PHARMACY BENEFIT COVERAGE GUIDELINE – 5.01.543

General Medical Necessity Criteria for Companion Diagnostics Related to Drug Approval

Effective Date: May 1, 2019
Last Revised: April 18, 2019
Replaces: N/A

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Introduction

A companion diagnostic test is specific type of medical test. It determines whether a person would respond to a particular drug. Only certain drugs have a companion diagnostic test. These are drugs, such as chemotherapy treatments, that usually have serious side effects. Companion diagnostic tests help doctors weigh if a drug’s benefits could be greater than its risks or side effects. Companion diagnostic tests help people who would respond to treatment get the drugs they need while avoiding unnecessary treatment and side effects among those who wouldn’t. This policy discusses when companion diagnostic tests may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Coverage Guidelines

The following coverage criteria apply to drugs with companion diagnostic tests, whenever there is not a specific medical policy covering the situation. If a drug-specific medical policy addresses the case circumstances, that policy will take precedence over this more general policy.
**Medical Necessity**

For drugs that have a specific companion diagnostic test, the test may be considered medically necessary when:

- The diagnostic test has been performed
- Test results predict that the drug will be of benefit to the patient for whom it is prescribed
- The drug is prescribed for a labeled indication in a patient that meets the FDA-approved criteria for prescribing it

Such companion diagnostic tests may be considered medically necessary for any patient in whom use of the drug is contemplated and the test informs whether use of the drug is expected to yield benefit to that patient.

Other uses of these tests are considered not medically necessary.

**NOTE:** Requests for approval of the drug should be accompanied by documentation of test results. In cases where the FDA has approved a drug with a specific branded companion test, determination of medical necessity may be based on that test, or any reasonable equivalent, whether specifically named in the label or not.

**Coding**

N/A

**Related Information**

**Personalized Medicine**

Personalized medicine is a general term that may be used to refer to any set of strategies used to select therapeutic approaches that are tailored to specific patients. Therapies may be identified by any clinically valid means, including demographic factors, genetic, phenotypic or biochemical markers, imaging techniques, etc.
Companion Diagnostics

Companion diagnostics are specific tests used to predict responsiveness of a patient to specific drugs or other treatments. In a more restrictive sense, the term is usually used to refer to genomic, proteomic or metabolomic testing. Genetic tests may identify a single nucleotide polymorphism (SNP) or a panel of SNPs that correlate strongly with positive response.

Evaluation of Companion Diagnostics

Evidence demonstrating the value of a companion diagnostics is categorized in three stages:

**Analytic validity** – How accurately and reliably the test measures the genotype or other marker of interest.

**Clinical validity** – How consistently and accurately the test detects or predicts the intermediate or final clinical outcomes of interest.

**Clinical utility** – How likely the test is to significantly improve patient outcomes.

Demonstration of clinical validity is normally expected when vetting a companion diagnostic; however, clinical utility requires longer term studies and will probably not be validated for months or years following product launch.

Benefit Application

This coverage is managed through the Pharmacy benefit.

Rationale

Development of new technologies such as whole genome assay studies (GWAS) and biobanking of clinical trial tissue samples have greatly increased the potential for identifying companion diagnostics. A previously identified marker may also be found to correlate with therapeutic outcomes, such as the Philadelphia chromosome and Bcr-Abl mutation, which have been found to have a high predictive value for response to imatinib and other targeted kinase inhibitors. The
intent of this policy is broadly inclusive; covering any diagnostic methodology specified in the drug’s approved labeling, regardless of whether it is a specific proprietary test or a generic one.

The completion of the human genome sequencing project a decade ago launched a period of rapid growth in the field. The impact of modern high throughput sequencing and DNA microarray chips has dramatically increased the power of genetics research and the resulting pool of information. In the past six years, more than 1000 regions of the human genome have been associated with specific traits and diseases. In this decade, commercialized specific diagnostic test and drug pairs are beginning to emerge from the pipeline and receive final FDA approval. These represent the first of a flood of such products expected to follow.

In some cases, eg, imatinib and the Bcr-Abl mutation, the pairing will be unquestionable, and review for medical necessity may prove unnecessary. In others, potential off-label uses will develop rapidly and prescriber demand may precede the corresponding scientific evidence. For instance, ivacaftor, a recently approved novel therapy for cystic fibrosis patients, acts to improve function of CFTR chloride transport channels in patients with a G551D point mutation. This is only one of over 23 identified polymorphisms that may result in cystic fibrosis. Ivacaftor is currently under investigation for use in several other mutations, but results of these studies are not yet available; however, requests for these off-label uses are already beginning to be made. This example illustrates the need to manage off-label use. With the growing number of new diagnostic/drug pairs being approved, a more generalized approach to managing utilization is required.

