FEP 2.04.130 ST2 Assay for Chronic Heart Failure and Heart Transplant Rejection

Effective Date: October 15, 2018
Related Policies: 2.01.68 Laboratory Tests for Heart Transplant Rejection

ST2 Assay for Chronic Heart Failure and Heart Transplant Rejection

Description
Clinical assessment and noninvasive imaging of chronic heart failure can be limited in accurately diagnosing patients with heart failure because symptoms and signs can poorly correlate with objective methods of assessing cardiac dysfunction. For management of heart failure, clinical signs and symptoms (e.g., shortness of breath) are relatively crude markers of decompensation and occur late in the course of an exacerbation. Thus, circulating biomarkers have potential benefit in heart failure diagnosis and management. A protein biomarker, soluble suppression of tumorigenicity-2 (sST2), has elicited interest as a potential aid to predict risk and manage therapy of heart failure as well as to manage in patients in the setting of heart transplant.

OBJECTIVE
The objective of this evidence review is to evaluate the ability of soluble suppression of tumorigenicity-2 assays to determine prognosis and/or to guide treatment in patients with chronic heart failure and to determine prognosis and/or to predict acute cellular rejection in patients undergoing heart transplantation.

POLICY STATEMENT
The use of the Presage ST2 Assay to evaluate the prognosis of patients diagnosed with chronic heart failure is considered investigational.

The use of the Presage ST2 Assay to guide management (e.g., pharmacologic, device-based, exercise) of patients diagnosed with chronic heart failure is considered investigational.

The use of the Presage ST2 Assay in the post cardiac transplantation period, including but not limited to predicting prognosis and predicting acute cellular rejection, is considered investigational.

BENEFIT APPLICATION
Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient’s existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.
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Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

In 2011, the Presage® ST2 Assay kit (Critical Diagnostics) was cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process for use with clinical evaluation as an aid in assessing the prognosis of patients diagnosed with chronic heart failure. The assay had already received Conformite Europeenne Mark in January 2011. The Presage® ST2 Assay kit is provided in a microplate configuration. The kit contains a ready-to-use 96-well microtiter plate coated with mouse monoclonal antihuman sST2 antibodies; a recombinant human sST2 standard calibrator (lyophilized); a standard diluent; an anti-ST2 biotinylated antibody reagent (mouse monoclonal antihuman sST2 antibodies) in phosphate-buffered saline; a sample diluent; a tracer concentrate and tracer diluent; a wash concentrate; a tetramethylbenzidine reagent; a stop solution; and 2 levels of controls provided in a sealed, lyophilized format (high and low control).

RATIONALE

Summary of Evidence

For individuals who have chronic heart failure who receive the sST2 assay to determine prognosis and/or to guide management, the evidence includes correlational studies and a meta-analysis. Relevant outcomes are overall survival, quality of life, and hospitalization. Most of the evidence is from reanalysis of existing randomized controlled trials and not from studies specifically designed to evaluate the predictive accuracy of sST2. Studies have mainly found that elevated sST2 levels are statistically associated with elevated risk of mortality. A pooled analysis of study results found that sST2 significantly predicted overall mortality and cardiovascular mortality. Several studies, however, found that sST2 test results did not provide additional prognostic information compared with N-terminal pro B-type natriuretic peptide levels. Moreover, no comparative studies were identified on the use of the sST2 assay to guide management of patients diagnosed with chronic heart failure. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have heart transplantation who receive sST2 assay to determine prognosis and/or to predict acute cellular rejection, the evidence includes a small number of retrospective observational studies on the Presage ST2 Assay. Relevant outcomes are overall survival, morbid events, and hospitalization. No prospective studies were identified that provide high-quality evidence on the ability of sST2 to predict transplant outcomes. One retrospective study (N=241) found that sST2 levels were associated with acute cellular rejection and mortality; another study (N=26) found that sST2 levels were higher during an acute rejection episode than before rejection. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

The American College of Cardiology Foundation and American Heart Association published joint evidence-based guidelines (2013), informed by a systematic review of the literature, on the management of heart failure. The review stated that soluble suppression of tumorigenicity-2 (sST2) is a biomarker for myocardial fibrosis that predicts hospitalization and death in patients with heart failure and provides additive prognostic information to natriuretic peptide levels. In the ambulatory heart failure setting, the guidelines were based on a class IIb recommendation with level B evidence for the use of sST2 as an option to provide additive prognostic information to established clinical evaluation and biomarkers. The guidelines did not address other uses of sST2.
U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

7. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. Aug 2012;14(8):803-869. PMID 22828712
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POLICY HISTORY

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>March 2015</td>
<td>New Policy</td>
<td>Policy created with literature review through October 22, 2014. Two new Policy statements: The use of the Presage® ST2 Assay is considered investigational for evaluating the prognosis of patients with chronic heart failure, to guide management of patients with heart failure, and for use in the post cardiac transplantation period.</td>
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<tr>
<td>September 2018</td>
<td>Update Policy</td>
<td>Policy updated with literature review through March 6, 2018; references 24 and 34 added. Policy statements unchanged.</td>
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