Whole Exome and Whole Genome Sequencing for Diagnosis of Genetic Disorders

Introduction

Our DNA contains all of our genetic material, and makes us who we are. Our DNA contains about 20,000 genes which are packaged into 46 chromosomes (23 pairs). Genes are very important because they tell our cells how to make proteins. Although there are tens of thousands of genes, they make up only about 1% of our entire DNA. A large part of our DNA doesn’t code for any proteins. The protein-coding genes are also called “exomes”.

The entire collection of DNA is called the “whole genome”. If a person was only talking about the genes themselves that are contained within the whole genome, they are called the “whole exome”.

“Whole genome sequencing” is a test that looks at the entire genome, including parts of the DNA that don’t contain any genes. “Whole exome sequencing” is a test that only looks at the exomes, which is that part of the DNA that contains genes that code for proteins. As an analogy, an entire football game would be your whole genome. Only the game highlights (1% of the game) would be the exomes. Whole genome sequencing would be like watching the entire football game from start to finish, while whole exome sequencing would be like watching only the game highlights the next day.

Whole genome and whole exome sequencing tests have been used to help diagnose genetic disorders in people. Whole genome sequencing is always considered to be investigational. Not
enough good quality medical studies have been done to show that whole genome sequencing is reliable and helpful in diagnosing genetic conditions. However, whole exome sequencing may be medically necessary in some situations. This policy describes when whole exome sequencing may be 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

The policy statement is intended to address the use of whole exome and whole genome sequencing for the diagnosis of genetic disorders in patients with suspected genetic disorders and for population-based screening.

This policy does not address the use of whole exome and whole genome sequencing for preimplantation genetic diagnosis or screening, prenatal (fetal) testing, or testing of cancer cells.

<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole exome sequencing</td>
<td>Whole exome sequencing may be considered medically necessary for the evaluation of unexplained congenital or neurodevelopmental disorders in children under the age of 18 when ALL of the following criteria are met:</td>
</tr>
<tr>
<td></td>
<td>• The patient has been evaluated by a clinician with expertise in clinical genetics and counseled about the potential risks of genetic testing.</td>
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<tr>
<td></td>
<td>AND</td>
</tr>
<tr>
<td></td>
<td>• There is potential for a change in management and clinical outcome for the individual being tested.</td>
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<td></td>
<td>AND</td>
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<td></td>
<td>• A genetic etiology is felt to be the most likely explanation for the patient’s signs and symptoms despite previous genetic testing (eg, chromosomal microarray analysis and/or targeted single-gene testing), OR when previous genetic testing has</td>
</tr>
</tbody>
</table>
Service | Medical Necessity
--- | ---
 | failed to yield a diagnosis, and the affected individual is faced with invasive procedures or testing as the next diagnostic step (eg, muscle biopsy).
Whole exome sequencing is considered investigational for the diagnosis of genetic disorders in all other situations.

Service | Investigational
--- | ---
Whole genome sequencing | Whole genome sequencing is considered investigational for the diagnosis of genetic disorders.
Whole exome sequencing, Whole genome sequencing | Whole exome sequencing and whole genome sequencing are considered investigational for screening of asymptomatic individuals for genetic disorders.

## Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CPT</strong></td>
<td>Germline disorders, gene rearrangement detection by whole genome next-generation sequencing, DNA, whole blood, report of specific gene rearrangement(s)</td>
</tr>
<tr>
<td>0012U</td>
<td>Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis</td>
</tr>
<tr>
<td>81415</td>
<td>Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (eg, parents, siblings) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>81416</td>
<td>Exome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)</td>
</tr>
<tr>
<td>81417</td>
<td>Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis</td>
</tr>
<tr>
<td>81425</td>
<td>Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>81427</td>
<td>Genome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (eg, updated knowledge or unrelated condition/syndrome)</td>
</tr>
<tr>
<td>81479</td>
<td>Unlisted molecular pathology code</td>
</tr>
</tbody>
</table>

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**Related Information**

**Definition of Terms**

**Exon:** The specific part of a gene that is involved with making a protein

**Exome:** The complete set of exons

**Gene:** A hereditary unit found within the DNA that tells the body how to make proteins

**Genome:** The entire collection of DNA

**Genotype:** The entire set of genes that a person has within their DNA; their “genetic makeup”

**Phenotype:** The observable physical characteristics of a person that are caused by their genes (eg, hair color, whether their ear lobes are attached or free, etc.).

