Genetic Testing for Neurofibromatosis

BCBSA Ref. Policy: 2.04.137

Effective Date: April 1, 2018
Last Revised: March 20, 2018
Replaces: 12.04.137

RELATED MEDICAL POLICIES:
12.04.116 Invasive Prenatal (Fetal) Diagnostic Testing
12.04.305 Preimplantation Genetic Testing in Embryos
12.04.518 Preconception Testing for Carrier Status of Genetic Diseases

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

Neurofibromatosis is a genetic condition affecting the nervous system. It generally affects the growth and formation of nerve cells and causes tumors to grow on nerves. The tumors are usually noncancerous but sometimes can become cancerous. The tumors can occur anywhere in the nervous system, such as the brain, spinal cord, and nerves. Neurofibromatosis is most often diagnosed in childhood or early adulthood. Diagnosis can usually be made based on the patient’s physical signs and symptoms. There are times, however, where a firm diagnosis can’t be made. A genetic test may be needed in such a situation. This policy describes when a genetic test may be considered medically necessary for neurofibromatosis.

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
Testing Purpose | Medical Necessity
--- | ---
Diagnosis is suspected | Genetic testing for neurofibromatosis (NF) may be considered medically necessary when the diagnosis is suspected due to clinical signs and/or symptoms, but a definitive diagnosis cannot be made without genetic testing.

At-risk relatives with no signs of disease | Genetic testing for neurofibromatosis in at-risk relatives* with no signs and/or symptoms of the disorder may be considered medically necessary when a definitive diagnosis cannot be made without genetic testing AND one of the following criteria is met:
- A close relative (i.e., first, second, or third-degree relative)** has a known NF variant

**OR**
- A close relative has been diagnosed with neurofibromatosis but their genetic status is unavailable

*See Benefit Application

** See Definition of Terms

Prenatal testing | Prenatal testing (either prior to embryo implantation or in utero) may be considered medically necessary when one of the biological parents has clinically diagnosed neurofibromatosis or has a known NF gene mutation.

Criteria not met | Genetic testing for neurofibromatosis is considered investigational when criteria in this policy are not met.

Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>CPT</td>
<td>Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of &gt;10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)</td>
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<tr>
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<td>Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or</td>
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<td>Code</td>
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<td>81408</td>
<td>Molecular pathology procedure, Level 9 (eg, analysis of &gt;50 exons in a single gene by DNA sequence analysis)</td>
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<td>Includes the following test: NF1 (neurofibromin 1) (eg, neurofibromatosis, type 1), full gene sequence.</td>
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**Related Information**

**Definition of Terms**

**Close blood relatives - degrees of relationship:** Close blood relatives are on the same side of the family, either maternal (mother) or paternal (father). The maternal and paternal sides of the family should be considered independently for familial patterns of inheritance.

<table>
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<td>1st</td>
<td>Parents, siblings (brother/sister), and children</td>
</tr>
<tr>
<td>2nd</td>
<td>Grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings (brother/sister)</td>
</tr>
<tr>
<td>3rd</td>
<td>Great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins</td>
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</table>
**Mutation scanning:** Mutation scanning is a process by which a particular segment of DNA is screened to identify sequence variants. Variant gene regions are then further analyzed (e.g., by sequencing) to identify the sequence alteration. Mutation scanning allows for screening of large genes and novel sequence variants.

**Neurofibromas:** Neurofibromas are tumors of the peripheral nerves.

**Schwann cells:** Schwann cells cover the nerve fibers in the peripheral nervous system and form the myelin sheath.

**Schwannomas:** Tumors that begin in Schwann cells that help form the myelin sheath.

**Simplex disease:** Simplex disease is a single occurrence of a disease in a family.

**Somatic mosaicism:** Somatic mosaicism is the occurrence of 2 genetically distinct populations of cells within an individual, derived from a postzygotic mutation. Unlike inherited variants, somatic mosaic variants may affect only a portion of the body and are not transmitted to progeny.

**Genetic Counseling**

Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual’s family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

**Testing Strategy**

For evaluation of neurofibromatosis type 1 (NF1), testing for a variety of pathogenic variants of NF1, preferably through a multistep variant detection protocol, is indicated. If no NF1
pathogenic variants are detected in patients with suspected NF1, testing for SPRED1 variants is reasonable.

