



# BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

## Positron Emission Tomography (PET) Miscellaneous (Non-cardiac, Non-oncologic) Applications

**Policy #** 00104

Original Effective Date: 01/28/2002  
Current Effective Date: 11/04/2013

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

*Note: Positron Emission Tomography (PET) Cardiac Applications are considered in medical policy 00103.*

*Note: Positron Emission Tomography (PET) Oncology Applications are considered in medical policy 00105.*

### When Services May Be Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider positron emission tomography (PET) using 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (FDG) in the diagnosis of chronic osteomyelitis to be **eligible for coverage**.

Based on review of available data, the Company may consider positron emission tomography (PET) using 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (FDG) in the assessment of selected patients with epileptic seizures who are candidates for surgery to be **eligible for coverage**.

### Patient Selection Criteria

Coverage eligibility for the use of positron emission tomography (PET) in the assessment of selected patients with epileptic seizures will be considered when the following criteria are met:

- Complex partial epileptic seizures that have failed to respond to medical therapy; and
- Resection of a suspected epileptogenic focus located in a region of the brain accessible to surgery has been recommended; and
- Conventional techniques for seizure localization must have been tried and provided data that suggested a seizure focus, but were not sufficiently conclusive to permit surgery; and
- The purpose of the positron emission tomography (PET) examination should be to avoid subjecting the patient to extended preoperative electroencephalographic (EEG) recording with implanted electrodes or to help localize and minimize the number of sites for implanted electrodes to reduce the morbidity of that procedure.

### When Services Are Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of positron emission tomography (PET) for all other miscellaneous indications, including but not limited to the following, to be **investigational**:\*

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## *Central Nervous System (CNS) diseases*

- Autoimmune disorders with CNS manifestations, including:
  - Behçet's syndrome
  - Lupus erythematosus
- Cerebrovascular diseases, including:
  - Arterial occlusive disease (arteriosclerosis, atherosclerosis)
  - Carotid artery disease
  - Cerebral aneurysm
  - Cerebrovascular malformations (AVM and Moya Moya disease)
  - Hemorrhage
  - Infarct
  - Ischemia
- Degenerative motor neuron diseases, including:
  - Amyotrophic lateral sclerosis
  - Friedreich's ataxia
  - Olivopontocerebellar atrophy
  - Parkinson's disease
  - Progressive supranuclear palsy
  - Shy-Drager syndrome
  - Spinocerebellar degeneration
  - Steele-Richardson-Olszewski disease
  - Tourette's syndrome
- Dementias, including:
  - Alzheimer's disease (AD)
  - Multi-infarct dementia
  - Pick's disease
  - Frontotemporal dementia (FTD)
  - Dementia with Lewy-Bodies
  - Presenile dementia
- Demyelinating diseases, such as multiple sclerosis
- Developmental, congenital, or inherited disorders, including:
  - Adrenoleukodystrophy
  - Down's syndrome
  - Huntington's chorea
  - Kinky-hair disease (Menkes' syndrome)
  - Sturge-Weber syndrome (encephalofacial angiomas) and the phakomatoses
- Miscellaneous
  - Chronic fatigue syndrome
  - Sick building syndrome
  - Post traumatic stress disorder
- Nutritional or metabolic diseases and disorders, including:
  - Acanthocytosis
  - Hepatic encephalopathy
  - Hepatolenticular degeneration

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- o Metachromatic leukodystrophy
- o Mitochondrial disease
- o Subacute necrotizing encephalomyopathy
- Psychiatric diseases and disorders, including:
  - o Affective disorders
  - o Depression
  - o Obsessive-compulsive disorder
  - o Psychomotor disorders
  - o Schizophrenia
- Pyogenic infections, including:
  - o Aspergillosis
  - o Encephalitis
- Substance abuse, including the CNS effects of alcohol, cocaine and heroin
- Trauma, including brain injury and carbon monoxide poisoning
- Viral infections, including:
  - o Acquired immune deficiency syndrome (AIDS)
  - o Acquired immune deficiency syndrome (AIDS) dementia complex
  - o Creutzfeldt-Jakob syndrome
  - o Progressive multifocal leukoencephalopathy
  - o Progressive rubella encephalopathy
  - o Subacute sclerosing panencephalitis
- Mycobacterium infection
- Migraine
- Anorexia nervosa
- Cerebral blood flow in newborns
- Vegetative versus "locked-in" state
- Pulmonary diseases
  - o Adult respiratory distress syndrome
  - o Diffuse panbronchiolitis
  - o Emphysema
  - o Obstructive lung disease
  - o Pneumonia
- Musculoskeletal diseases
  - o Spondylodiscitis
  - o Joint replacement follow-up
- Other
  - o Giant cell arteritis
  - o Vasculitis
  - o Inflammatory bowel disease
  - o Sarcoidosis

