**Genetic Testing for Macular Degeneration**

**DISCLAIMER**

Our medical policies are designed for informational purposes only and are not an authorization, explanation of benefits or a contract. Receipt of benefits is subject to satisfaction of all terms and conditions of the coverage. Medical technology is constantly changing, and we reserve the right to review and update our policies periodically.

**POLICY**

Genetic testing for macular degeneration is considered **investigational**.

**POLICY GUIDELINES**

**GENETICS NOMENCLATURE UPDATE**

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society’s nomenclature is recommended by the Human Variome Project, the HUman Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—“pathogenic,” “likely pathogenic,” “uncertain significance,” “likely benign,” and “benign”—to describe variants identified that cause Mendelian disorders.

**Table PG1. Nomenclature to Report on Variants Found in DNA**

<table>
<thead>
<tr>
<th>Previous</th>
<th>Updated</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutation</td>
<td>Disease-associated</td>
<td>Disease-associated change in the DNA sequence</td>
</tr>
<tr>
<td>Variant</td>
<td></td>
<td>Change in the DNA sequence</td>
</tr>
<tr>
<td>Familial variant</td>
<td></td>
<td>Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives</td>
</tr>
</tbody>
</table>

**Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification**

<table>
<thead>
<tr>
<th>Variant Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic</td>
<td>Disease-causing change in the DNA sequence</td>
</tr>
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</table>
GENETIC COUNSELING

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

CODING

If testing is specific to particular genes that have been codified and does not involve any risk algorithm, the test can be reported with the tier 2 CPT code(s).

Under code 81401:

* APOE (*apolipoprotein E*) (e.g., hyperlipoproteinemia type III, cardiovascular disease, Alzheimer disease), common variants (e.g., *2, *3, *4)

* CFH/ARMS2 (*complement factor H/age-related maculopathy susceptibility 2*) (e.g., macular degeneration), common variants (e.g., Y402H [CFH], A69S [ARMS2]).

Under 81405:

* HTRA1 (*HtrA serine peptidase 1*) (e.g., macular degeneration), full gene sequence.

Under code 81408:

* ABCA4 (*ATP-binding cassette, sub-family A [ABC1], member 4*) (e.g., Stargardt disease, age-related macular degeneration), full gene sequence.

If the specific test is not listed in tier 2, the unlisted molecular pathology code 81479 would be reported. If the test involves multiple analytes and an algorithm, the unlisted multianalyte assay with algorithmic analysis (MAAA) code 81599 would be reported.

BENEFIT APPLICATION

BLUECARD/NATIONAL ACCOUNT ISSUES

Some Plans may have contract or benefit exclusions for genetic testing.

BACKGROUND

MACULAR DEGENERATION

Macular degeneration, the leading cause of severe vision loss in people older than age 60 years, occurs when the central portion of the retina (the macula) deteriorates. Because the disease develops as a person ages, it is often referred to as age-related macular degeneration (AMD). AMD has an estimated prevalence of 1 in 2000 in the United States and affects individuals of European descent more frequently than African Americans in the United States.
There are 2 major types of AMD, known as the dry form and the wet form. The dry form is much more common, accounting for 85% to 90% of all cases of AMD, and it is characterized by the buildup of yellow deposits called drusen in the retina and slowly progressive vision loss. The condition typically affects vision in both eyes, although vision loss often occurs in 1 eye before the other. AMD is generally thought to progress along a continuum from dry AMD to neovascular wet AMD, with approximately 10% to 15% of all AMD patients eventually developing the wet form. Occasionally patients with no prior signs of dry AMD present with wet AMD as the first manifestation of the condition.

The wet form of AMD is characterized by the growth of abnormal blood vessels from the choroid underneath the macula, and is associated with severe vision loss that can rapidly worsen. The abnormal vessels leak blood and fluid into the retina, which damages the macula, leading to permanent loss of central vision.

