Clinical Policy Title: Autonomic nervous system monitoring for neuropathy

Clinical Policy Number: 09.01.01

**Effective Date:** September 1, 2013
**Initial Review Date:** February 18, 2013
**Most Recent Review Date:** April 19, 2017
**Next Review Date:** April 2018

Policy contains:
- Autonomic nervous system
- Diabetes
- Neuropathy

**Related policies:**
None.

**ABOUT THIS POLICY:** Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state and federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

**Coverage policy**

Select Health of South Carolina considers the use of autonomic nervous system (ANS) monitoring for neuropathy to be clinically proven and, therefore, medically necessary when overseen and interpreted by a physician of the appropriate specialty (neurologist or cardiologist) and when the following criteria are met:

<table>
<thead>
<tr>
<th>Autonomic nervous system tested</th>
<th>Medically appropriate test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular system</td>
<td>• Heart rate response to standing (HRSTAND).</td>
</tr>
<tr>
<td></td>
<td>• Heart rate response to the valsalva maneuver (HRVM).</td>
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<tr>
<td>Direct nerve measurement</td>
<td>• Heart rate response to deep breathing (HRDB).</td>
</tr>
<tr>
<td>Sudomotor function tests</td>
<td>• Resting heart rate variability (resting HRV).</td>
</tr>
<tr>
<td></td>
<td>• Blood pressure response to standing.</td>
</tr>
<tr>
<td>Peripheral sensory perception threshold tests</td>
<td>• Needle insertion nerve conduction studies.</td>
</tr>
<tr>
<td></td>
<td>• Sympathetic skin response test (SSR).</td>
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<tr>
<td></td>
<td>• Quantitative sudomotor axon reflex test (QSART).</td>
</tr>
<tr>
<td></td>
<td>• Vibration perception threshold test.</td>
</tr>
<tr>
<td></td>
<td>• Thermal perception threshold test.</td>
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</tbody>
</table>
Limitations:

All other uses of ANS monitoring for neuropathy are not medically necessary.

Alternative covered services:

- Physician office visits.
- Appropriate therapy sessions.

Background

Dysfunction of the ANS, including neuropathy, may involve conditions that affect either the sympathetic or parasympathetic nerves. The resulting deregulation may be clinically insignificant or may manifest as a number of symptoms based upon the body organs affected.

ANS dysfunction that affects the cardiovascular system may result in either rapid resting heart rate or slowing. Blood pressure may drop on standing, a condition called “orthostatic hypotension.” Any cardiovascular effects may result in syncope, or loss of consciousness. ANS dysfunction affecting other organs may result in genitourinary symptoms (e.g., urinary incontinence, erectile dysfunction, incomplete voiding/neurogenic bladder), gastrointestinal symptoms (gastroparesis, diarrhea or constipation), sweating problems with excessive or inadequate sweat production that can affect body temperature control, or vision difficulties from inappropriate pupillary constriction.

ANS neuropathy may be caused by symptoms, a patient’s general health, family history, recent/current medications, exposure to poisons, alcohol consumption, and sexual history. These factors should be assessed by the attending physician. Checking the skin, pulse, sensation, and reflexes may also offer clues in the diagnosis of ANS neuropathy. Diagnosis can be made through nerve conduction studies that check speed of nerves sending messages, through electrodes placed on the skin over the nerve; electromyography in which a thick needle is inserted into the skin and muscle and an oscilloscope is used to stimulate the nerves; or through nerve and skin biopsies.

A number of diseases may account for ANS dysfunction. Autonomic neuropathy is an important, but not well-recognized complication of diabetes. Its clinical manifestations include orthostatic hypotension, exercise intolerance, gastroparesis, diarrhea, constipation, and urinary incontinence. The disorder is linked with sudden unexplained deaths in young people, even though the condition is relatively rare. In diabetic adults, autonomic neuropathy is a strong predictor of mortality, mostly due to cardiovascular disease, nephropathy, and hypoglycemia (Tang, 2013).

