Medical Policy

BlueCross BlueShield of Kansas
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Title: High-Sensitivity C-Reactive Protein

Professional
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DESCRIPTION

C-reactive protein (CRP) is an acute phase reactant that has long been used to monitor inflammatory processes, such as infection and autoimmune diseases. Recent studies have suggested that low-level chronic inflammation may play a role in atherogenesis, and thus measurement of CRP has been investigated in various settings of cardiovascular disease.

C-reactive protein (CRP) is an acute phase reactant produced by the liver that has long been used to monitor inflammatory processes, such as infection and autoimmune diseases. Recent studies have suggested that low-level chronic inflammation may play a role in atherogenesis, and thus measurement of CRP has been investigated in various settings of cardiovascular disease, i.e., in patients with known cardiovascular disease, in patients with risk factors for cardiovascular disease, and as a general risk assessment tool for cardiovascular disease. Conventional methodologies for measuring CRP in acute

inflammatory diseases have a detection limit of 3-5 mg/dL. However, in the setting of the low levels of chronic inflammation in otherwise healthy individuals, this level of detection is not adequate. To be used as a risk assessment tool, a greater precision at lower levels of CRP is needed such that the range of values collected in epidemiologic studies can be subdivided into quartiles and quintiles; in this way, the data from large epidemiologic studies can be applied to individual patients. Such technologies, collectively known as high-sensitivity C-reactive protein (hs-CRP), include enzyme-linked immunosorbent assays (ELISA) and various other techniques based on monoclonal antibodies.

Regulatory Status

While the ELISA test is still primarily used as a research tool, various immunoassays have been automated and are commercially available. Several of the high-sensitivity C-reactive protein tests have received 510(k) marketing clearance from the U.S. Food and Drug Administration (FDA).

POLICY

A. Measurement of high-sensitivity C-reactive protein is considered **experimental / investigational** as a method of cardiac risk stratification.

B. Measurement of high-sensitivity C-reactive protein is considered **experimental / investigational** for determining clinically significant inflammation. Standard C-reactive protein is sufficient for this purpose.

RATIONALE

The most recent update included a literature review for the period of August 2010 through July 15, 2011.

Evaluation of the clinical utility of a risk factor involves the following steps:

1. Standardization of the measurement of the risk factor.

2. Determination of its contribution to risk assessment. As a risk factor, it is important to determine whether the novel risk factor (i.e., high-sensitivity C-reactive protein [hs-CRP]) independently contributes to risk assessment compared to established risk factors.

In addition, it is important to understand the relationship of any novel risk factor with other “”emerging” risk factors. There are many potential novel risk factors that could be incorporated into existing risk assessment guidelines. These include measurements of lipid subclasses (e.g., apo B, low density lipoprotein [LDL] size, etc.), inflammatory markers (e.g., CRP, fibrinogen, plasminogen activator, etc.), as well as other potential cardiac-related measurements (e.g., B-natriuretic peptide [BNP], homocysteine, etc.). Any one of these markers may individually contribute to risk assessment models. However, the optimal combination of markers for risk assessment can only be understood by evaluating multiple potential markers in a multivariate fashion.

3. Determination of how the novel risk assessment will be used in the management of the patient, compared to standard methods of assessing risk, and whether any subsequent changes in patient management result in an improvement in patient outcome.

The above attributes are reviewed in relation to hs-CRP.

1. Standardization of the measurement of the risk factor.

Several studies have evaluated automated methods of measuring hs-CRP and compared them to enzyme-linked immunosorbent assays (ELISA), considered the gold standard. (1,2) These studies suggest a high correlation between the automated assays and the ELISA assay. In addition, serial measurement levels of hs-CRP have shown minimal variability among healthy adults. (3)

2. Determination of its contribution to risk assessment.

A large number of prospective epidemiologic studies have reported that measurement of hs-CRP is an independent risk factor for cardiovascular disease in a variety of clinical settings. For example, results of the Multiple Risk Factor Intervention Study (MRFIT) demonstrated that among male smokers there was a correlation between hs-CRP and coronary heart disease mortality. (4) Similarly, a direct positive correlation between hs-CRP and future coronary events was observed among apparently healthy men participating in the Physicians' Health Study. (5,6) Results from the Women's Health Study report similar findings in women. (7) These studies also suggest levels of hs-CRP were independent of other recognized cardiovascular risk factors and that risk models incorporating measurements of lipids and hs-CRP were better at predicting risk than risk assessment based on lipid levels alone. Elevated levels of hs-CRP have also been found to be independent risk factors of cardiovascular risk in those with both chronic stable and unstable angina. (8,9)

A TEC Special Report completed in 2002 (10) concluded that a large body of well-done observational cohort studies demonstrates an association between C-reactive protein levels and risk of future coronary heart disease (CHD) events. There are, however, uncertainties as to the exact role CRP plays in the pathogenesis of CHD and the reliability of CRP assessment.

