Bcr-Abl Kinase Inhibitors

Number 5.01.518  
Effective Date May 1, 2017  
Revision Date(s) 05/01/17; 01/01/17; 06/09/15; 07/14/14; 3/11/13; 11/13/12; 11/10/11; 11/09/10; 08/10/10; 12/08/09; 8/12/10  
Replaces N/A  
*This coverage is managed through the Pharmacy benefit.

Note: Initial approval period for agents listed below will be 3 months. Continued approval beyond the first 3 months will require documentation showing objective response to therapy.

Imatinib (Gleevec®)

*Imatinib (Gleevec®) may be considered medically necessary for:
- Treatment of adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase, accelerated phase or blast crisis;
- Treatment of pediatric patients with Ph+ chronic phase CML whose disease has recurred after stem cell transplant;
- Treatment of adult and pediatric patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL);
- Adult patients with myelodysplastic/ myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements;
- Adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown;
- Adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown;
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP) or aggressive desmoid tumors;
- Single-agent therapy or in combination with cisplatin or sirolimus for the treatment of recurrent chordoma;
- Single-agent therapy for the treatment of Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor;
- Treatment of patients with Kit (CD117) positive GIST, melanoma and other tumors;
- Treatment of patients with Ph+ NHL – Lymphoblastic lymphoma.

Dasatinib (Sprycel®) and Nilotinib (Tasigna®)

*Dasatinib (Sprycel®) and nilotinib (Tasigna®) may be considered medically necessary in patients with resistance or intolerance to prior therapy with imatinib for:
- Treatment of adults with chronic, accelerated, or blast phase Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML);
Treatment of adults with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL); and
Treatment of patients with gastrointestinal stromal tumor (GIST).

**Bosutinib (Bosulif™)**

*Bosutinib (Bosulif™)* may be considered medically necessary in patients with resistance or intolerance to prior therapy with imatinib for:

- Treatment of adults with chronic, accelerated, or blast phase Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML).

**Ponatinib (Iclusig™)**

*Ponatinib (Iclusig™)* may be considered medically necessary for:

- Treatment of adults with chronic, accelerated, or lymphoid blast phase Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML); or
- Treatment of adults with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL).

Treatment with ponatinib may be considered medically necessary ONLY in patients that have demonstrated resistance or intolerance to prior therapy with:

- Imatinib; AND
- One other tyrosine kinase inhibitor (dasatinib, nilotinib or bosutinib).

All other uses of imatinib, dasatinib, nilotinib, bosutinib or ponatinib are considered investigational.

**Omacetaxine (Synribo™)**

*Omacetaxine (Synribo™)* may be considered medically necessary for:

- Treatment of adults with chronic or accelerated phase chronic myeloid leukemia.

Treatment with omacetaxine may be considered medically necessary ONLY in patients that have demonstrated resistance or intolerance to prior therapy with:

- Imatinib; AND
- At least one other tyrosine kinase inhibitor (dasatinib, nilotinib, bosutinib or ponatinib).

All other uses of omacetaxine are considered investigational.

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**Related Policies**

<table>
<thead>
<tr>
<th>Policy Code</th>
<th>Title</th>
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<tr>
<td>5.01.517</td>
<td>Use of Vascular Endothelial Growth Factor Receptor (VEGF) Inhibitors and Other Angiogenesis Inhibitors in Oncology Patients</td>
</tr>
<tr>
<td>5.01.534</td>
<td>Multiple Receptor Tyrosine Kinase Inhibitors</td>
</tr>
<tr>
<td>5.01.544</td>
<td>Prostate Cancer Targeted Therapies</td>
</tr>
<tr>
<td>5.01.603</td>
<td>Epidermal Growth Factor Receptor (EGFR) Inhibitors</td>
</tr>
</tbody>
</table>

**Policy Guidelines**
**Imatinib (Gleevec®)**

Patients that have not demonstrated objective response to imatinib therapy after three months are considered imatinib-resistant for purposes of prescribing an alternative therapy.

**Dasatinib (Sprycel®), nilotinib (Tasigna®), bosutinib (Bosulif™) and ponatinib (Iclusig™)**

Patients that have not demonstrated objective response to dasatinib, nilotinib or bosutinib therapy after three months are considered resistant for purposes of prescribing ponatinib therapy.