**Benefit Application**

Some plans may have contract or benefit exclusions for genetic testing.

When possible, genetic testing for neurofibromatosis should be performed in an affected family member. In this way, at-risk family members who have no signs of the disease can be tested to look for the specific gene variant found in the affected family member. However, coverage for testing of the affected index case (proband) depends on contract benefit language.

Specific contract language must be reviewed and considered when determining coverage for testing. In some cases, coverage for testing the index case may be available through the contract that covers the unaffected, at-risk individual who will benefit from knowing the results of the genetic test.

**Evidence Review**

**Description**

Neurofibromatoses are autosomal dominant genetic disorders associated with tumors of the peripheral and central nervous systems. There are 3 clinically and genetically distinct forms: neurofibromatosis (NF) type 1 (NF1), NF type 2 (NF2), and schwannomatosis. The potential benefit of genetic testing for NF is to confirm the diagnosis in an individual with suspected NF who does not fulfill diagnostic clinical diagnostic criteria. It may also be useful to determine future risk of NF in asymptomatic at-risk relatives.

**Background**

*Neurofibromatosis Type 1*

NF1 (also known as von Recklinghausen disease) is one of the most common dominantly inherited genetic disorders, with an incidence at birth of 1 in 3000 individuals.
Clinical Characteristics

The clinical manifestations of NF1 show extreme variability. Variations are seen between unrelated individuals, among affected individuals within a single family, and within a single person at different times in life. NF1 is characterized by multiple café-au-lait spots, axillary and inguinal freckling, multiple cutaneous neurofibromas, and Lisch nodules in the iris. Segmental NF1 is limited to 1 area of the body. Many individuals with NF1 only develop cutaneous manifestations of the disease and Lisch nodules.

Cutaneous Manifestations

Café-au-lait macules occur in nearly all affected individuals, and intertriginous freckling occurs in almost 90%. Café-au-lait macules are common in the general population, but when more than 6 are present, NF1 should be suspected. Café-au-lait spots are often present at birth and increase in number during the first few years of life.

Neurofibromas

Neurofibromas are benign tumors of Schwann cells that affect virtually any nerve in the body and develop in most people with NF1. They are divided into cutaneous and plexiform types. Cutaneous neurofibromas, which develop in almost all people with NF1, are discrete, soft, sessile, or pedunculated tumors. Discrete cutaneous and subcutaneous neurofibromas are rarely seen before late childhood. They may vary from a few to hundreds or thousands, and the rate of development may vary greatly from year to year. Cutaneous neurofibromas do not carry a risk of malignant transformation, but may be a major cosmetic problem in adults.

Plexiform neurofibromas, which occur in about half of individuals with NF1, are more diffuse growths that may be locally invasive. They can be superficial or deep and, therefore, the extent cannot be determined by clinical examination alone; magnetic resonance imaging (MRI) is the method of choice for imaging plexiform neurofibromas.¹ Plexiform neurofibromas represent a major cause of morbidity and disfigurement in individuals with NF1. They tend to develop and grow in childhood and adolescence and then stabilize throughout adulthood.¹ Plexiform neurofibromas can compress the spinal cord or airway and can transform into malignant peripheral nerve sheath tumors. Malignant peripheral nerve sheath tumors occur in approximately 10% of affected individuals.¹
**Central Nervous System Tumors**

Optic gliomas, which can lead to blindness, usually develop in the first 6 years of life. Symptoms may include loss of visual acuity or proptosis, but the gliomas may not become symptomatic until later in childhood or in adulthood.

While optic pathway gliomas are particularly associated with NF1, other central nervous system (CNS) tumors, including astrocytomas and brainstem gliomas, are also frequently seen in NF1.

**Other Findings**

Other findings in NF1 include:

- Intellectual disability occurs about twice as often as in the general population, and features of autism spectrum disorder are seen in up to 30% of children with NF1.
- Musculoskeletal features include dysplasia of the long bones, most often the tibia and fibula, which is almost always unilateral. Generalized osteopenia is more common in people with NF1 and osteoporosis is more common and occurs at a younger age than in the general population.\(^1\)
- Cardiovascular involvement often includes hypertension. Vasculopathies may involve arteries of the heart, brain, or major systemic arteries, and can have serious or fatal consequences. Pulmonic valve stenosis may occur, and congenital heart defects and hypertrophic cardiomyopathy are also often seen in individuals with NF1 whole gene deletions.\(^1\) Adults may develop pulmonary hypertension, often in association with parenchymal lung disease.
- Lisch nodules are harmless hamartomas of the iris.