Since the 2002 TEC Assessment, numerous studies have confirmed the independent predictive ability of CRP for cardiovascular disease. Analysis of data from the Cardiovascular Health Study, consisting of 5,020 patients without baseline cardiovascular disease followed up for 12 years, examined whether hs-CRP was an independent predictor of future cardiovascular events (11). An elevated hs-CRP (greater than 3 mg/l) was an independent predictor of cardiovascular death in patients with preexisting carotid atherosclerosis (relative risk [RR] 1.72, 95% confidence interval [CI] 1.46-2.01) but was not an independent predictor of outcomes in patients without preexisting carotid atherosclerosis.

Not all prospective cohort studies have concluded that CRP is an independent predictor for cardiovascular disease. Olsen et al. (12) followed up 2,656 individuals from Denmark over a period of 9.4 years and evaluated the incremental predictive ability of a number of emerging risk markers, including hs-CRP, N-terminal BNP, and urine albumin/creatinine ratio. When controlled for both traditional risk markers, N-terminal BNP added significant predictive information for future cardiovascular events while hs-CRP did not (HR 1.17, p=NS).

More recent literature has focused on the predictive ability of CRP when considered together with other emerging risk factors. These studies examined different combinations of potential risk factors and used different methods of analyzing the predictive relationship among these factors. Ridker and colleagues (13) evaluated the predictive ability of hs-CRP in relationship to the emerging lipid measures apo B and apo A-I in 15,632 women enrolled in the Women's Health Initiative. This study concluded that hs-CRP added significant predictive information above that of apo B or apo A-I. However, these analyses of "additional predictive ability" were performed individually for each of the lipid measurements rather than in a fully integrated multivariate model.

Wang and colleagues (14) evaluated 10 potential biomarkers (i.e., hs-CRP, BNP, N-terminal pro-atrial natriuretic peptide, aldosterone, renin, fibrinogen, D-dimer, plasminogen-activator inhibitor type I, homocysteine, and the urinary albumin/creatinine ratio) in 3,209 participants in the Framingham Heart Study. In a multivariate model including all 10 potential biomarkers, CRP was not an independent predictor for cardiovascular events but was an independent predictor of overall mortality. This study also included an analysis of the incremental predictive ability of these markers for classification accuracy, using the C-statistic (similar to receiver operating characteristic [ROC] analysis). For cardiovascular events, the C-statistic (analogous to "area under the curve" in ROC analysis) was 0.76 in a model including age, sex, and conventional risk measurements. This C-statistic rose only slightly to 0.77 when the experimental biomarkers were entered into the model. The authors therefore concluded that the additional predictive ability of these novel biomarkers was modest at best.

Ridker et al. (15) published the Reynolds Risk Score, which is an empirically derived prediction model for cardiovascular outcomes based on data from 24,558 initially healthy women enrolled in the Women's Health Study and followed up for a median of 10.2 years. A total of 35 potential predictors of cardiovascular disease were considered as potential predictors in both derivation and validation models. Hs-CRP was 1 of 9 independent predictors of cardiovascular events that were included in the final model. Zakai et al. (16) evaluated 13 potential biomarkers for independent predictive ability compared to established risk factors, using data from 4,510 individuals followed up for 9 years in the Cardiovascular Health Study. Hs-CRP was one of 7 biomarkers that had incremental predictive ability above established risk factors. The adjusted hazard ratio for each standard deviation increase in hs-CRP was 1.13 (95% CI: 1.05-1.21).