**Coding**

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Prescription drug, oral, chemotherapeutic, NOS (includes: Bosulif, Gleevec, Iclusig, Sprycel, and Tasigna)</th>
</tr>
</thead>
<tbody>
<tr>
<td>J8999</td>
<td>Not otherwise classified, antineoplastic drugs (Synribo)</td>
</tr>
<tr>
<td>S0088</td>
<td>Imatinib [Gleevec] 100mg</td>
</tr>
</tbody>
</table>

**Description**

Cancer is characterized by the uncontrolled growth and spread of malignant cells. Nearly 1.4 million Americans will be diagnosed with cancer this year, and approximately 570,000 will die of the disease. The good news is, survival rates for cancer are on the rise, increasing from 50% to 64% over the last 30 years.

Conventional cytotoxic cancer chemotherapy has been one of the major medical advances realized in the last few decades. Although directed toward certain biologic targets thought to be involved in cellular growth and proliferation, typically they have not discriminated well between rapidly dividing normal cells (eg, bone marrow, gastrointestinal tract) and tumor cells, frequently resulting in toxicities. In addition, tumor responses to traditional cytotoxic cancer chemotherapies can be unpredictable and brief.

“Targeted chemotherapies” (eg, monoclonal antibodies, tyrosine kinase inhibitors, antisense inhibitors of growth factor receptors) are the newest therapeutic approach. These agents have been designed to interfere with molecular targets that have a role in tumor growth and progression (eg, tyrosine kinase, vascular endothelial growth factor, epithelial growth factor, farnesyl transferase inhibition). These targets are typically preferentially located on/in tumor cells, thus these therapies have a higher specificity for tumor cells. The promise of these agents is they will provide a broader therapeutic index with less toxicity. They may also be useful in combination with traditional cytotoxic chemotherapies, immunotherapies or radiation to produce additive or synergistic activity without overlap in toxicity profiles.

The Philadelphia Chromosome mutation was first described in 1960 as a translocation of parts of chromosomes 9 and 22. The result is that part of the BCR ("breakpoint cluster region") gene from chromosome 22 (region q11) is fused with part of the ABL gene on chromosome 9 (region q34). Abl stands for "Abelson", the name of a leukemia virus which carries a similar protein. The result of the translocation is a protein of p210 or sometimes p185 (p simply stands for "protein"; the numbers represent the apparent molecular weight of the mutant proteins in kDa). The fused "bcr-abl" gene is located on the resulting, shorter chromosome 22. Because abl carries a domain that can add phosphate groups to tyrosine residues (tyrosine kinase) the bcr-abl fusion gene is also a tyrosine kinase. The bcr region is also a serine/threonine kinase.

The fused bcr-abl protein interacts with the interleukin-3 receptor beta(c) subunit. The bcr-abl transcript is constitutively active. In turn, bcr-abl activates a number of cell cycle-controlling proteins and enzymes, speeding up cell division. Moreover, it inhibits DNA repair, causing genomic instability and potentially causing blast crisis in CML.

The bcr-abl kinase inhibiting agents currently available are as follows:

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Pharmacology</th>
<th>How Given</th>
<th>FDA-approved Uses</th>
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[TOP]
<table>
<thead>
<tr>
<th>Drug Description</th>
<th>Gene Target</th>
<th>Route</th>
<th>Event-Free Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>imatinib (Gleevec®)</td>
<td>Bcr-abl kinase inhibitor</td>
<td>Oral (Rx)</td>
<td>Philadelphia chromosome + CML, ALL, PDGFR-associated MDS/MPD, KIT+ (CD117) cancers</td>
</tr>
<tr>
<td>dasatinib (Sprycel®)</td>
<td>Bcr-abl kinase inhibitor</td>
<td>Oral (Rx)</td>
<td>Philadelphia chromosome + CML, ALL, KIT+ GIST</td>
</tr>
<tr>
<td>nilotinib (Tasigna®)</td>
<td>Bcr-abl kinase inhibitor</td>
<td>Oral (Rx)</td>
<td>Philadelphia chromosome + CML, KIT+ GIST</td>
</tr>
<tr>
<td>Bosutinib (Bosulif™)</td>
<td>Bcr-abl kinase inhibitor</td>
<td>Oral (Rx)</td>
<td>Philadelphia chromosome + CML</td>
</tr>
<tr>
<td>Ponatinib (Iclusig™)</td>
<td>Bcr-abl kinase inhibitor</td>
<td>Oral (Rx)</td>
<td>Philadelphia chromosome + CML</td>
</tr>
</tbody>
</table>