Tests for ANS abnormalities become part of the diagnostic strategy and must be selected based on the specific set of symptoms. A given test may be appropriate in one setting but not another. Not all of the tests available are well studied. The level of evidence for any given test is based on the reliability and reproducibility of that modality. Tests for autonomic dysfunction may be used for
diagnosis, prognosis or monitoring of the condition. Appropriate application and interpretation of ANS testing requires a detailed knowledge of the testing criteria and a match between the tests of suspected clinical/functional impairment with the autonomic activity being tested. Autonomic testing may be indicated to exclude or confirm rarer autonomic disorders.

**Searches**

Select Health of South Carolina searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on February 28, 2017. Search terms were: “autonomic nervous system” and “neuropathy.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

An American Academy of Neurology (AAN) practice parameter found that autonomic testing should be considered in evaluating patients with 1) polyneuropathy to document ANS involvement; and 2) suspected autonomic neuropathies. Both applications were given a level “B” grade by the expert panel (AAN, 2009).

A publication from the National Heart, Lung, and Blood Institute asserted that ANS function is assessed by measuring resting heart rate, heart rate variability, or heart rate recovery after exercise. These measures can identify correlates of ANS dysfunction for patients, such as obesity, diabetes, and heart failure (Lauer, 2009).

Recommendations from the Neuropathy Study Group of the Italian Society of Diabetology were produced because diabetic autonomic neuropathy is not often diagnosed. These recommendations include information on how and when to perform the recommended tests, and how to interpret them.
A Hayes review from 2014 assessed 23 studies (n=6141) on ANS monitoring for neuropathy. Diabetics was the topic of 17 of these studies, and 20 of 23 focused on adults. The types of tests included 1) cardiovascular tests; 2) nerve/muscle fiber conduction tests; 3) sudomotor function tests; 4) peripheral sensory perception threshold tests; 5) laser Doppler skin blood flow studies; 6) pupillary function tests; 7) gastric emptying tests; and 8) serum autonomic neurotransmitter tests. The proportion of abnormalities in persons with a disorder versus healthy persons were compared for each. Hayes rated the efficacy of most tests as “moderate” when sufficient data was available (Hayes, 2014).

Diabetes is perhaps the most studied condition for efficacy of ANS testing. In particular, cardiovascular autonomic neuropathy is one of the most serious complications of diabetes, as damage to the autonomic nerve fibers in heart vessels can result in heart rate and vascular abnormalities (Vinik, 2007).

One study of 151 Type 1 diabetes patients assessed the association of various risk factors to the disease. These included neuropathy and diabetic neuropathy; both were highly significant predictors of the disease (Tannus, 2014). Another review found an under-diagnosis of cardiovascular autonomic neuropathy in persons with diabetes due to low interest in an unfamiliar complication; skepticism of therapies; lack of understanding diagnostic utility; and need for education and training – in spite of evidence of predictive value of neuropathy for the disease. A related issue is the lack of uniformity of treatment (Rolim, 2013).

A study of 490 persons age 50 – 75 with diabetes followed for a median of 13.6 years found that cardiac autonomic dysfunction, described using 10 measures, was strongly associated with risk of cardiovascular mortality, and recommended such measures be monitored in diabetics (Beijers, 2009). A related article found that the impact of hypoglycemia on cardiovascular autonomic function could explain the risk of cardiovascular mortality among diabetics (Adler, 2009). Another study documented that more diabetics on intensive therapy had neuropathy than those on standard therapy (Duckworth, 2009).

Individuals with the metabolic syndrome have alterations in the function of the ANS, and these alterations are linked with greater risk of aspects of the syndrome, such as obesity, hypertension, and insulin resistance – although the issue of whether these alterations are contributors or a consequence of the syndrome remain unresolved (Licht, 2010).