Kozan et al. (17) evaluated the ability of hs-CRP to impact classification of cardiac risk. These authors classified 1,817 hypertensive patients from the Intensive/Initial Cardiovascular Examination Regarding Blood Pressure Levels: Evaluation of Risk Groups (ICEBERG) study into risk categories according to the European Society of Hypertension/European Society of Cardiology guidelines. The addition of hs-CRP to risk prediction models significantly increased the absolute number of patients classified into "high" or "very high" risk categories by 11–13%.

Numerous studies were identified through 2010-2011 that continued to evaluate the predictive ability of hs-CRP in different clinical situations. For example, studies reported that hs-CRP is an independent predictor of future cardiac events for patients with acute MI, (18) following stenting with drug-eluting stents (19-20), post-coronary artery bypass graft (CABG) surgery, (20) and following vascular surgery. (21) In addition, elevated CRP levels were reported to be predictive of total and ischemic stroke among middle-aged Japanese individuals. (22) These studies extend the literature on the predictive ability of hs-CRP to different populations.

3. Determination of how risk assessment will be used in the management of the patient.

There are fewer studies that examine the impact of CRP on management, the most prominent of which is the JUPITER trial. Several earlier studies demonstrated that CRP levels decline in association with statin treatment. For example, Ridker and colleagues reported that among patients with primary hypercholesterolemia, 8 weeks of cerivastatin therapy was associated with a reduction in CRP levels independent of reduction in lipid levels (23). Some authors have suggested that elevated hs-CRP levels may lead to improved compliance with physician recommendations regarding diet, exercise, and smoking cessation, but this hypothesis is still untested.

Measurement of hs-CRP has been included as an outcome measure in interventional studies (24-28). Ridker and colleagues evaluated the relationships between the LDL cholesterol and CRP levels achieved after treatment with statin drugs and the risk of recurrent myocardial infarction (MI) or cardiovascular death in 3,745 patients with acute coronary syndromes (28). Patients who had low CRP levels after statin therapy had better clinical outcomes than those with higher CRP levels, regardless of the resultant level of LDL cholesterol. Nissen and colleagues examined the outcomes of moderate and intensive statin therapy in patients with documented coronary artery disease (27). Lipoprotein and CRP levels were measured at baseline and at follow-up. The primary outcome was the progression of atherosclerosis, as assessed by ultrasonography. The decrease in CRP levels was independently and significantly correlated with the rate of progression. Sattar et al. (29) used data from the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) to evaluate whether hs-CRP levels were associated with degree of response to statin therapy. While this analysis reported that hs-CRP levels were a predictor of adverse cardiovascular outcomes, there was no correlation between hs-CRP levels and response to statin therapy.

McMurray and colleagues (30) performed a retrospective analysis of the CORONA trial, stratifying patients into high (greater than 2.0) or low (less than 2.0) CRP groups. The CORONA trial randomly assigned 4,961 patients with heart failure to rosuvastatin or placebo and followed patients for the development of major adverse cardiovascular events. The retrospective analysis of this trial compared the degree of benefit from statin therapy in the low CRP group with the degree of benefit in the high CRP group. For patients with high CRP, there was a significant reduction in adverse cardiovascular events for patients treated with rosuvastatin (HR 0.87; 95% CI: 0.77–0.98), while for patients with low CRP, there was no benefit reported (HR 1.09; 95% CI: 0.89–1.3). Statistical testing for interaction between CRP and treatment was marginally significant at p=0.062.

A re-analysis of the Heart Protection Study (HPS) was published in 2011 that evaluated the benefit of statin therapy according to CRP levels (31). The 20,536 participants in the HPS were stratified into six groups by baseline CRP level, and major cardiovascular events were compared among the different CRP groups. There was an overall relative risk reduction of 24% for the entire population. Among the different CRP strata, the relative risk reduction did not differ substantially, and there was no evidence for an interaction of LDL and CRP levels. Even among the group of patients with the lowest CRP and lowest LDL levels, there was a 27% reduction (95% CI 11-40%, p<0.0001) in cardiovascular events. This study does not support the hypothesis that the benefit of statin therapy varies according to CRP level.