Imatinib (Gleevec®) is a protein-tyrosine kinase inhibitor that inhibits the bcr-abl tyrosine kinase, the abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in chronic myelogenous leukemia (CML). This inhibition prevents proliferation and induces apoptosis of the abnormal cells. Gleevec® is also an inhibitor of the receptor tyrosine kinases for platelet-derived growth factor (PDGF) and stem cell factor (SCF), and c-kit. In vitro, Gleevec® inhibits proliferation and induces apoptosis in gastrointestinal stromal tumors (GIST) cells, which express an activating c-kit mutation.

Dasatinib (Sprycel®) and nilotinib are inhibitors of multiple protein-tyrosine kinases, including BCR-ABL, SRC family, c-KIT, EPHA2 and PDGFR-beta). Based on modeling studies, Sprycl is predicted to bind to multiple conformations of the ABL kinase.

Imatinib, approved in 2001, revolutionized treatment of CML. The imatinib molecule fits tightly into the ATP binding site of the BCR-ABL tyrosine kinase, interfering with function of the abnormal protein. Thus it is called a BCR-ABL tyrosine kinase inhibitor or BCR-ABL TKI. Long term follow-up of some of the first imatinib patients shows an 8-year event-free survival of 81%. However, 17% of patients do not respond to imatinib, and of those that do, 15% later lose their response. Primary resistance (failure to achieve remission in 3-6 months) may be caused by excessive plasma protein binding, or reduced drug transport into the cell. Secondary resistance is thought to be most commonly due to acquired mutations in the drug binding site of the BCR-ABL TK protein. Mutations in imatinib-resistant patients have been mapped and sequenced. Second and third generation TKI’s – dasatinib, nilotinib, later bosutinib, and most recently ponatinib - have been developed to overcome imatinib-resistant mutations. In vitro binding and growth inhibition studies for these drugs are available for an ever-increasing number of mutations.

There is increasing evidence that mutations in the BCR-ABL gene correspond to success or failure of different TKI’s. However, this information has limits on clinical usefulness. Over 80% of patients do well on first-line agents and do not harbor mutations. Of patients that fail imatinib therapy, Parker et al. were able to detect mutations in 28% of patients by sequencing, and 32% by mass spectrometry. Soverini et al. estimated that 29% of patients with imatinib failure harbor a detectable mutation in the BCR-ABL binding site. Branford et al. report a 10-20% mutation detection rate by sequencing, and of those for whom a mutation was detected, 43% had a mutation that was useful to guide clinical decisions. Mutations are now detected in about half of imatinib resistant patients, and of those mutations that are detected, 20-25% are useful for guiding treatment choice. Differences in defining treatment failure, as well as increasing numbers of mutations in advancing disease, may account for variability in reported percentages.

New methods of mutation detection are developing. Mass spectrometry can be used to identify mutations that are at too low a clonal level to be detected by sequencing. Denaturing high-performance liquid chromatography (D-HPLC) is also more sensitive but does not characterize the mutation, and may be used to screen samples before sequencing. A rapid PCR method is available to detect the T315I mutation, which is resistant to all TKI’s except ponatinib. Whether patients could be screened for this single mutation to guide therapy has not been tested.