**Variant:** a change to a gene. Also called a mutation.

**Whole Exome Sequencing:** A genetic test that looks at all of the protein-coding genes within the DNA

**Whole Genome sequencing:** A genetic test that looks at all of a person's DNA, including the parts that don’t contain genes

**Trio Testing**

Testing of the child and both parents can increase the chance of finding a definitive diagnosis.
Genetic Counseling

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Evidence Review

Description

Whole exome sequencing (WES) sequences the portion of the genome that contains protein-coding DNA, while whole genome sequencing (WGS) sequences both coding and noncoding regions of the genome. WES and WGS have been proposed for use in patients presenting with disorders and anomalies that have not been explained by standard clinical workup. Potential candidates for WES and WGS include patients who present with a broad spectrum of suspected genetic conditions.

Background

*Whole Exome Sequencing and Whole Genome Sequencing*

Whole exome sequencing (WES) is targeted next-generation sequencing of the subset of the human genome that contains functionally important sequences of protein-coding DNA, while whole genome sequencing (WGS) uses next-generation sequencing techniques to sequence both coding and noncoding regions of the genome. WES and WGS have been proposed for use in patients presenting with disorders and anomalies not explained by standard clinical workup. Potential candidates for WES and WGS include patients who present with a broad spectrum of suspected genetic conditions.
Given the variety of disorders and management approaches, many potential health outcomes may result from having a definitive genetic diagnosis. In general, the outcomes of a molecular genetic diagnosis include (1) impacting the search for a diagnosis, (2) deciding on appropriate follow-up that can benefit a child by reducing morbidity, and (3) affecting reproductive planning for parents and potentially the affected patient.

The standard diagnostic workup for patients with suspected Mendelian disorders may include combinations of radiographic, electrophysiologic, biochemical, biopsy, and targeted genetic evaluations. The search for a diagnosis may thus become a time-consuming and expensive process.

**WES and WGS Technology**

WES or WGS using next-generation sequencing technology can help to efficiently obtain a genetic diagnosis in patients. WES is limited to most of the protein-coding sequence of an individual (~85%), is composed of about 20,000 genes and 180,000 exons (protein-coding segments of a gene), and constitutes approximately 1% of the genome. It is believed that the exome contains about 85% of heritable disease-causing mutations. WES has the advantage of speed and efficiency relative to Sanger sequencing of multiple genes. However, WES also shares some limitations with Sanger sequencing. For example, it will not identify the following: intronic sequences or gene regulatory regions; chromosomal changes; large deletions; duplications; or rearrangements within genes, nucleotide repeats, or epigenetic changes. WGS uses techniques similar to WES, but includes noncoding regions. WGS has greater ability to detect large deletions or duplications in protein-coding regions compared with WES, but it requires greater data analytics. Technical aspects of WES and WGS are evolving, including the development of databases such as the National Institutes of Health’s ClinVar database ([http://www.ncbi.nlm.nih.gov/clinvar/](http://www.ncbi.nlm.nih.gov/clinvar/)) to catalog variants, uneven sequencing coverage, gaps in exon capture before sequencing, and difficulties with narrowing the large initial number of variants to manageable numbers without losing likely candidate mutations. The variability contributed by the different platforms and procedures used by different clinical laboratories offering exome sequencing as a clinical service is unknown.