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## Background/Overview

Positron emission tomography images biochemical and physiological functions by measuring concentrations of radioactive chemicals that are partially metabolized in the body region of interest. Radiopharmaceuticals used for PET are generated in a cyclotron or nuclear generator and introduced into the body by intravenous injection or by respiration. A variety of PET radiopharmaceuticals have been investigated; however, only a few have received approval by the U.S. Food and Drug Administration (FDA) for clinical use. The scanners used for PET imaging are somewhat similar to those used for x-ray computed tomography (CT), but PET requires complicated technology and computerized mathematical models of physiologic functions and tracer kinetics for the generation of images.

*Note: This policy only addresses the use of radiotracers detected with the use of dedicated full-ring PET scanners. Radiotracers such as fluorodeoxyglucose (FDG) may be detected using single-photon emission computed tomography (SPECT) cameras, a hybrid PET/SPECT procedure that may be referred to as FDG-SPECT or molecular coincidence detection.*

## FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

The 1997 U.S. Food and Drug Administration Modernization Act (FDAMA) established FDA authority over the safety and effectiveness of locally manufactured radiotracers and developed streamlined regulations for good manufacturing practices (GMP) with which each PET facility must comply.

The following radiotracers have been approved by the FDA:

- <sup>18</sup>F-FDG for evaluation of glucose metabolism in oncology
- <sup>18</sup>F-FDG for evaluation of myocardial hibernation
- <sup>13</sup>N-ammonia for evaluation of myocardial blood flow
- 82-rubidium chloride injection (NDA-19-414) was approved in 1989 "for assessing regional myocardial perfusion in the diagnosis and localization of myocardial infarction."
- <sup>18</sup>F FDG (NDA 20-306) was approved in 1994 for "the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures."
- <sup>18</sup>F sodium fluoride injection (NDA 17-042) was approved in 1972 for "injection as a bone imaging agent to define areas of altered osteogenic activity." The original company ceased making this drug product in 1975, and it is now being marketed again by PETNET Solutions (a Siemens company).

In September 2005, the FDA issued a draft rule and draft guidance on current good manufacturing practice for PET drug products. The final current good manufacturing practices (CGMP) regulation for the production of PET drugs was issued on December 9, 2009 and takes effect on December 12, 2011. More detailed information available online at:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm085783.htm>.

Centers for Medicare and Medicaid Services (CMS)

National Coverage Determination (NCD) for FDG-PET for Dementia and Neurodegenerative Diseases (220.6.13): "Medicare covers FDG-PET scans for either the differential diagnosis of fronto-temporal dementia (FTD) and Alzheimer's disease (AD) under specific requirements; OR, its use in a CMS-approved



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practical clinical trial focused on the utility of FDG-PET in the diagnosis or treatment of dementing neurodegenerative diseases". Specific requirements for each indication are clarified in the document.

## **National Coverage Determination (NCD) for FDG-PET for Infection and Inflammation (220.6.16)**

"The CMS is continuing its national non-coverage of FDG-PET for the requested indications. Based upon our review, CMS has determined that the evidence is inadequate to conclude that FDG-PET for chronic osteomyelitis, infection of hip arthroplasty, and fever of unknown origin improves health outcomes in the Medicare populations, and therefore has determined that FDG-PET for chronic osteomyelitis, infection of hip arthroplasty, and fever of unknown origin is not reasonable and necessary under section 1862(a)(1)(A) of the Social Security Act."