Despite the wealth of information on mutations and in vitro sensitivity, there are no published prospective clinical trials on the clinical usefulness of mutational analysis to select a TKI. Studies to date are retrospective or observational. For example, in the phase II efficacy trial of Nilotinib in imatinib-resistant patients, mutation data were collected at baseline and thereafter. Patients who had no mutation detected, or mutations with high in vitro sensitivity to nilotinib, had a better response than those with mutations that were resistant to nilotinib in vitro (mutations Y253H, E255K/V, F359C/F). Omacetaxine, a protein translation inhibitor, has been recently approved by the FDA as second-line therapy, and other potential treatments for imatinib-resistant patients are being tested.
As patients who are successful on primary therapy are maintained for longer periods with molecular markers below the level of detection, the question has arisen as to whether they may actually be able to discontinue TKI therapy. In one pilot study, 100 patients who had been on imatinib for >2 years with complete molecular response discontinued treatment. At one year, 41% remained in complete molecular response. All of the 69% that relapsed remained sensitive to imatinib.

**NCCN Compendium and Other Practice Guidelines**

The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium is based directly on the NCCN Clinical Practice Guidelines in Oncology. The compendium lists specific panel recommendations for off-label uses of drugs, and each recommendation is supported by a level of evidence category.

The NCCN Categories of Evidence and Consensus used in the recommendations are:

- **Category 1**: The recommendation is based on high level evidence (eg, randomized controlled trials) and there is uniform NCCN consensus.
- **Category 2A**: The recommendation is based on lower level evidence and there is uniform NCCN consensus.
- **Category 2B**: The recommendation is based on lower level evidence and there is nonuniform NCCN consensus (but no major disagreement).
- **Category 3**: The recommendation is based on any level of evidence but reflects major disagreement.

In June 2008, the NCCN Compendium became one of four references for Centers for Medicare and Medicaid Services (CMS) for oncology coverage policy. In its national coverage decision CMS states that, in general, a use identified by the NCCN Compendium is medically accepted if the indication is a Category 1 or 2A as defined by NCCN. A use is not medically accepted if the indication is a Category 3 in NCCN. The local CMS contractor, Noridian Administrative Services (NAS), has issued an additional coverage statement regarding Category 2B: “NAS recognizes NCCN Categories of Evidence Levels Category 1 and Category 2A ONLY as medically accepted indications. If a provider chooses to use NCCN level 2B in support of a chemotherapeutic drug used off-label in an anti-cancer chemotherapeutic regimen, NAS expects that the provider will make available to NAS significant peer-reviewed Phase II or Phase III studies demonstrating such support. In the absence of such studies, level 2B evidence does not support such use.”

**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 services representative to determine whether there are any benefit limitations applicable to this service or supply.

**Benefit Application**

N/A

**Rationale**

The effectiveness of dasatinib (Sprycel®) is based on hematologic and cytogenetic response rates. There are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased
survival. To date, Sprycel® has been studied in four uncontrolled Phase II pivotal clinical trials and one Phase II pilot study in patients in all phases of CML, as well as BRC-ABL+ (Ph+) ALL.

Two Phase II studies evaluated the efficacy and safety of Sprycel® in patients with chronic phase CML who were previously treated with imatinib (Gleevec®). One randomized, non-comparative pilot study enrolled patients (N=150) after failure of low-dose Gleevec® (ie, <600 mg/day). One other single-arm study enrolled patients (N=186) who were resistant to or intolerant of Gleevec® at any dose. The primary endpoint in both studies was the rate of major cytogenetic response (MCyR). In the pilot study, 35% of Sprycel®-treated patients achieved a MCyR at 12 weeks and 21% achieved a complete cytogenetic response (CCyR). In the single-arm study 39% of patients achieved a MCyR.

Three single-arm Phase II studies were performed to evaluate the safety and efficacy of Sprycel® in patients with advanced stage CML and BRC-ABL+ (Ph+) ALL who were resistant to or intolerant of Gleevec. The primary endpoint in these studies was the rate of major hematologic response (MaHR) and overall hematologic response (OHR).

The safety and efficacy of nilotinib has been studied in one uncontrolled, open-label, phase II pivotal clinical trial in imatinib-resistant and -intolerant patients with all phases of CML, as well as Ph+ ALL. Hematologic and cytogenetic response rates ranged from 16%-74%. In a preliminary report from another single-arm, open-label, phase II study, nilotinib has also shown activity in patients with all phases of Ph+ CML and Ph+ ALL who were unresponsive or intolerant to both imatinib and dasatinib. No controlled clinical trials for the agent are available at this time.