Patients with obstructive sleep apnea have increased levels of sympathetic activity, resulting in ANS imbalance, potentially predisposing them to greater risk of cardiac arrhythmias (Aytemir, 2007).

Some new monitors have been developed to track ANS activity. One is a pleth-wave derived parameter, the Perfusion Index, was tested on 20 patients, and Index modifications occurred (Del Buono, 2016). Another is a low power generic small wireless sensor node to monitor physiological
signals of responses of the ANS (Brown, 2009).

**Policy updates:**

A total of four clinical guidelines/other and 12 peer-reviewed references were added to this version of the policy.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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</thead>
</table>
| Hayes (2014) | **Key points:**  
- Literature review of 23 studies (n=6141); diabetics were the subject in 17 of 23, adults were the subject in 20 of 23.  
- Tests included 1) cardiovascular tests; 2) nerve/muscle fiber conduction tests; 3) sudomotor function tests; 4) peripheral sensory perception threshold tests; 5) laser Doppler skin blood flow studies; 6) pupillary function tests; 7) gastric emptying tests; and 8) serum autonomic neurotransmitter tests.  
- Efficacy of most tests rated “moderate”; some had insufficient data, and not rated. |
| Casellini (2013) | **Key points:**  
- 83 DM patients with and without diabetic neuropathy and 210 healthy controls.  
- Neuropathy impairment score-lower legs (NIS-LL), quantitative autonomic function testing (QAFIT) and quantitative sensory testing (QST) were performed.  
- Sudomotor function testing (Sudoscan) measures electrochemical skin conductance of hands and feet through reverse iontophoresis.  
- Sudomotor testing is sensitive tool to detect neuropathy in patients and can be performed in 3 – 5 minutes. |
| Beijers (2009) | **Key points:**  
- Study of 490 diabetics ages 50 – 75, followed for 13.6 years (median)  
- Ten parameters of cardiovascular autonomic dysfunction graded for each subject  
- Cardiovascular autonomic dysfunction significantly raised risk of cardiovascular mortality (risk ratio = 1.74). |
| AAN (2009) | **Key points:**  
- Role of autonomic testing, nerve biopsy, and skin biopsy in diagnosing distal symmetric polyneuropathy.  
- Autonomic testing should be considered in evaluating patients with suspected autonomic neuropathies.  
- Autonomic testing should be considered in evaluating patients with polyneuropathy to document autonomic nervous system involvement. |
References

Professional society guidelines/other:


Peer-reviewed references:


Del Buono R, Cappiello D, Pascarella G, Agro FE. The monitoring of the autonomic nervous


CMS National Coverage Determinations (NCDs):

70.2.1 Services provided for the Diagnosis and Treatment of Diabetic Sensory Neuropathy with Loss of Protective Sensation (aka Diabetic Peripheral Neuropathy). July 1, 2002.
    erageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=neuropathy&KeyWordLookUp=Title&KeyW
    ordSearchType=And&bc=gAAAAACAAA AAAAA%3d%3d&. Accessed March 2, 2017.

Local coverage determinations (LCDs):

Autonomic Function Testing
    ticleType=All&PolicyType=Final&s=All&KeyWord=autonomi c+function+testing&KeyWordLookUp=Title&KeyWord
    SearchType=And&bc=gAAAAAA AAAAAA%3d%3d&. Accessed March 2, 2017.

    cleType=All&PolicyType=Final&s=All&KeyWord=autonomic+function+testing&KeyWordLookUp=Title&KeyWordSearch
    Type=And&bc=gAAAAAA AAAAAA%3d%3d&. Accessed March 2, 2017.

L35395 Autonomic Function Tests Novitas Solutions, Inc.
L34500 Medicine: Autonomic Function Tests Cahaba Government Benefit Administrator’s, LLC.
L33609 Autoimmune Function Tests. First Coast Service Options, Inc.

October 1, 2015. https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=autonomic+function+tests&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAAAA AAAAAA%3d%3d&. Accessed March 2, 2017.