In 2013, the American College of Medical Genetics and Genomics, Association for Molecular Pathology, and College of American Pathologists convened a workgroup to develop standard terminology for describing sequence variants. Guidelines that were developed by this workgroup, published in 2015, describe criteria for classifying pathogenic and benign sequence variants based on types of data into 5 categories: pathogenic, likely pathogenic, uncertain significance, likely benign, and benign.²
Summary of Evidence

For individuals who have unexplained multiple congenital anomalies or a neurodevelopmental disorder and receive WES, the evidence includes large case series and a within-subject comparison. Relevant outcomes are test accuracy and validity, functional outcomes, changes in reproductive decision making, and resource utilization. Patients who have multiple congenital anomalies or a developmental disorder with a suspected genetic etiology, but the specific genetic alteration is unclear or unidentified by standard clinical workup, may be left without a clinical diagnosis of their disorder, despite a lengthy diagnostic workup. For a substantial proportion of these patients, WES may return a likely pathogenic variant. Several large series and a number of smaller series report diagnostic yields of WES ranging from 25% to 60%, depending on the individual’s age, phenotype, and previous workup. One comparative study found a 44% increase in yield compared with standard testing strategies. Many of the studies have also reported changes in patient management, including medication changes, discontinuation of or additional testing, ending the diagnostic odyssey, and family planning. However, the wide variance in diagnostic yield confers uncertainty. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have a suspected genetic disorder lacking multiple congenital anomalies or a neurodevelopmental phenotype who receive WES, the evidence includes small case series. Relevant outcomes are test accuracy and validity, functional outcomes, changes in reproductive decision making, and resource utilization. There are increasing reports of use of WES to identify a molecular basis for disorders other than multiple congenital anomalies or neurodevelopmental disorders. The diagnostic yields in these studies range from as low as 3% to 60%. One concern with WES is the possibility of incidental findings. Some studies have reported on the use of a virtual gene panel with restricted analysis of disease-associated genes, and WES data allows reanalysis as new genes are linked to the patient phenotype. Overall, there are a limited number of patients who have been studied for any specific disorder, and clinical use of WES for these disorders is at an early stage. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with a suspected genetic disorder who receive WGS, the evidence includes case series. Relevant outcomes are test accuracy and validity, functional outcomes, changes in reproductive decision making, and resource utilization. WGS has increased coverage and diagnostic yield compared with WES, but the technology is limited by the amount of data generated and greater need for storage and analytic capability. Several authors have proposed that as WGS becomes feasible on a larger scale, it may in the future become the standard first-
tier diagnostic test. At present, there is limited data on the clinical use of WGS. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02380729</td>
<td>Mutation Exploration in Non-acquired, Genetic Disorders and Its Impact on Health Economy and Life Quality</td>
<td>200</td>
<td>Dec 2017</td>
</tr>
<tr>
<td>NCT02077894</td>
<td>Whole Exome and Whole Genome Sequencing for Genotyping of Inherited and Congenital Eye Cond</td>
<td>310</td>
<td>Sep 2018</td>
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<tr>
<td>NCT02699190</td>
<td>LeukoSEQ: Whole Genome Sequencing as a First-Line Diagnostic Tool for Leukodystrophies</td>
<td>50</td>
<td>Apr 2020</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

Practice Guidelines and Position Statements

The American College of Medical Genetics and Genomics (ACMG) states that diagnostic testing with whole exome sequencing (WES) and whole genome sequencing (WGS) should be considered in the clinical diagnostic assessment of a phenotypically affected individual when:

- “The phenotype or family history data strongly implicate a genetic etiology, but the phenotype does not correspond with a specific disorder for which a genetic test targeting a specific gene is available on a clinical basis.

- “A patient presents with a defined genetic disorder that demonstrates a high degree of genetic heterogeneity, making WES or WGS analysis of multiple genes simultaneously a more practical approach.

- “A patient presents with a likely genetic disorder but specific genetic tests available for that phenotype have failed to arrive at a diagnosis.
• “A fetus with a likely genetic disorder in which specific genetic tests, including targeted sequencing tests, available for that phenotype have failed to arrive at a diagnosis.”