Although no head-to-head clinical trials between the second-generation TKIs nilotinib and dasatinib are available, their safety profiles appear to differ. Nilotinib notably carries a boxed warning for QT prolongation and sudden death and the need to take the drug on an empty stomach (avoid food two hours before and within one hour after dose). A greater incidence of grade 3/4 elevated serum lipase and electrolyte abnormalities were reported with nilotinib. While a greater incidence of grade 3/4 myelosuppression, bleeding-related events, and fluid retention were reported with dasatinib.

Management guidelines developed by the National Comprehensive Cancer Network (NCCN) recommend use of either dasatinib or nilotinib in patients with imatinib-resistant or -intolerant Ph+ CML (all phases).

**2010 Update-The NCCN Drug Compendium**

The Company recognizes indications and uses of drugs listed in the NCCN Drugs and Biologics Compendium with Categories of Evidence and consensus of 1 and 2A as proven and Categories of Evidence and Consensus of 2B and 3 as unproven. However, Category 2B uses may be considered for coverage if they are substantiated by provider submission of significant peer-reviewed Phase II or Phase III studies demonstrating treatment effectiveness.

This policy is in agreement with July 2010 NCCN Drugs and Biologics Compendium recommendations of 1 and 2A.

**2011 Update**

A literature search was conducted from October 2010 to September 2011. No major new developments were found.

Emerging evidence in CML patients suggests that response rates can be increased by careful attention to therapeutic drug monitoring. Hehlmann and colleagues randomized 1014 newly-diagnosed CML patients to receive 400mg/day, 800mg/day tolerability adjusted or 400mg/day plus alpha interferon. Patients receiving the higher dose imatinib had a higher rate of MMR at 12 months than with imatinib 400 mg/d (59% [95% CI: 53% to 65%]) v 44% [95% CI: 37% to 50%]; P < .001) or imatinib 400 mg/d plus IFN-α (59% v 46% [95% CI: 40% to 52%]; P = .002). Median dose in the 800-mg/d arm was 628 mg/d with a maximum dose of 737 mg/d during months 4 to 6 and a maintenance dose of 600 mg/d. All three treatment approaches were well tolerated with similar grade 3 and 4 adverse events. The authors concluded that treatment of early-phase CML with imatinib can be optimized by giving early high-dose therapy followed by rapid adaptation to good tolerability. MMR at 12 months was strongly correlated with survival at 1 and 3 years.
2012 Update
A literature search was conducted from October 2011 to October 2012. No major new developments were found.

The TOPS trial published this year further elucidated the relationship between Imatinib trough plasma levels and achievement of complete cytogenetic response (CCyR) and major molecular response (MMR). The clinical significance of this in terms of practice changes remains to be assessed.

Ibrahim et al. demonstrated an incremental benefit from sequential administration of imatinib followed by one of the newer tyrosine kinase inhibitors after imatinib failure.

2013 Update
A complete review was prepared for the Premera Pharmacy and Therapeutics Committee in January 2013. Focus was on the role of the newer agents in this class and the possibility of using genetic testing to predict resistance to imatinib or some of the other drugs in this class. Unfortunately, the technology was not sufficiently developed for use in routine clinical practice.

The medical necessity criteria for imatinib, dasatinib and nilotinib were updated to include currently labeled indications, and indications were added for bosutinib and ponatinib. These were also compared with current NCCN Compendium listings.

The European Leukemia Net (ELN) guidelines recommend imatinib as first-line therapy, with nilotinib or dasatinib as second line. Bosutinib and ponatinib have now also been approved as second-line agents.

2014 Update
A literature search was conducted from January 2013 to June 2014. No major new developments were found.

2015 Update
A literature search was conducted from June 2014 to May 2015. No major new developments were found. Reference list updated.

2016 Update
A literature search was conducted from July 1, 2015 to December 5, 2016. No major new developments were found. Reference list updated.