## **Rationale/Source**

Policies on PET were originally based on 4 TEC Assessments that addressed various applications of PET. In terms of miscellaneous (i.e., non-cardiac, non-oncologic) applications of PET, PET using FDG was initially considered medically necessary for the assessment of selected patients with epileptic seizures and investigational for other indications. Based on additional literature, the policy was changed in 2007 to state that PET for diagnosing chronic osteomyelitis may be considered medically necessary. The key literature identified in updated literature searches is described below:

### **Epilepsy**

A 2007 meta-analysis on the use of FDG-PET for preoperative evaluation of patients with temporal lobe epilepsy found that ipsilateral PET hypometabolism had a predictive value for a good outcome of 86%. The authors note, however, the difficulty of the analysis because of differences in study design and lack of precise patient data, which made the incremental value of PET unclear. Positron emission tomography may not add value for patients well-localized by ictal scalp electroencephalography and magnetic resonance imaging (MRI).

### **Chronic Osteomyelitis**

In 2005, Termaat and colleagues published a systematic review and meta-analysis of diagnostic imaging to assess chronic osteomyelitis. The authors reviewed studies on 6 imaging approaches to chronic osteomyelitis, including fluorodeoxyglucose PET (FDG-PET) and concluded that PET is the most accurate mode (pooled sensitivity: 96% [95% (confidence interval) CI: 88–99%]; pooled specificity: 91% [95% CI: 81–95%]) for diagnosing chronic osteomyelitis. Leukocyte scintigraphy was adequate in the peripheral skeleton (sensitivity: 84% [95% CI: 72–91%]; specificity: 80% [95% CI: 61–91%]) but was inferior in the axial skeleton (sensitivity: 21% [95% CI: 11–38%]; specificity: 60% [95% CI: 39–78%]). The assessment of PET was based on 4 prospective, European studies published between 1998 and 2003, with a total of 1,660 patients. However, the study populations varied and included the following: 1) 57 patients with suspected spinal infection referred for FDG-PET and who had previous spinal surgery but not "recently"; 2) 22 trauma patients scheduled for surgery who had suspected metallic implant-associated infection; 3) 51 patients with recurrent osteomyelitis or osteomyelitis symptoms for more than 6 weeks, 36 in the peripheral skeleton and 15 in the central skeleton; and 4) 30 consecutive non-diabetic patients referred for possible chronic osteomyelitis. The results appeared to be robust across fairly diverse clinical populations, which strengthen the conclusions.



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## Alzheimer's Disease and Dementia

The CMS issued a decision memorandum on April 16, 2003, that would not support coverage of FDG-PET in AD because the evidence did not demonstrate its use for improved patient outcomes. This decision was based, in part, on a technology assessment conducted at Duke University through the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center. This assessment used decision-analysis modeling to examine whether the use of FDG-PET would improve health outcomes when used for diagnosis of AD in 3 clinical populations: patients with dementia, patients with mild cognitive impairment, or subjects with no symptoms but a first-degree relative with AD. Positron emission tomography was considered to have an 88% sensitivity (95% confidence interval [CI]: 79–94%) and 87% specificity (95% CI: 77–93%) for diagnosing AD. The report concluded that outcomes for all 3 groups of patients were better if all patients were treated with agents such as cholinesterase inhibitors rather than using FDG-PET to select patients for treatment based on PET results, since the complications of treatment were relatively mild, and treatment was considered to have some degree of efficacy in delaying the progression of AD. Thus, the adverse effect of not treating subjects with AD who had false-negative PET results was influential in this analysis. However, this conclusion was sensitive to the toxicity associated with treatment.

In October 2003, CMS agreed to reconsider its policy on PET for AD and dementia. On September 15, 2004, Medicare made public its final decision memorandum announcing a positive national coverage decision for a subset of patients "with a recent diagnosis of dementia and documented cognitive decline of at least 6 months, who meet diagnostic criteria for both AD and FTD, who have been evaluated for specific alternative neurodegenerative diseases or causative factors, and for whom the cause of the clinical symptoms remains uncertain." For its reconsideration, CMS requested an update of the original AHRQ assessment which concluded that no new publications provided direct evidence to evaluate the use of PET to either differentiate among different types of dementia or to identify those patients with mild cognitive impairment who were at greatest risk to progress to AD. In addition, Medicare considered a consensus report by the Neuroimaging Work Group of the Alzheimer's Association and proceedings of an expert panel discussion of neuroimaging in AD, convened by the National Institute of Aging and Medicare.

