test  


<table>
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<tr>
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<td><strong>Drug</strong></td>
<td><strong>Medical Necessity</strong></td>
</tr>
</tbody>
</table>
| Artane® (trihexphenidyl) | o Artane® (trihexphenidyl) may be considered medically necessary for the treatment of hyperkinetic disorder when the following conditions are met:  
|                  | • Patient is 18 years of age or older  
|                  | AND  
|                  | • Patient has failed previous treatment with all of the following, unless contraindicated or otherwise medically inappropriate:  
|                  | o Trihexphenidyl  
|                  | AND  
|                  | o Diazepam  
|                  | AND  
|                  | o Haloperidol  
|                  | AND  
|                  | o Risperdal® (risperidone)  
|                  | AND  
|                  | o Fluoxetine® (fluoxetine)  
|                  | AND  
|                  | o Sertraline® (sertraline) |

**Signifor® LAR (pasireotide)** may be considered medically necessary for the treatment of acromegaly when the following conditions are met:  
• Patient has had a trial and treatment failure with all of the following, unless contraindicated or otherwise medically inappropriate:  
  o Ketoconazole  
  AND  
  o Cabergoline  
  AND  
  o Metopirone® (metylapone) or Lysodren® (mitotane)  

**Somavert**® (pegvisomant) SC  
Somavert® (pegvisomant) may be considered medically necessary for the treatment of acromegaly when the following conditions are met:  
• Patient is 18 years of age or older  
AND  
• Had an inadequate response to surgery or radiation therapy  
OR  
• Surgery and radiation therapy is not appropriate  

**Korlym® (mifepristone)** oral  
Korlym® (mifepristone) may be considered medically necessary for treatment of hyperglycemia in patients with Cushing’s disease when the following conditions are met:  
• Patient is 18 years of age or older  
AND  
• Patient has type 2 diabetes mellitus or glucose intolerance
Drug Medical Necessity

AND

- Hyperglycemia is secondary to Cushing’s disease

AND

- Patient has failed pituitary surgery, or is not a surgical candidate

Drug Investigational

Signifor® (pasireotide), Signifor® LAR (pasireotide), Somavert® (pegvisomant), Korlym® (mifepristone)

All other uses of Signifor® (pasireotide), Signifor® LAR (pasireotide), Somavert® (pegvisomant), and Korlym® (mifepristone) for conditions not outlined in this policy are considered investigational.

Length of Approval

<table>
<thead>
<tr>
<th>Approval</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial authorization</td>
<td>All drugs listed in policy may be approved up to 1 year.</td>
</tr>
<tr>
<td>Re-authorization criteria</td>
<td>Future re-authorization of all drugs listed in policy may be approved up to 1 year 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, physical evaluation and medication history

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**

Signifor® (pasireotide) and Korlym® (mifepristone) are managed through the Pharmacy benefit. Signifor® LAR (pasireotide) and Somavert® (pegvisomant) are managed through both the Pharmacy benefit and Medical 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 glucocorticoids 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 <2.5 mcg/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.

**Somavert® (pegvisomant)**

Somavert selectively binds to growth hormone (GH) receptors on cell surfaces, where it blocks the binding of endogenous GH, and thus interferes with GH signal transduction. Inhibition of GH action results in decreased serum concentrations of insulin-like growth factor-I (IGF-I), as well as other GH-responsive serum proteins, including IGF binding protein-3 (IGFBP-3), and the acid-labile subunit (ALS).

Somavert has been studied in a randomized, double-blinded, placebo-controlled, 12-week study evaluating the safety and efficacy of Somavert 10 mg, 15 mg, or 20 mg in patients with acromegaly. Following withdrawal from previous medical therapy, the 80 patients randomized to treatment with Somavert received a subcutaneous (SC) loading dose, followed by 10, 15, or 20 mg/day SC. The three groups that received Somavert showed dose-dependent reductions in serum levels of IGF-I, free IGF-I, IGFBP-3, and ALS compared with placebo at all post-baseline visits. After 12 weeks of treatment, the mean serum IGF-I concentration decreased from baseline by 4.0%, 26.7%, 50.1%, and 62.5% in the placebo, 10 mg, 15 mg, and 20 mg arms, respectively. This difference was significant in all treatment arms compared to placebo. Normalization of serum IGF-I concentrations were achieved in 10%, 54%, 81%, and 89% of subjects in the placebo, 10 mg, 15 mg, and 20 mg arms, respectively. In patients treated with Somavert 15 mg or 20 mg daily, there were significant decreases in ring size, soft-tissue swelling, the degree of excessive perspiration, and fatigue.

Somavert is contraindicated in patients with a history of hypersensitivity to any of its components.
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.

2019 Update

A literature search was conducted from November 1, 2018 through August 28, 2019. Reviewed all FDA-approved indications for drugs in policy and made additional updates to Signifor® LAR (pasireotide) to clarify Signifor® LAR is indicated for both acromegaly and Cushing’s disease. Policy criteria rewritten and revised for Korlym® (mifepristone) to reflect prescribing information. Added policy criteria for Somavert® (pegvisomant). References updated.
References

17. Korlym® (mifepristone) prescribing information. Corcept Therapeutics; Menlo Park, CA. February 2012.

**History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/14/13</td>
<td>New policy. Add to Prescription Drug section. Pasireotide (Signifor)® and mifepristone (Korlym)® considered medically necessary to treat Cushing’s disease when criteria are met.</td>
</tr>
<tr>
<td>12/17/14</td>
<td>Annual Review. Policy updated with literature review; no change in policy statement.</td>
</tr>
<tr>
<td>06/09/15</td>
<td>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.</td>
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<tr>
<td>01/19/16</td>
<td>Coding update. New HCPCS code J2502, effective 1/1/16, added to policy.</td>
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<tr>
<td>01/01/17</td>
<td>Annual Review, approved December 13, 2016. Policy updated with literature review.</td>
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<tr>
<td>12/01/17</td>
<td>Annual Review, approved November 21, 2017. Policy was updated with literature review. Reference added. No policy changes were made.</td>
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<tr>
<td>12/01/18</td>
<td>Annual Review, approved November 21, 2018. No changes; references update.</td>
</tr>
<tr>
<td>10/01/19</td>
<td>Annual Review, approved September 10, 2019. Criteria updated for Korlym® (mifepristone), Signifor® (pasireotide) and Signifor® LAR (pasireotide). New policy criteria added for Somavert® (pegvisomant).</td>
</tr>
</tbody>
</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). ©2019 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.

If you if you believe that Premera has failed to provide these services or discriminate 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 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 S09F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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 S09F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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).

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Oromo (Cushite):