The JUPITER trial. The JUPITER trial (32) was a multicenter randomized, controlled trial that enrolled 17,802 patients (men age 50 or older and women age 60 or older) from more than 1,300 sites in 26 countries and evaluated the efficacy of statin therapy in patients selected for elevated

CRP and normal LDL levels. The main eligibility criteria included an elevated CRP (greater than 2.0 mg/dL), "normal" LDL (less than 130 mg/dL), and no previous history of heart disease or diabetes mellitus. Patients were randomly assigned to treatment with rosuvastatin or placebo, and follow-up was planned for 4 years. The primary outcome measure was a composite of cardiovascular death, MI, stroke, unstable angina (UA), and revascularization. A second composite outcome was also reported for hard events, i.e., cardiovascular death, MI, and stroke. The trial was stopped early at 1.9 years due to interim analysis that showed benefit in the statin group.

The results reported in the publication were primarily framed in terms of relative risks (RR). For death/MI/stroke/UA/revascularization, the RR was 0.56 (95% CI: 0.46-0.69) for patients treated with rosuvastatin. For death/MI/stroke, the RR was 0.53 (95% CI: 0.40-0.69) for rosuvastatin treatment. There was an increase in physician-reported incidence of diabetes mellitus in the rosuvastatin group (3.0% vs. 2.4%, respectively) as well as a slight increase in mean hemoglobin A1c (5.9 vs. 5.8%, respectively).

The absolute risk for the main composite outcome, calculated from numbers reported in the publication, was 142/8,901 (1.6%) in the statin group versus 251/8,901 (2.8%) in the placebo group. This represents an absolute risk reduction of 1.2% for this outcome and a number needed to treat of 83.3 to prevent 1 event over a 2-year period. For the composite of death/MI/stroke, the absolute risk was 83/8,901 (0.9%) in the statin group versus 157/8,901 (1.8%) in the placebo group. The absolute risk reduction for this outcome was 0.9% with a number needed to treat of 111.

This study establishes that patients with high CRP and normal LDL levels will benefit from treatment with statins. In considering whether this trial should prompt changes in recommendations for selecting and treating patients with statins, several questions remain. First and foremost is the question of whether the absolute risk of cardiovascular disease for this population is high enough to warrant treatment with statins. The concept of selecting patients for treatment based on their absolute risk of cardiovascular disease has precedent in the most recent NCEP recommendations, (33) which base the decision for statin treatment on the 10-year risk of MI or cardiovascular death. It is not possible to directly calculate the 10-year risk for MI/cardiovascular death for patients in the JUPITER study since this composite outcome was not reported. The closest outcome given is for death/MI/stroke (1.8% over 1.9 years), which would extrapolate to a mean risk of 9.5% over 10 years, assuming stable risk over time. This crude calculation suggests that approximately half of the patients enrolled in the trial would reach this threshold of a 10-year risk of 10%. This estimate is consistent with data reported in the JUPITER publication that approximately 50% of patients in the trial had a calculated Framingham 10-year risk of greater than 10%.

A second question is whether selecting patients primarily with CRP level is the optimal method for risk stratification and selection for statin treatment. The Framingham risk score is currently the most common method used and is endorsed by the latest NCEP guidelines (33). This method does have limitations and numerous recent studies have demonstrated that this risk prediction model can be improved by the addition of additional predictors of risk. However, the optimal method for risk prediction has yet to be established, and none of the newer risk prediction models have achieved widespread use. The JUPITER trial does not attempt to compare methods for risk prediction or selection for statin treatment and therefore offers no new information on this question.

Finally, it is not clear whether the relatively large relative risk reduction reported in this trial is due to selection of patients based on high CRP levels. While it is possible that patients selected for high CRP do benefit more from statin therapy than do other populations, the evidence from this trial does not prove that contention. In particular, it may be just as likely, or more likely, that the high relative risk reduction is the result of treatment with rosuvastatin rather than the result of patient selection. Rosuvastatin is the most potent available statin in reducing LDL levels, and this may translate into a larger magnitude of benefit in preventing cardiovascular disease. Since rosuvastatin has been used less extensively than other statins in large clinical trials, it is not yet possible to determine whether this degree of risk reduction is typical of rosuvastatin treatment.

In summary, the JUPITER trial is an important trial that adds to our knowledge concerning the utility of CRP in clinical care and establishes that patients with high CRP and normal LDL levels will benefit from statin treatment. However, because of the uncertainties discussed here, it does not provide sufficient evidence to warrant deviation from the current guidelines regarding selection and treatment of patients with statins. The interpretation of the JUPITER trial remains controversial, and published studies (34-35) continue to debate its interpretation.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

In 2010, input was received from 2 physician specialty societies (5 reviewers) and 5 academic medical centers. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. The input received did not demonstrate strong, uniform clinical support for use of hs-CRP for any application related to cardiovascular disease. The potential use that received the most support, although not uniform, was in evaluating patients with an intermediate risk of cardiovascular disease.