**Diagnosis**

Although the clinical manifestations of NF1 are extremely variable and some are age-dependent, the diagnosis can usually be made based on clinical findings, and genetic testing is rarely needed.\(^1\)

The clinical diagnosis of NF1 should be suspected in individuals who meet the criteria developed by the National Institute of Health (NIH). The criteria are met when an individual has two or more of the following features:
• Six or more café-au-lait macules greater than 5mm in greatest diameter in prepubertal individuals and greater than 15mm in postpubertal individuals
• Two or more neurofibromas of any type or one plexiform neurofibroma
• Freckling in the axillary or inguinal regions
• Optic glioma
• Two or more Lisch nodules (raised, tan-colored hamartomas of the iris)
• A distinctive osseous lesion such as sphenoid dysplasia or tibial pseudarthrosis
• A first degree relative with NF1 as defined by the prior criteria

In adults, the clinical diagnostic criteria are highly specific and sensitive for a diagnosis of NF1.\(^1\)

Approximately half of the children with NF1 and no known family history of NF1 meet the NIH criteria for the clinical diagnosis by 1 year of age. Almost all meet the criteria by 8 years of age because many features of NF1 increase in frequency with age. Children who have inherited NF1 from an affected parent can usually be diagnosed within the first year of life because the diagnosis only requires 1 diagnostic clinical feature in addition to a family history of the disease. This feature is usually multiple café-au-lait spots which are present in infancy in more than 95% of individuals with NF1.\(^1\)

A diagnosis of NF1 should be suspected in young children with multiple café-au-lait spots even if they have no other features of NF1 and they do not have a parent with signs of NF1. These children should be followed clinically.\(^2\) A definitive diagnosis of NF1 using NIH criteria can be made in most children by 4 years of age.\(^1\)

**Genetics**

NF1 is caused by dominant loss-of-function variants in the NF1 gene, which is a tumor suppressor gene located at chromosome 17q11.2. This gene encodes neurofibromin, a negative regulator of RAS activity. About half of affected individuals have it as a result of a de novo NF1 variant. Penetrance is virtually complete after childhood; however, expressivity is highly variable.

The variants responsible for NF1 are very heterogeneous and include nonsense and missense single-nucleotide changes, single base insertions or deletions, splicing variants (≈30% of cases), whole gene deletions (≈5% of cases), intragenic copy number variants, and other structural
rearrangements. Several thousand pathogenic NF1 variants have been identified, however, none is frequent.¹

Management

Patient management guidelines for NF1 have been developed by the American Academy of Pediatrics, the National Society of Genetic Counselors and other expert groups.¹³

After an initial diagnosis of NF1, the extent of the disease should be established by personal medical history and physical examination. Particular attention should be paid to features of NF1, such as ophthalmologic evaluation including slit lamp examination of the irides, developmental assessment in children, and other studies as indicated on the basis of clinically apparent signs or symptoms.¹

Surveillance recommendations for an individual with NF1 include having a regular annual visit with a skin examination looking for new peripheral neurofibromas, signs of plexiform neurofibroma or progression of existing lesions. The individual should also be checked for hypertension and undergo other studies (eg, MRI) as indicated based on clinically apparent signs or symptoms. An appropriate specialist should also monitor abnormalities of the central nervous system, skeletal system, and/or cardiovascular system. In children, recommendations include an annual ophthalmologic examination in early childhood (less frequently in older children and adults), and regular developmental assessment.

Long-term care for individuals with NF1 aims at early detection and symptomatic treatment of complications.

It is recommended that radiotherapy be avoided, if possible, because radiotherapy in individuals with NF1 appears to be associated with a high risk of developing malignant peripheral nerve sheath tumor within the field of treatment.

Legius Syndrome

Clinical Characteristics

A few clinical syndromes may overlap clinically with NF1. In most cases, including Proteus syndrome, Noonan syndrome, McCune-Albright syndrome, and LEOPARD syndrome, patients will be missing key features or will have features of the other disorder. However, the Legius syndrome is a rare autosomal-dominant disorder characterized by multiple café-au-lait macules,
intertriginous freckling, macrocephaly, lipomas, and potential attention-deficit/hyperactivity disorder. Misdiagnosis of Legius syndrome as NF1 might result in overtreatment and psychological burden on families about potential serious NF-related complications.