In 2005, a meta-analysis compared the ability of FDG-PET, SPECT, and structural MR imaging to predict patients' conversion from mild cognitive impairment to AD. Using 24 articles identified among studies published between 1990 to April 2008 (6 on FDG-PET, published 2001-2005), the authors found no statistically significant difference among the 3 modalities in pooled sensitivity, pooled specificity, or negative likelihood ratio, FDG-PET had the highest odds ratio and positive likelihood ratio. However, there was strong evidence of between-study heterogeneity and marked asymmetry in the funnel plot (with studies missing from the bottom left quadrant), reducing confidence in the results. Efforts to identify sources of heterogeneity (e.g., publication year, age, male-female ratio, follow-up interval, years of education, mean mini-mental state examination (MMSE) score at baseline) yielded no significant results; only the imaging technique was associated with the log odds ratio. (In an apparent error, the article states that "[N]o statistically significant difference was found ( $P > .05$ ) for each technique in pooled sensitivity and LR- [emphasis added]. Also, in Table 5, the odds ratio for FDG-PET is reported as 40.146, 95% CI: 18.53 ~ 6.97. The last number appears to be incorrect.)

Research continues on efforts to use PET to identify AD and differentiate it from other types of dementia. For example, a 2008 multicenter, international study with 548 patients, including normal patients and those

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with mild cognitive impairment, AD, frontotemporal dementia, and dementia with Lewy bodies, used Neurological Statistical Image Analysis (Neurostat, University of Washington) to process the results. Excluding the patients with mild cognitive impairment, the sample was split in half, with key PET findings identified on half of the data set and validated on the second half of the data set. The disease-specific PET patterns correctly classified 94% normal patients, 95% AD, 92% dementia with Lewy bodies, 94% frontotemporal dementia ( $p < 0.001$ ). The PET patterns were also 98% sensitive and 92% specific ( $p < 0.001$ ) in distinguishing mild cognitive impairment from normal patients. While interesting, these findings need to be replicated on a less selected sample, i.e., one in which mild cognitive impairment (MCI) patients are included in the mix. Also, the reference standard used was clinical diagnosis, so the incremental value, if any, of PET imaging over clinical judgment alone could not be determined. More generally, evidence of clinical utility would require demonstrating that PET improved diagnostic accuracy and that earlier or more accurate diagnosis led to treatment changes that improved health outcomes.

One of the challenges in evaluating the use of PET to distinguish among dementias is to identify what serves as the reference standard. Durand-Martel and colleagues noted in 2010 that the sensitivity of clinical diagnosis for AD varies between 75% and 98%, with an average of 82%. Therefore, comparing PET results to clinical diagnosis can be confounded by the fact that the clinical diagnosis itself may not be accurate. Durand-Martel et al. asserted that autopsy results should serve as the reference standard in studies on the use of FDG-PET for dementia; they identified only 5 studies with 20 patients or more in which results of both FDG-PET imaging and autopsy were presented.

There is also research on alternative radiotracers to FDG in identifying AD. In particular, there is interest in amyloid PET tracers, because beta amyloid is the principal component of AD plaques in the brain. However, in 2008, the FDA did not approve the use of this type of tracer, because the detection of beta amyloid is not specific for AD. The correlation between retention during PET imaging of Pittsburgh Compound-B (PIB), one of the best known and investigated amyloid tracers, and cognition is "fairly weak." Using both FDG and an amyloid tracer might improve differentiation of AD. Pittsburgh Compound-B has an extremely short half-life, making it necessary to produce the tracer in the same facility as it is used.

Another recent research interest is the potential use of PET scan results as a biomarker for progression to AD. It is difficult to evaluate treatments that may prevent or delay the onset of dementia in individuals with mild cognitive impairment because a relatively small number of study participants will progress to AD during the follow-up period. A 2011 study by Herholz and colleagues in the U.K. used a quantitative PET score previously devised by this research group to evaluate disease progression; a software program was available to calculate the score. The prospective study included 94 patients with MCI, 40 patients with mild AD and 44 healthy controls. Participants received 4 PET scans and clinical assessments over 2 years. By the 2-year follow-up, 30 of 94 (32%) had progressed to MCI, 7 (7%) reverted to normal cognitive function and 57 (61%) remained MCI. Two of 44 (4.5%) healthy controls had progressed to MCI. All of the individuals with AD at baseline remained in that category. The proportion of patients with abnormal PET scores at baseline was 85% in the AD group, 40% in the MCI group, and 11% in the control group. An abnormal PET score at baseline had a sensitivity to predict disease progression of 0.57 and a specificity of 0.67. The area under the receiver-operating characteristic (ROC) curve was 0.75 for PET scores. Areas under the ROC curve for predicting disease progression for the outcome measures Mini-Mental State Examination (MMSE) and the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-cog), were 0.66

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and 0.68, respectively. Conclusions about the utility of using this PET score in clinical practice cannot be drawn from the Herholz study; additional research is needed that evaluates whether patient management decisions using the PET score results in improved health outcomes.