Summary

The existing observational evidence establishes that CRP is an independent predictor of cardiovascular disease across a wide spectrum of patient populations. The evidence also suggests that using CRP as a component of a risk assessment tool will result in a more accurate cardiac risk prediction. There is no scientific literature that directly tests the hypothesis that measurement of C-reactive protein to assess CHD risk results in improved patient outcomes. In addition, there appears to be no generally accepted risk assessment tool available using C-reactive protein that translates into risk estimates to which established treatment guidelines can be applied (e.g., Adult Treatment Panel III sponsored by the National Cholesterol Education Program).

There is some clinical trial evidence reporting that patients with high CRP levels benefit more than patients with low CRP levels, but this is not a consistent finding across all trials. These data are primarily derived from post-hoc analysis of existing randomized, controlled trials that originally selected patients on factors other than CRP. The JUPITER trial selected patients based on elevated CRP levels and demonstrated that these patients have a relatively large benefit from rosuvastatin treatment. However, these trials do not provide sufficient guidance to alter clinical practice. The impact of altering selection criteria for statin therapy based on CRP levels is unclear. Patients with low CRP levels may benefit less from statin treatment; however, it is unclear whether withholding statins in this situation will improve or worsen outcomes. The majority of existing guidelines from

major specialty societies and national organizations do not recommend using CRP as a factor in selecting patients for statin treatment.

None of the new literature identified prompts reconsideration of the current policy statement, which considers this testing investigational.

Practice Guidelines and Position Statements

In 2011, the American College of Preventive Medicine published recommendations for cardiovascular screening of adults. (36) These guidelines recommend using the Framingham Risk Score to assess risk and guide therapy. They do not recommend adding non-traditional risk factors, including hs-CRP, to measurement with the Framingham Risk Score.

In 2010, the American College of Cardiology Foundation and the American Heart Association published recommendations on assessing cardiovascular risk in asymptomatic patients. (37) These recommendations supported the use of hs-CRP for intermediate risk individuals in two situations:

- In men 50 years of age or older, or women 60 years of age or older, with low-density lipoprotein cholesterol less than 130 mg/dL; not on lipid-lowering, hormone replacement, or immunosuppressant therapy; without clinical CHD, diabetes, chronic kidney disease, severe inflammatory conditions, or contraindications to statins, measurement of CRP can be useful in the selection of patients for statin therapy. (Class IIa recommendations) (*Level of Evidence: B*).
- In asymptomatic intermediate-risk men 50 years of age or younger, or women 60 years of age or younger, measurement of CRP may be reasonable for cardiovascular risk assessment. (Class IIb recommendation) (*Level of Evidence: B*)

The American Academy of Family Physicians (AAFP) concluded (2011) that the current evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors discussed in this statement to screen asymptomatic men and women with no history of coronary heart disease (CHD) to prevent CHD events. (38) The nontraditional risk factors included in this recommendation are high-sensitivity C-reactive protein (hs-CRP), ankle-brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima-media thickness (carotid IMT), coronary artery calcification (CAC) score on electron-beam computed tomography (EBCT), homocysteine level, and lipoprotein(a) level.

The US Preventive Services Task Force (USPSTF) concluded (2009) that the current evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors discussed in this statement to screen asymptomatic men and women with no history of coronary heart disease (CHD) to prevent CHD events. (39) The nontraditional risk factors included in this recommendation are high-sensitivity C-reactive protein (hs-CRP), ankle-brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima-media thickness (carotid IMT), coronary artery calcification (CAC) score on electron-beam computed tomography (EBCT), homocysteine level, and lipoprotein(a) level.