**Genetics**

Legius syndrome is associated with pathogenic loss-of-function variants in the *SPRED1* gene on chromosome 15, which is the only known gene associated with Legius syndrome.

**Management**

Legius syndrome typically follows a benign course and management generally focuses on treatment of manifestations and prevention of secondary complications. Treatment of manifestations includes behavioral modification and/or pharmacologic therapy for those with attention-deficit/hyperactivity disorder; physical, speech, and occupational therapy for those with identified developmental delays; and individualized education plans for those with learning disorders.

**Neurofibromatosis Type 2**

NF2 (also known as bilateral acoustic neurofibromatosis and central neurofibromatosis) is estimated to occur in 1 in 33,000 individuals.

**Clinical Characteristics**

NF2 is characterized by bilateral vestibular schwannomas and associated symptoms of tinnitus, hearing loss, and balance dysfunction. Average age of onset is 18 to 24 years, and almost all affected individuals develop bilateral vestibular schwannomas by age 30 years. Affected individuals may also develop schwannomas of other cranial and peripheral nerves, ependymomas, meningiomas, and, rarely, astrocytomas. The most common ocular finding, which may be the first sign of NF2, is posterior subcapsular lens opacities; they rarely progress to visually significant cataracts.

Most patients with NF2 present with hearing loss, which is usually unilateral at onset. Hearing loss may be accompanied or preceded by tinnitus. Occasionally, features such as dizziness or
imbalance are the first symptom. A significant proportion of cases (20%-30%) present with an intracranial meningioma, spinal, or cutaneous tumor. The presentation in pediatric populations may differ from adult populations, in that, in children, vestibular schwannomas may account for only 15% to 30% of initial symptoms.

**Diagnosis**

The diagnosis of NF2 is usually based on clinical findings, with diagnosis depending on presence of one of the following modified NIH diagnostic criteria:

- Bilateral vestibular schwannomas
- A first-degree relative with NF2

**AND**

- Unilateral vestibular schwannoma

**OR**

- Any 2 of: meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacities

- Multiple meningiomas

**AND**

- Unilateral vestibular schwannoma

**OR**

- Any two of: schwannoma, glioma, neurofibroma, cataract

**Genetics**

NF2 is inherited in an autosomal dominant manner; approximately 50% of individuals have an affected parent and the other 50% have NF2 as a result of a de novo variant.

Between 25% and 33% of individuals with NF2 caused by a de novo mutation have somatic mosaicism. Variant detection rates are lower in simplex cases and in an individual in the first generation of a family to have NF2 because they are more likely to have somatic mosaicism.
Somatic mosaicism can make clinical recognition of NF2 difficult and results in lower variant detection rates. Clinical recognition of NF2 in these patients may be more difficult because these individuals may not have bilateral vestibular schwannomas. Variant detection rates may be lower because molecular genetic test results may be normal in unaffected tissue (eg, lymphocytes), and molecular testing of tumor tissue may be necessary to establish the presence of somatic mosaicism.1

Management

In an individual diagnosed with NF2, it is recommended that an initial evaluation establish the extent of the disease, typically using cranial MRI, hearing evaluation, and ophthalmologic and cutaneous examinations.

Counseling is recommended for insidious problems with balance and underwater disorientation, which can result in drowning.

Hearing preservation and augmentation are part of the management of NF2, as is early recognition and management of visual impairment from other manifestations of NF2. Therefore, routine hearing and eye examination should be conducted.

Surveillance measures for affected or at-risk individuals include doing an annual MRI beginning at around age 10 and continuing until at least the fourth decade of life.

