



MEDICAL COVERAGE GUIDELINES
SECTION: LABORATORY

ORIGINAL EFFECTIVE DATE: 11/28/06
LAST REVIEW DATE: 01/22/19
LAST CRITERIA REVISION DATE: 02/06/18
ARCHIVE DATE:

PARANEOPLASTIC NEUROLOGICAL DISORDER ANTIBODY TESTING

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Paraneoplastic neurological disorders are rare syndromes that are caused by, or associated with, an underlying neoplasm and may affect any part of the central or peripheral nervous system. Paraneoplastic neurological syndromes (PNS) typically affect middle-aged to older adults and are most common in individuals with lung, ovarian, lymphatic, or breast cancer. Immunologic factors have been investigated in the development of PNS because antineuronal autoantibodies and T-cell responses against nervous system antigens have been defined for many of these disorders. About one-third of the affected individuals do not have detectable antibodies and 5-10% have an atypical antibody that is not well characterized. Despite the presumed autoimmune etiology of PNS, the results of various forms of immunotherapy have been disappointing. Rapid detection and immediate treatment of the underlying tumor appears to offer the best chance of stabilizing the individual and preventing further neurological deterioration.

Criteria:

- Antibody testing for paraneoplastic neurological disorders is considered ***experimental or investigational*** based upon:
1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
 2. Insufficient evidence to support improvement of the net health outcome, and
 3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
 4. Insufficient evidence to support improvement outside the investigational setting.

Antibody tests include, *but are not limited to*:

- Amphiphysin
- Anti-Tr
- CAR
- CASPR2
- CV2
- GAD65
- Ganglionic AChR
- Hu
- LGI1
- LEMS (VGCC)
- MaTa
- NMDA Receptor (NR1)
- Ri
- VGKC
- Yo
- Zic4

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Resources:

1. Athena Diagnostics. Paraneoplastic Neurological Disorders. Accessed 01/28/2018, 02/02/2017, 01/30/2015, 02/18/2014, 02/01/2013, 12/01/08, 08/29/2006.
2. de Beukelaar JW, Sillevs Smitt PA. Managing paraneoplastic neurological disorders. *Oncologist*. 2006 Mar 2006;11(3):292-305.
3. Donaldson R, Li J, Li Y. Clinical significance of cation channel antibodies in motor neuron disease. *Muscle & nerve*. Aug 2016;54(2):228-231.
4. Dropcho EJ. Update on paraneoplastic syndromes. *Curr Opin Neurol*. 2005 Jun 2005;18(3):331-336.
5. Garcia-Reitboeck P, Thompson G, Johns P, Al Wahab Y, Omer S, Griffin C. Upbeat nystagmus in anti-Ma2 encephalitis. *Pract Neurol*. Feb 2014;14(1):36-38.
6. Graus F, Delattre JY, Antoine JC, et al. Recommended diagnostic criteria for paraneoplastic neurological syndromes. *J Neurol Neurosurg Psychiatry*. 2004 Aug 2004;75(8):1135-1140.
7. Greene M, Lai Y, Baella N, Dalmau J, Lancaster E. Antibodies to Delta/notch-like epidermal growth factor-related receptor in patients with anti-Tr, paraneoplastic cerebellar degeneration, and Hodgkin lymphoma. *JAMA Neurol*. Aug 2014;71(8):1003-1008.
8. Honnorat J. Onconeural antibodies are essential to diagnose paraneoplastic neurological syndromes. *Acta Neurol Scand Suppl*. 2006 2006;183:64-68.
9. Mirabelli-Badenier M, Biancheri R, Morana G, et al. Anti-NMDAR encephalitis misdiagnosed as Hashimoto's encephalopathy. *Eur J Paediatr Neurol*. Jan 2014;18(1):72-74.
10. Ontaneda D, Fox RJ. Is neuromyelitis optica with advanced age of onset a paraneoplastic disorder? *Int J Neurosci*. Jul 2014;124(7):509-511.
11. Tebo AE, Haven TR, Jackson BR. Autoantibody diversity in paraneoplastic syndromes and related disorders: The need for a more guided screening approach. *Clinica chimica acta; international journal of clinical chemistry*. Aug 01 2016;459:162-169.
12. UpToDate. Overview of paraneoplastic syndromes of the nervous system. 12/06/2016, 10/05/2015, 02/05/2014.



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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ 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: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's 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, DC 20201, 1-800-368-1019, 800-537-7697 (TDD). Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nilinígíí Blue Cross Blue Shield of Arizona haada yit'éego bina'idííkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yina'idííkidgo beehaz'áanii hólg díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilínígóó. Ata' halne'ígíí kojí' bich'í' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أية تكلفة. للتحدث مع مترجم اتصل بـ 877-475-4799.