A meta-analysis pooled 7 studies of FDG PET and 6 studies of PET with carbon-11 PIB for prediction of conversion to AD among patients with MCI. Areas under the ROC curve were 0.88 for FDG PET and 0.85 for PIB PET. This report lacks comparisons with other means of predicting conversion from MCI to AD. It also lacks a discussion of how PET might influence treatment decisions and whether use of PET improves health outcomes.

It should be noted that much of the present interest in detecting AD early is to develop and test treatments that might affect the progression of the disease. This is clearly an important goal, but several important challenges must be overcome before PET imaging is routinely used in clinical practice to detect preclinical AD, so that treatment can be started. At the same time, other methods of diagnosing AD that do not involve imaging are also being explored.

Due to the lack of direct evidence that this imaging technique will result in a change in management that will improve patient outcomes, PET for AD and dementia is considered investigational.

## **Vasculitis**

A systematic review of literature on PET and PET/CT in patients with large-vessel vasculitis was published in 2011 by Treglia and colleagues. The investigators identified 32 studies with a total of 604 vasculitis patients. The authors did not pool findings of the studies. They concluded that PET and PET/CT may be useful for initial diagnosis and assessment of severity of disease and that the role of these imaging methods in monitoring treatment response is unclear. They also concluded that "given the heterogeneity between studies with regard to PET analysis and diagnostic criteria, a standardization of the technique is needed." The studies cited in support of using PET for diagnosing large vessel vasculitis had small sample sizes; one study included 25 vasculitis patients and 44 controls; the others had total sample sizes of fewer than 20 patients.

Lehmann and colleagues in Germany published a study after the Treglia review. Positron emission tomography scans of 20 patients with giant cell arthritis or Takayasu arthritis, and 20 healthy controls were retrospectively reviewed by 2 experienced nuclear medicine experts on a blinded basis. Positron emission tomography was found to have a sensitivity of 65% and a specificity of 80% for identifying patients with a known large vessel vasculitis diagnosis. The 2 reviewers agreed on the diagnosis in 34 of 40 (85%) of scans; the interrater agreement (Cohen's kappa) was 0.70. The authors concluded that, due to the low sensitivity and specificity, the diagnosis of large vessel vasculitis should not be based solely on PET findings. Study limitations include being retrospective and not including individuals with suspected, rather than established, large vessel vasculitis.

## **Other indications**

Recent review articles on the use of PET with spinal infections; inflammatory diseases more generally; fever of unknown origin; hyperinsulinemic hypoglycemia; mycobacterium infection; inflammatory bowel disease; and multiple sclerosis indicate insufficient evidence on the benefit of PET for these indications. Many of the studies cited in the reviews were small, retrospective, published in the 1990s to early 2000s and/or many



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studies did not directly compare one modality to another in the same patient group or connect the PET results in individual patients to improved clinical outcomes.

A 2008 meta-analysis on using FDG-PET to diagnose prosthetic joint infection following hip or knee replacement reported pooled estimates of the sensitivity of PET in detecting infection of 82.1% (95% CI: 68.0–90.8%) and a pooled specificity of 86.6% (95% CI: 79.7–91.4%). The authors note, however, that the results should be interpreted with caution because of significant heterogeneity identified among the 11 studies included (which confers substantial uncertainty on the pooled estimates). Efforts to identify sources of heterogeneity were mostly unsuccessful; there were differences in performance based on location of prostheses (hip vs. knee) and whether filtered back projection or iterative reconstruction was used. The authors stated that a large, multicenter trial is needed to evaluate the use of FDG-PET for identifying infection around joint prostheses. Both this study and another study on the same clinical issue found that the specificity of PET was significantly greater for hip prostheses than for knee prostheses. The articles also noted that these studies were based on the use of PET alone. Computed tomography is generally not useful in evaluating potential infections around joint prostheses because of the artifacts caused by the metallic implants, so additional research would be needed on combined PET/CT. The second study compared the accuracy of PET with a triple-phase scan and with white blood cell imaging. The authors concluded that the latter is the most accurate but also the most complex and time-consuming, while the former is readily available and the easiest to perform. However, these comparisons are open to question because the methods were poorly described and the authors appeared to mix together results from single-arm studies on one modality with comparative studies.