Treatment of manifestations includes surgical resection of small vestibular schwannomas, which may often be completely resected with preservation of hearing and facial nerve function. Larger tumors are often managed expectantly with debulking or decompression when brain stem compression, deterioration of hearing, and/or facial nerve dysfunction occur.5

Radiotherapy should be avoided, because radiotherapy of NF2-associated tumors, especially in childhood, may induce, accelerate, or transform tumors.5

Evaluation of At-Risk Relatives

Early identification of relatives who have inherited the family-specific NF2 variant allows for appropriate screening using MRI for neuroimaging and audiologic evaluation, which result in earlier detection and improved outcomes.5 Identification of at-risk relatives who do not have the family-specific NF2 variant eliminates the need for surveillance.
**Schwannomatosis**

Schwannomatosis is a rare condition defined as multiple schwannomas without any vestibular schwannomas, which would be diagnostic of NF2. Individuals with schwannomatosis may develop intracranial, spinal nerve root, or peripheral nerve tumors. Familial cases are inherited in an autosomal dominant manner, with highly variable expressivity and incomplete penetrance. Clinically, schwannomatosis is distinct from NF1 and NF2, although some individuals eventually fulfill diagnostic criteria for NF2. SMARCB1 variants have been shown to cause 30% to 60% of familial schwannomatosis but only a small number of simplex disease.

**Summary of Evidence**

For individuals who have suspected NF who receive genetic testing for NF, the evidence includes clinical validation studies of a multistep diagnostic protocol and genotype-phenotype correlation studies. Relevant outcomes are test accuracy and validity, symptoms, morbid events, and functional outcomes. A multistep variant testing protocol identifies more than 95% of pathogenic variants in NF1; for NF2, the variant detection rate approaches more than 70% in simplex cases and exceeds 90% for familial cases. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic, with a close relative(s) with an NF diagnosis, who receive genetic testing for NF, there is no direct evidence. Relevant outcomes are test accuracy and validity, symptoms, morbid events, and functional outcomes. For individuals with a known pathogenic variant in the family, testing of at-risk relatives will confirm or exclude the variant with high certainty. While direct evidence on the clinical utility of genetic testing for NF is lacking, a definitive diagnosis resulting from genetic testing can direct patient care according to established clinical management guidelines, including referrals to the proper specialists, treatment of manifestations, and surveillance. Testing of at-risk relatives will lead to initiation or avoidance of management and/or surveillance. Early surveillance may be particularly important for patients with NF2 because early identification of internal lesions by imaging is expected to improve outcomes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this policy are listed in Table 2.
Table 2. Summary of Key Trials

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<td>Whole Exome Sequencing (WES) of NF2-associated in Comparison to Sporadic Vestibular Schwannomas - Correlation With Clinical Data</td>
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<td>Sep 2021</td>
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NCT: national clinical trial

Practice Guidelines and Position Statements

American Academy of Pediatrics

In 2008, the American Academy of Pediatrics published diagnostic and health supervision guidelines for children with neurofibromatosis type 1.\(^3\)

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, 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. Lab tests for NF are available under the auspices of 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


<table>
<thead>
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<th>Date</th>
<th>Comments</th>
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<td>04/01/16</td>
<td>Policy created with literature review through November 12, 2015. Genetic testing for neurofibromatosis (NF) may be considered medically necessary in individuals with suspected NF and in at-risk relatives in whom the diagnosis cannot be made without genetic testing.</td>
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<td>04/06/16</td>
<td>Deleted policy, renumbered to 12.04.522 – it was erroneously numbered 12.04.137. No change in coverage statements.</td>
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<td>04/01/17</td>
<td>Annual Review, approved March 14, 2017. Appendix table removed. Policy updated with literature review through November 7, 2016; references 9-14 and 18-21 added. Added policy guideline stating if NF1 pathogenic variants are not detected in patients with suspected NF1, testing for SPRED1 variants is reasonable. Policy statements unchanged.</td>
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<td>Annual Review, approved March 20, 2018. Policy updated with literature review through November 2017; references 2, 14, and 24-25 added; references 1 and 4-5 updated. Policy statements unchanged.</td>
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포함하고 있습니다. 본 통지서에는 짧지만 되는 날짜들이 있을 수
있습니다. 귀하의 신청과 커버리지를 계약 유지를 위한 지침이 있기
때문에 일정한 마감일까지 짧은 기간이 있을 수 있습니다.
귀하의 이러한 정보와 도움은 귀하의 안정을 유지할 수 있는
권리가 있습니다. 800-722-1471 (TTY: 800-842-5357)로 전화해 보세요.

Latvian (Latvian):
Saprotim, ka šis ziņojums ietver svarīgas informācijas.
Premera Blue Cross nodrošina jums porceļš jautājumos un noklausas.
Tikai, ja jums ir specifikās jautājumi par noteikumu vai
lietotāja darbību, varat pievienoties 800-722-1471 (TTY: 800-842-5357).