In 2008, the American Diabetes Association and American College of Cardiology Foundation noted that additional biomarkers (e.g., C-reactive protein [CRP], fibrinogen, and homocysteine) have been evaluated to determine their prognostic significance; however, their independent predictive power and clinical utility are still unclear. (40) In particular, CRP is often elevated in people with cardiometabolic risk, but here, too, the utility of its measurement in individuals already known to be at high risk is unknown. The American Heart Association/Centers for Disease Control and

Prevention (AHA/CDC) Scientific Statement was published in January 2003. (41) The recommendations of the AHA/CDC are summarized in the following table. In their report, the AHA/CDC offered several recommendations:

Recommendation of AHA/CDC Regarding Role of hs-CRP Measurements in Clinical Practice

Class IIa Recommendations

- Measurement of hs-CRP is an independent marker of risk, and, in those judges at intermediate risk by global risk assessment (10%–120% risk of CHD per 10 years), at the discretion of the physician, may help direct further evaluation and therapy in the primary prevention of cardiovascular disease (CVD). The benefits of such therapy based on this strategy remain uncertain.
- In patients with stable coronary disease or acute coronary syndromes, hs-CRP measurement may be useful as an independent marker of prognosis for recurrent events, including death, myocardial infarction (MI), and restenosis after percutaneous cardiac interventions. The benefits of therapy based on this strategy remain uncertain.

Class IIb Recommendations

- Measurement of hs-CRP is an independent marker of risk and may be used at the discretion of the physician, as part of a global coronary risk assessment in adults without known CVD. The benefits of this strategy remain uncertain. (Compared to the Class IIa recommendation above, this statement includes a broader population of patients.)
- hs-CRP levels may be useful in motivating patients to improve lifestyle behaviors. The benefits of this strategy remain uncertain.

As noted here, none of the recommendations received a Class I recommendation, and the AHA/CDC recognize that the benefits of using hs-CRP as a cardiac risk assessment tool are uncertain. The policy statement, indicating that hs-CRP is investigational, is based on this acknowledged lack of direct evidence linking a risk assessment incorporating hs-CRP to changes in therapy and ultimately to improvement in health outcomes. The strongest recommendation by the CHD/AHA (i.e., IIa) suggests that the results of hs-CRP may help identify patients at intermediate risk who may benefit from primary prevention of CVD. It is estimated that 30–40% of the population may fall into this intermediate risk group. If the results of the hs-CRP measurement are considered high, patients may then be offered various interventions, frequently including the initiation of statin therapy. Therefore, the use of hs-CRP as one component of a risk assessment tool may ultimately result in considerably more patients being placed on life-long drug therapy.

The following comments regarding hs-CRP and standard CRP are from UpToDate. The level of CRP that is truly normal or innocuous is not known. CRP levels vary with age, sex, and race. It is useful to regard CRP levels from 0.3 to 1.0 mg/dL (3 to 10 mg/L) as minor CRP elevation. Higher values are felt to reflect clinically significant inflammation. Values between 0.3 and 1 mg/dL may reflect minor degrees of inflammation such as that seen in periodontitis, but may also reflect obesity, cigarette smoking, diabetes mellitus, uremia, hypertension, low levels of physical activity, oral hormone replacement therapy, sleep disturbance, chronic fatigue, low alcohol consumption, depression, aging, or other apparently non-inflammatory states. One common misunderstanding has been the incorrect belief that hs-CRP is different in some way from the CRP that has been measured for many years. It is not. "High-sensitivity" only means that the concentration of CRP was determined using an assay designed to measure very low levels of CRP. Minor CRP elevation (concentrations between 3 and 10 mg/L) has been generally regarded as a marker of what has

been called low-grade inflammation. However, this poorly defined state, sometimes referred to as mini-inflammation or subclinical inflammation, occurs in many conditions where there are minor degrees of metabolic malfunction, such as obesity and insulin resistance, and in such circumstances is not a marker of inflammation as we have traditionally thought of it. (42)

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

86141 C-reactive protein; high sensitivity (hsCRP)

DIAGNOSIS

Experimental / investigational for all diagnoses related to this policy.

REVISIONS

03-01-2011	Updated Description section
	Updated Rationale section
	Updated References section
08-23-2011	Updated Description section
	Updated Rationale section
	Updated References section
01-30-2012	In Policy section: Added the criteria, "B. Measurement of high-sensitivity C-reactive protein is considered experimental / investigational for determining clinically significant inflammation. Standard C-reactive protein is sufficient for this purpose."
	Updated Rationale section
	Updated References section
10-31-2013	Description section reviewed
	Rationale section reviewed
	References reviewed

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