References


**Appendix**

N/A

**History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/12/08</td>
<td>Add to Prescription Drug Section - New PR policy.</td>
</tr>
<tr>
<td>12/16/08</td>
<td>Minor Update - Corrected table under description.</td>
</tr>
<tr>
<td>12/08/09</td>
<td>Replace Policy - Additional wording regarding NCCN added to Description and Rationale. No change to policy statements. Reference added.</td>
</tr>
<tr>
<td>11/09/10</td>
<td>Replace Policy - Reviewed by OAP in August 2010 – The policy statement has been reworded for purposes of clarification, listing the specific types of tumors covered under the medically necessary indication; the intent remains the same. A literature review was conducted; references added. Reviewed by P&amp;T on September 2010.</td>
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<tr>
<td>11/10/11</td>
<td>Replace Policy – Policy updated with literature review; no change in policy statement. Reference 11 added. Reviewed by P&amp;T on September 27, 2011.</td>
</tr>
<tr>
<td>11/13/12</td>
<td>Replace policy. Policy updated with literature review; no change in policy statements. References 12 and 13 added.</td>
</tr>
<tr>
<td>03/11/13</td>
<td>Replace policy. Policy section updated with medically necessary statements for dasatinib, dasatinib, nilotinib and omacetaxine. The medical necessity criteria for imatinib, dasatinib and nilotinib were updated to include currently labeled indications, and indications were added for bosutinib and ponatinib. Policy Guidelines and Rationale sections updated; references added. Reviewed by P&amp;T on March 7, 2013. HCPCS codes C9297, 9399 and J9999 added.</td>
</tr>
<tr>
<td>08/15/13</td>
<td>Update Related Policies. Add 5.01.534.</td>
</tr>
<tr>
<td>12/06/13</td>
<td>Update Related Policies. Add 5.01.544.</td>
</tr>
<tr>
<td>07/31/14</td>
<td>Annual review. Policy updated with literature review. No change in policy statements.</td>
</tr>
<tr>
<td>12/03/14</td>
<td>Update Related Policies. Add 5.01.517.</td>
</tr>
<tr>
<td>06/09/15</td>
<td>Annual review. Policy updated with literature review. No change in policy statements.</td>
</tr>
<tr>
<td>01/01/17</td>
<td>Annual review, changes approved December 13, 2016. Policy updated with literature review. No change in policy statements. Note added that coverage is managed through the Pharmacy benefit.</td>
</tr>
<tr>
<td>05/01/17</td>
<td>Annual review, changes approved April 11, 2017. A statement outlining the length of therapy for initial and subsequent approval has been added to the policy.</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).
Discrimination Is Against the Law

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  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

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If you believe that Premera has failed to provide these services or discriminated 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 425-918-5992. TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

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, HH Building Washington, DC. 20201, 1-800-368-1019, 800-537-7697 (TDD) Complaint forms are available at:

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).

Arabic (Amharic):
لا يوجد هذا الإشعار معلومات هامة. قد يوجد هذه المعلومات معلومات مهمة يغوصها ملوك أو
الغلافة التي تيغوصها على مها مجاب معاقيون عبر مرنوا في Premera Blue Cross. نوك والمعلومات عن هذه المعلومات والمعلومات على كيف تكون هذه المعلومات تفويض مرنوا لون لكون آية vs
- 800-722-1471 (TTY: 800-842-5357) متساوية

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

Oromo (Cushite):
Oromoo (Cushite):

Français (French):

Kreyòl ayisyen (Creole):
Avi siila a gen Enfòmasyon Enpòtan laidann. Avi siila a kapab geny enn enfòmasyon enpòtan konsènan aplikasyon lwa oso konsènan kouvèti asiirans lan atravè Premera Blue Cross. Kapab geny enn k li e enpòtan nan avi siila a. Ou ka gen pou pran kék akso an vosan sèt la, difen pou ka jenbe kouvèti asiirans sante lwa oso pou yo ka ede e avèk depans yo. Se dwa w pou resewwa enfòmasyon sa a ak asiirans k lo lang ou pale a, san ou pa gen pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Hmoob (Hmong):

Iloko (Ilocano):
Daytoy a Pakdaak ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaak magbalin nga adda ket naglaon iti napateg nga impormasion maipanggep iti aplikasyonowy nungu coverage babaen iti Premera Blue Cross. Daytoy ket balmin dagiti importante a palsa iti daytoy a pakdaak. Magbalin nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding nga adda aldaw tapno mapagalantayino a coverage ti salun-ayo nungu tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagasaaa nga awan ti bayadanoy. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):