Northern Sotho (Northern Sotho):
Aan die publiek word gewe de belangrike inligting van hierdie brief.
Premera Blue Cross verseker die bene van hierdie brief, maar dit
het ook duidelike tydperkaries vir die publiek om hul eksemplers
talleer en hul ade verwys..

Polish (Polish):
To ogłoszenie może zawierać ważne informacje. To ogłoszenie może
zawierać ważne informacje odnośnie systemu壁纸 lub zakresu
świadczeń poprzez Premera Blue Cross. Prosimy zwrócić uwagę na
kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie
przekroczyć terminów w przypadku utraty polisy ubezpieczeniowej lub
pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej
informacji we własnym języku. Zadzwoń 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 dados importantes neste aviso.
Talvez seja necessário que você tome providências dentro de
determinados prazos para manter sua cobertura de saúde e ajuda de
custos. Você tem o direito de obter esta informação e ajuda em seu idioma

Punjabi (Punjabi):
ਨਾਥ ਵਿੱਚ ਫਸਲ ਨੀ ਦਿੱਤੀ ਸਾਹਮੀ ਮਦਦਾਂ ਦੀ ਸੰਖਭੇ ਅਨੁਸਾਰ ਪ੍ਰੈਮਰਾ ਬ੍ਰੂਲ ਕ੍ਰੀਸ੍ਸ ਦੀ ਕੁਝ ਵਿਅਕੀਤਾ ਦੇ ਗਲਦੇ ਹਨ। 
ਨਾਥ ਵਿੱਚ ਫਸਲ ਨੀ ਦਿੱਤੀ ਸਾਹਮੀ ਮਦਦਾਂ ਦੀ ਸੰਖਭੇ ਅਨੁਸਾਰ ਪ੍ਰੈਮਰਾ ਬ੍ਰੂਲ ਕ੍ਰੀਸ੍ਸ ਦੀ ਕੁਝ ਵਿਅਕੀਤਾ ਦੇ ਗਲਦੇ ਹਨ। 

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

Română (Romanian):
Prezentă notificare conține informații importante. Această notificare poate
conține informații importante privind cererea sau acoperirea asigurării
dumneavoastră de sănătate prin Premera Blue Cross. Poți consulta datele
în această notificare. Este posibil să fie nevoie să acționați până la anumite
termini limită pentru a vă menține acoperirea asigurării de sănătate sau
asistența privativă 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 направить запросы 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

Tagalog (Tagalog):
Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang
paunawa na ito ay maaring nagagamit ng mahalagang impormasyon
tungkol sa iyong aplikasyon o pagasig ko sa pamamagitan ng Premera Blue
Cross. Maaring magaangalang ka na magsagawa ng habagat sa ilang mga
itanag na panahon unang mapanatili ang iyong pagasig ko sa kalusugan o
tulong sa walang gastos. May karapatan ka na makakuha ng ganitong impormasyon
at tungol sa iyong wika ng walang gastos. Tunawag sa 800-722-1471
(TTY: 800-842-5357).

ไทย (Thai):
ประกาศนี้มีข้อมูลสําคัญเกี่ยวกับการขอสิทธิ์ในการขอรับการช่วยเหลือ
การสูญเสียของ Premera Blue Cross และนี่คือวิธีการที่คุณควรจะ
ดำเนินการในกรณีที่คุณมีปัญหาเกี่ยวกับการสูญเสียการช่วยเหลือที่
มีอยู่ คุณมีสิทธิ์ที่จะได้รับข้อมูลและคำแนะนำที่เกี่ยวกับการสูญเสียได้ โทร
800-722-1471 (TTY: 800-842-5357).

Українська (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).

Việt Nam (Vietnamese):
Thông báo này cung cấp thông tin quan trọng. Thông báo này có thể
thông tin quan trọng về đơn xin tham gia hoặc hỗ trợ bảo hiểm của quý vị qua
chương trình Premera Blue Cross. Xin xem ngay quan trọng thông báo này. Quí vị có thể phải thực hiện thêm thông báo đúng trong thời hạn
dễ phụ trách bảo hiểm sức khỏe hoặc được trợ giúp về chăm sóc sức khỏe của quý vị. 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).