A 2011 systematic review addressed use of PET in evaluating disease activity in patients with sarcoidosis. The report does not include quality assessment of individual studies, a critical feature of a well-conducted systematic review. Only 3 small studies out of 9 reviewed included data from a comparator imaging modality, thus conclusions about comparative diagnostic performance cannot be reached.

## Ongoing clinical trials

Metabolic cerebral imaging in incipient dementia (NCT00329706) This is a randomized controlled trial (RCT) evaluating whether PET scanning can distinguish between patients with early Alzheimer's changes in their brains from patients with other types of cognitive impairment. All participants (estimated enrollment is n = 710) will undergo scanning with FDG-PET. They will be randomized to immediate release of the PET report or a 2-year delay in the release of the report. Outcomes include change in cognitive function, utilization of health resources, and prescriptions for Alzheimer's-specific therapies. The expected study completion date is January 2016.

## Summary

PET for selected patients with epilepsy and patients with chronic osteomyelitis may be considered eligible for coverage. There is insufficient evidence on the value of PET for other miscellaneous (non-cardiac, non-oncologic) indications. Studies are needed that demonstrate that PET will result in a change in management that will improve patient outcomes in order to determine that it is a clinically useful test.

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# BlueCross BlueShield of Louisiana

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Positron Emission Tomography (PET) Miscellaneous (Non-cardiac, Non-oncologic) Applications

Policy # 00104

Original Effective Date: 01/28/2002

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## Coding

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Code Type	Code
CPT	78608, 78609, 78811, 78812, 78813, 78814, 78815, 78816
HCPCS	A9526, A9552, A9580
ICD-9 Diagnosis	All diagnoses

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ICD-9 Procedure	92.01, 92.02, 92.03, 92.09, 92.11, 92.12, 92.14, 92.15, 92.16, 92.17, 92.18, 92.19
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## **Policy History**

Original Effective Date: 01/28/2013

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12/06/2001 Medical Policy Committee review  
01/28/2002 Managed Care Advisory Council approval  
06/24/2002 Format revision. No substance change to policy.  
07/06/2004 Medical Director review  
07/20/2004 Medical Policy Committee review. Format revision. No substance change to policy.  
07/26/2004 Managed Care Advisory Council approval  
07/13/2005 Medical Director review  
07/19/2005 Medical Policy Committee review  
08/24/2005 Managed Care Advisory Council approval  
07/07/2006 Format revision including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.  
09/06/2006 Medical Director review  
09/20/2006 Medical Policy Committee approval. No changes to policy guidelines.  
06/13/2007 Medical Director review  
06/20/2007 Medical Policy Committee approval. Policy updated with literature search. Chronic osteomyelitis added as "may be considered medically necessary" and giant cell arteritis added as "investigational".  
07/02/2008 Medical Director review  
07/16/2008 Medical Policy Committee approval. No change to coverage eligibility.  
07/02/2009 Medical Director review  
07/22/2009 Medical Policy Committee approval. No change to coverage eligibility.  
01/01/2010 Coding Revision  
07/01/2010 Medical Policy Committee approval  
07/21/2010 Medical Policy Implementation Committee approval. Two additional dementia subtypes added to the investigational policy statement indications (frontotemporal dementia and dementia with Lewy Bodies).  
07/07/2011 Medical Policy Committee approval  
07/20/2011 Medical Policy Implementation Committee approval. Minor changes to policy statements (investigational indication for schizophrenia moved from dementias to psychiatric diseases and disorders; "vasculitis" added to investigational "other" category).  
02/15/2012 Coding updated.  
06/28/2012 Medical Policy Committee review  
07/27/2012 Medical Policy Implementation Committee approval. Added (Non-cardiac, Non-oncologic) to the policy title. Mycobacterium infection and inflammatory bowel disease added as investigational indications.  
08/01/2013 Medical Policy Committee review  
08/21/2013 Medical Policy Implementation Committee approval. Sarcoidosis added as an investigational indication.

Next Scheduled Review Date: 08/2014

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

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- A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
  2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  3. reference to federal regulations.

\*\*Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. in accordance with nationally accepted standards of medical practice;
- B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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