As genetic science advances rapidly into this field, investigators are encountering new orders of magnitude of complexity. Despite the milestones achieved since 2001, we are still far from understanding the mechanisms behind most of the diseases being studied. Given the desperation of patients and physicians faced with incurable chronic diseases, experimentation beyond the limits of evidence-based medicine is bound to occur. This policy is designed to provide a simple administrative means of ensuring that clinical practice does not outpace research.

2013 Update

No changes were found that indicate need for change to this policy.
2014 Update

No information was found that indicates a need for changes to coverage contained herein.

2016 Update

No information was found that indicates a need for changes to coverage contained herein.

2017 Update

No information was found that indicates a need for changes to coverage contained herein.

2018 Update

No information was found that indicates a need for changes to coverage contained herein.

2019 Update

No information was identified that would indicate change to coverage criteria.

References


## History

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<tr>
<td>10/09/12</td>
<td>New policy. Add to Prescription Drug section.</td>
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<tr>
<td>02/05/13</td>
<td>Code update. Codes 81205 – 81208 and 81235 added to policy; these are new codes effective 1/1/13.</td>
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<tr>
<td>07/08/13</td>
<td>Minor Update – Clarification was added to the policy that it is managed through the member’s pharmacy benefit; this is now listed in the header and within the coding section.</td>
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<tr>
<td>12/09/13</td>
<td>Replace policy. Policy updated with review; no changes to policy statement.</td>
</tr>
<tr>
<td>01/20/14</td>
<td>Update Related Policies. Add 12.04.506.</td>
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<tr>
<td>11/20/14</td>
<td>Annual review. Covered to Benefit Coverage Guideline template; no change in coverage criteria.</td>
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<tr>
<td>02/10/15</td>
<td>Coding update. CPT code 81235 removed from the policy; this applies to policy 2.04.125.</td>
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<td>10/13/15</td>
<td>Annual Review. Policy reviewed; no change in policy statements.</td>
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<td>04/01/16</td>
<td>Update Related Policies. Remove 12.04.38 as it was deleted and replaced with 12.04.517.</td>
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<tr>
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<td>Annual review, approved December 13, 2016. Policy reviewed; no change in policy statements.</td>
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<td>07/01/17</td>
<td>Policy moved into new format. No changes to policy statement.</td>
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<tr>
<td>09/01/17</td>
<td>Annual Review, approved August 22, 2017. No changes to policy statements. Minor change to title for clarification.</td>
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<tr>
<td>07/01/18</td>
<td>Annual Review, approved June 5, 2018. No changes to policy statement.</td>
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<tr>
<td>01/15/19</td>
<td>Minor update, removed 12.04.517 from Related Policies as it was archived.</td>
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<tr>
<td>05/01/19</td>
<td>Annual Review, approved April 18, 2019. No change to policy statement. Removed CPT codes 81205, 81206, 81207, and 81208.</td>
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**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.
Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - 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

If you need these services, contact the Civil Rights Coordinator.

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:
- Civil Rights Coordinator - Complaints and Appeals
  PO Box 91102, Seattle, WA 98111
  Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357

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 509F, HHH Building, Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at:
- 200 Independence Avenue SW, Room 509F, HHH Building, Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
- PO Box 91102, Seattle, WA 98111

You can also file a complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, by mail, phone, fax, or TTY. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, by phone at 800-722-1471, TTY 800-842-5357.

This Notice has Important Information.

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).

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 提交的申請或保險的重要訊息。本通知可能有重要的日期。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).


Tagalog (Tagalog):

Tiếng Việt (Vietnamese):

Român (Romanian):

Русский (Russian):
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Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud de cobertura a través de Premera Blue Cross. Es posible que haya fechas claves 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).

日本語 (Japanese):
この通知には重要な情報が含まれています。この通知には、Premera Blue Crossの申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている情報は重要な日付を含む場合があります。健康保険や無料サポートを維持するには、特定の期間までに行動を取りなければならない場合があります。ご使用の言語による情報とサポートが無料で提供されます。800-722-1471 (TTY: 800-842-5357)まで電話ください。

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