Description
MPO is a white blood cell-derived inflammatory enzyme that measures disease activity from the luminal aspect of the arterial wall.

Briefly, when the artery wall is damaged, or inflamed, MPO is released by invading macrophages where it accumulates. MPO mediates the vascular inflammation that propagates plaque formation and activates protease cascades that are linked to plaque vulnerability. White blood cell activation in the bloodstream, in response to luminal injury of the artery wall including fissures, erosions or a degrading collagen cap, leads to MPO release in the bloodstream. This combination of detrimental effects demonstrates that MPO is actively involved in the progression of atherosclerosis. The Cleveland HeartLab MPO test measures free MPO in the bloodstream.

Clinical Use
The MPO test may be performed on individuals at intermediate or high risk for developing coronary heart disease who are any age with at least two major risk factors, those ≥65 years of age with one major risk factor, smokers, those with a fasting blood glucose of ≥100 mg/dL, or those who have metabolic syndrome.

Clinical Significance
- Elevated MPO levels predict the risk of heart disease in subgroups otherwise associated with low risk.
- Elevated MPO levels independently predict the risk of future cardiovascular events in patients presenting with an acute coronary syndrome.
- Individuals with elevated MPO levels are more than 2x as likely to experience cardiovascular mortality.
- MPO enhances cardiovascular risk prediction when used independently or alongside standard biomarker testing such as hsCRP.
- MPO levels are not likely to be elevated due to chronic infections or rheumatologic disorders due to the fact that free MPO in the blood is a specific marker of vascular inflammation and vulnerable plaque/erosions/fissures.

Sample Type
The MPO test should be performed on an EDTA plasma sample.

Commercial Insurance or Medicare Coverage
Coverage guidelines, also known as NCD (National Coverage Determination) or LCD (Local Coverage Determination) have been established or posted by CMS (Medicare & Medicaid). Guidelines should be reviewed for coverage and limitations. Limited information has been provided by the majority of the larger carriers (Aetna, United HealthCare, Cigna, Blues).

Understanding Medical Necessity
The following ICD-9 codes for MPO are listed as a convenience for the ordering practitioner. The ordering practitioner should report the diagnosis code that best describes the reason for performing the test and provide the 4th and 5th ICD-9 digit as appropriate.

<table>
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<th>Diagnosis</th>
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<td>Diabetes Mellitus Type II or Unspecified,</td>
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<td>Not Stated as Uncontrolled</td>
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<td>of Vessel, Native or Graft</td>
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<td>Artery</td>
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<td>Other Abnormal Blood Chemistry</td>
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Treatment Considerations

These treatment considerations are for educational purposes only. Specific treatment plans should be provided and reviewed by the treating practitioner.

✔ Assess LDL-C levels.
- If not at goal, consider lipid-lowering therapy, ideally with a statin-based regimen if not contraindicated.

✔ Assess risk for pre-diabetes/diabetes.
- If abnormal fasting glucose or oral glucose tolerance test, consider PPAR agonists, metformin or DPP-IV inhibitor if not contraindicated.

✔ Assess the presence of coronary artery disease (CAD) with imaging techniques such as carotid intima media thickness testing (CIMT) or coronary artery calcium scoring.
- Consider aspirin therapy if not contraindicated.
- Consider clopidogrel if history of CAD (i.e., myocardial infarction or revascularization) and/or a history of cerebrovascular disease (i.e., TIA or stroke).

✔ Assess dental health (periodontal disease).
- Refer to dentist to identify gum disease.
  NOTE: Poor dental health may cause significant inflammation and is associated with the presence of atherosclerosis.

✔ Assess HDL-C levels.
- If not at goal, consider niacin or fenofibrate therapy.
- Assess CoQ10 levels as recent evidence suggests that low ApoA1 and/or HDL-C levels are associated with low CoQ10 levels.

✔ Assess smoking habits.
  NOTE: Smoking cessation is essential as individuals who smoke are at increased risk of heart disease and blood clots.

If asymptomatic, with all of the above factors ruled out, an elevated MPO value may in fact be the patient’s baseline. MPO levels should be monitored every 3-6 months.

✔ Assess blood pressure.
- If not at goal, consider initiating, or titrating, anti-hypertensive therapy.
  NOTE: An elevated blood pressure may contribute to endothelial dysfunction and coronary disease formation.

✔ Assess lifestyle habits.
- Consider diet/exercise/weight reduction efforts if appropriate.

✔ Assess the presence of inflammatory conditions such as Crohn’s disease, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).
  NOTE: Chronic inflammatory diseases may exhibit elevated MPO values due to increased vascular disease associated with these conditions. For example, RA is associated with a 5x increased risk for myocardial infarction.

✔ Assess the presence of vasculitis.
  NOTE: MPO values may be elevated in individuals with vasculitis as it is characterized by increased vascular inflammation.

✔ Assess the presence of bone marrow dyscrasias.
  NOTE: MPO values may be elevated in individuals with chronic lymphocytic leukemia or other leukemias, that cause increased white blood cell destruction.

✔ Assess level of exercise.
  NOTE: MPO values may be elevated in marathon runners and extreme athletes and may identify those with increased oxidative stress and basal levels of inflammation.

References
5. An elevated blood pressure may cause significant inflammation and is associated with the presence of atherosclerosis.