ACMG states that for screening purposes:

WGS/WES may be considered in preconception carrier screening, using a strategy to focus on genetic variants known to be associated with significant phenotypes in homozygous or hemizygous progeny.

ACMG has also recommended that that WGS and WES should not be used at this time as an approach to prenatal screening or as a first-tier approach for newborn screening.

In March 2013, ACMG finalized its recommendations for reporting incidental findings in WGS and WES. ACMG determined that reporting some incidental findings would likely have medical benefit for the patients and families of patients undergoing clinical sequencing, recommended that, when a report is issued for clinically indicated exome and genome sequencing, a minimum list of conditions, genes, and variants should be routinely evaluated and reported to the ordering clinician.

**American Academy of Neurology et al**

In 2014, the American Academy of Neurology and American Association of Neuromuscular and Electrodiagnostic Medicine issued evidenced-based guidelines for the diagnosis and treatment of limb-girdle and distal dystrophies. Their recommendations are shown in Table 2.

**Table 2. Guidelines on Limb-Girdle Muscular Dystrophy**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>For patients with suspected muscular dystrophy, clinicians should use a clinical approach to guide genetic diagnosis based on the clinical phenotype, including the pattern of muscle involvement, inheritance pattern, age at onset, and associated manifestations (eg, early contractures, cardiac or respiratory involvement).</td>
<td>B</td>
</tr>
<tr>
<td>In patients with suspected muscular dystrophy in whom initial clinically directed genetic testing does not provide a diagnosis, clinicians may obtain genetic consultation or perform parallel sequencing of targeted exomes, whole-exome sequencing, whole-genome screening, or next-generation sequencing to identify the genetic abnormality.</td>
<td>C</td>
</tr>
<tr>
<td>Recommendation</td>
<td>Level of Evidence</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Management of cardiac complications</strong></td>
<td></td>
</tr>
<tr>
<td>Clinicians should refer newly diagnosed patients with (1) limb-girdle muscular dystrophy (LGMD) 1A, LGMD 1B, LGMD 1D, LGMD 1E, LGMD 2C–K, LGMD 2M–P, … or (2) muscular dystrophy without a specific genetic diagnosis for cardiology evaluation, including electrocardiogram (ECG) and structural evaluation (echocardiography or cardiac magnetic resonance imaging [MRI]), even if they are asymptomatic from a cardiac standpoint, to guide appropriate management.</td>
<td>B</td>
</tr>
<tr>
<td>If ECG or structural cardiac evaluation (eg, echocardiography) has abnormal results, or if the patient has episodes of syncope, near-syncope, or palpitations, clinicians should order rhythm evaluation (eg, Holter monitor or event monitor) to guide appropriate management.</td>
<td>B</td>
</tr>
<tr>
<td>Clinicians should refer muscular dystrophy patients with palpitations, symptomatic or asymptomatic tachycardia or arrhythmias, or signs and symptoms of cardiac failure for cardiology evaluation.</td>
<td>B</td>
</tr>
<tr>
<td>It is not obligatory for clinicians to refer patients with LGMD 2A, LGMD 2B, and LGMD 2L for cardiac evaluation unless they develop overt cardiac signs or symptoms.</td>
<td>B</td>
</tr>
<tr>
<td><strong>Management of pulmonary complications</strong></td>
<td></td>
</tr>
<tr>
<td>Clinicians should order pulmonary function testing (spirometry and maximal inspiratory/expiratory force in the upright and, if normal, supine positions) or refer for pulmonary evaluation (to identify and treat respiratory insufficiency) in muscular dystrophy patients at the time of diagnosis, or if they develop pulmonary symptoms later in their course.</td>
<td>B</td>
</tr>
<tr>
<td>In patients with a known high risk of respiratory failure (eg, those with LGMD 2I …), clinicians should obtain periodic pulmonary function testing (spirometry and maximal inspiratory/expiratory force in the upright position and, if normal, in the supine position) or evaluation by a pulmonologist to identify and treat respiratory insufficiency.</td>
<td>B</td>
</tr>
<tr>
<td>It is not obligatory for clinicians to refer patients with LGMD 2B and LGMD 2L for pulmonary evaluation unless they are symptomatic.</td>
<td>C</td>
</tr>
<tr>
<td>Clinicians should refer muscular dystrophy patients with excessive daytime somnolence, nonrestorative sleep (eg, frequent nocturnal arousals, morning headaches, excessive daytime fatigue), or respiratory insufficiency based on pulmonary function tests for pulmonary or sleep medicine consultation for consideration of noninvasive ventilation to improve quality of life.</td>
<td>B</td>
</tr>
</tbody>
</table>