Autonomic Nervous System.
L35456 Nerve Blockade for Treatment of Chronic Pain and Neuropathy. Noridian Healthcare Solutions LLC.
Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>95921</td>
<td>Testing of autonomic nervous system function, cardiovagal innervation (parasympathetic function), including 2 or more of the following: heart rate response to deep breathing with recorded R-R interval, valsalva ratio, and 30:15 ratio</td>
<td></td>
</tr>
<tr>
<td>95922</td>
<td>Testing of autonomic nervous system function, vasomotor adrenergic innervation (sympathetic adrenergic function), including beat-to-beat blood pressure and R-R interval changes during valsalva maneuver and at least 5 minutes of passive tilt</td>
<td></td>
</tr>
<tr>
<td>95923</td>
<td>Testing of autonomic nervous system function, sudomotor, including 1 or more of the following: quantitative sudomotor axon reflex test (QSART), silastic sweat imprint, thermoregulatory sweat test, and changes in sympathetic skin potential</td>
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</tr>
<tr>
<td>95924</td>
<td>Combined parasympathetic and sympathetic adrenergic function testing with at least 5 minutes of passive tilt</td>
<td></td>
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<tr>
<td>95943</td>
<td>Simultaneous, independent, quantitative measures of both parasympathetic function and sympathetic function, based on time-frequency analysis of heart rate variability concurrent with time-frequency analysis of continuous respiratory activity, with mean heart rate and blood pressure measures, during rest, paced (deep) breathing, valsalva maneuvers, and head-up postural change</td>
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</tbody>
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<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>E08.43</td>
<td>Diabetes mellitus due to underlying condition with diabetic autonomic (poly)neuropathy</td>
<td></td>
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<tr>
<td>E08.49</td>
<td>Diabetes mellitus due to underlying condition with other diabetic neurological complication</td>
<td></td>
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<tr>
<td>E09.43</td>
<td>Drug or chemical induced diabetes mellitus with neurological complications with diabetic autonomic (poly)neuropathy</td>
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</tr>
<tr>
<td>E09.49</td>
<td>Drug or chemical induced diabetes mellitus with neurological complications with other diabetic neurological complication</td>
<td></td>
</tr>
<tr>
<td>E10.43</td>
<td>Type 1 diabetes mellitus with diabetic autonomic, (poly)neuropathy</td>
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</tr>
<tr>
<td>E10.49</td>
<td>Type 1 diabetes mellitus with other diabetic neurological complication</td>
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<tr>
<td>ICD-10 Code</td>
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<td>Comments</td>
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<tr>
<td>E11.43</td>
<td>Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy</td>
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<tr>
<td>E11.49</td>
<td>Type 2 diabetes mellitus with other diabetic neurological complication</td>
<td></td>
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<tr>
<td>E13.43</td>
<td>Other specified diabetes mellitus with diabetic autonomic (poly)neuropathy</td>
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<tr>
<td>E13.49</td>
<td>Other specified diabetes mellitus with other diabetic neurological complication</td>
<td></td>
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<tr>
<td>G60.3</td>
<td>Idiopathic progressive neuropathy</td>
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<tr>
<td>G90.1</td>
<td>Familial dysautonomia (Riley-Day Syndrome)</td>
<td></td>
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<tr>
<td>G90.2</td>
<td>Horner's syndrome</td>
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<tr>
<td>G90.3</td>
<td>Shy-Drager Syndrome</td>
<td></td>
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<tr>
<td>G90.4</td>
<td>Autonomic dysreflexia</td>
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<tr>
<td>G90.8</td>
<td>Other disorders of autonomic nervous system</td>
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<tr>
<td>G90.9</td>
<td>Disorder of the autonomic nervous system, unspecified</td>
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<table>
<thead>
<tr>
<th>HCPCS Level II Code</th>
<th>Description</th>
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<tbody>
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