LGMD: limb-girdle muscular dystrophy; ECG: electrocardiogram

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Whole exome or genome sequencing tests as a clinical service are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

References


### History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/11/13</td>
<td>New Policy. Whole exome sequencing is considered investigational for all indications. Policy renumbered from 2.04 to 12.04 to align with genetic testing category.</td>
</tr>
<tr>
<td>11/10/14</td>
<td>Annual Review. Policy updated with literature review through August 3, 2014. References 2, 4-5, and 8-13 added. Whole genome sequencing added to policy statement; whole genome sequencing considered investigational. New CPT codes, 81415-81417, 81425 and 81426, effective 1/1/15, added to the policy.</td>
</tr>
<tr>
<td>02/01/16</td>
<td>Coding update. Removed duplicate code 81416.</td>
</tr>
<tr>
<td>12/01/16</td>
<td>Annual Review, approved November 8, 2016. Policy updated with literature review through August 22, 2016; references 9, 11, 14, 16-18, and 20-22 added. Rationale revised. No change to the policy statement.</td>
</tr>
<tr>
<td>02/01/17</td>
<td>Annual Review, approved January 10, 2017. Policy updated with literature review through August 22, 2016; references 9, 11, 14, 16-18, and 20-22 added. Rationale revised. Whole exome sequencing, previously considered investigational, may now be considered medically necessary for diagnosis of individuals under the age of 18 with multiple congenital anomalies or a neurodevelopmental disorder. All other uses of whole exome and whole genome sequencing are considered investigational. Policy statement added that whole exome and whole genome sequencing are considered investigational for screening of asymptomatic individuals. Removed appendix table.</td>
</tr>
<tr>
<td>10/01/17</td>
<td>Coding update. Added new CPT code 0012U (effective 8/1/17).</td>
</tr>
<tr>
<td>10/06/17</td>
<td>Policy moved into new format; no change to policy statements.</td>
</tr>
<tr>
<td>12/01/17</td>
<td>Annual Review, approved November 9, 2017. Policy updated with literature search through August 2017; references 6-8, 19, 24-25, 27, and 30 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>03/09/18</td>
<td>Minor update, clarified medical necessity criteria.</td>
</tr>
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</table>
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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).

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).

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 maaring magaling na malalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na dapat na iisagawa sa ilang mga itinakdang panahon. Ua e taua e taula e talung ewalang may mga tulong na dapat na iisagawa.

Român (Romanian):

Thai (Thai):
ประกาศนี้มีข้อมูลสําคัญ ซึ่งอาจมีกําหนดการในประกาศนี้ มีกําหนดการในประกาศนี้ สามารถใช้สําหรับประกันสุขภาพของคุณผ่าน Premera Blue Cross และจะมีข้อมูลที่ใช้ในการแยกตัวคุณออกจากคุณหากคุณต้องการ ประกาศนี้มีข้อมูลสําคัญ ซึ่งอาจมีกําหนดการในประกาศนี้ มีกําหนดการในประกาศนี้ สามารถใช้สําหรับประกันสุขภาพของคุณผ่าน Premera Blue Cross.

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. Дозвоніться за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):