Major risk factors for AMD include older age, cigarette smoking, cardiovascular diseases, nutritional factors, and certain genetic markers. Age appears to be the most important risk factor, because the chance of developing the condition increases significantly as a person gets older. Smoking is another established risk factor. Other factors that may increase the risk of AMD include high blood pressure, heart disease, a high-fat diet, or one low in certain nutrients (e.g., antioxidants, zinc), and obesity.

Clinical Diagnosis
AMD can be detected by routine eye exam, with one of the most common early signs being the presence of drusen or pigment clumping. An Amsler Grid test, a pattern of straight lines that resembles a checkerboard, may also be used. In an individual with AMD, some of the straight lines may appear wavy or missing.

If AMD is suspected, fluorescein angiography and/or optical coherence tomography may be performed. Angiography involves injecting a dye into the bloodstream to identify leaking blood vessels in the macula. Optical coherence tomography captures a cross-sectional image of the macula and aids in identifying fluid beneath the retina and in documenting degrees of retinal thickening.

Treatment
There is currently no cure for macular degeneration, but certain treatments may prevent severe vision loss or slow disease progression. For dry AMD, there is no medical treatment; however, changing certain lifestyle risks may slow AMD onset and progression. The goal for wet (advanced) AMD is early detection and treatment aimed at preventing the formation of new blood vessels, or sealing the leakage of fluid from blood vessels that have already formed. Treatment options include laser photocoagulation, photodynamic therapy, surgery, anti-angiogenic drugs, and combination treatments. Anti-angiogenesis drugs block the development of new blood vessels and leakage from the abnormal vessels within the eye that cause wet macular degeneration and may lead to patients regaining lost vision. The Age-Related Eye Disease Study (2001), a large study performed by the National Eye Institute of the National Institutes of Health, showed that, for certain individuals (those with extensive drusen or neovascular AMD in 1 eye), high doses of vitamins C, E, β-carotene, and zinc may provide a modest protective effect against the progression of AMD.¹

Genetic Testing
It has been reported that genetic variants associated with AMD account for approximately 70% of the risk for the condition.²

More than 25 genes have been reported to influence the risk of developing AMD, discovered initially through family-based linkage studies, and subsequently through large-scale genome-wide association
studies. Genes influencing several biologic pathways, including genetic loci associated with the regulation of complement, lipid, angiogenic, and extracellular matrix pathways, have been found to be associated with the onset, progression, and bilateral involvement of early, intermediate, and advanced stages of AMD.\(^3\)

Loci based on common single nucleotide variants contribute to the greatest risk of AMD:

- the long (q) arm of chromosome 10 in a region known as 10q26 contains 2 genes of interest, \textit{ARMS2} and \textit{HTRA1}. Changes in both genes have been studied as possible risk factors for the disease; however, because the 2 genes are so close together, it is difficult to tell which is associated with AMD risk or whether increased risk results from variations in both genes.
- common and rare variants in the complement factor \textit{H (CFH)} gene.

Other confirmed genes in the complement pathway include \textit{C2}, \textit{C3}, \textit{CFB}, and \textit{CFI}.\(^3\)

On the basis of large genome-wide association studies, high-density lipoprotein cholesterol pathway genes have been implicated, including \textit{CETP} and \textit{LIpc}, and possibly \textit{LPL} and \textit{ABCA1}.\(^3\) The collagen matrix pathway genes \textit{COL10A1} and \textit{COL8A1}, apolipoprotein \textit{E (APOE)}, and the extracellular matrix pathway genes \textit{TIMP3} and \textit{FBN2} have also been linked to AMD. Genes involved in DNA repair (\textit{RAD51B}) and in the angiogenesis pathway (\textit{VEGFA}) have also been associated with AMD.

\textbf{Commercially Available Testing for AMD}

Commercially available genetic testing for AMD is aimed at identifying those individuals who are at risk of developing \textit{advanced} AMD.

Arctic Medical Laboratories offers Macula Risk\textsuperscript{®}, which uses patient clinical information and the patient’s genotype for 15 associated biomarkers in an algorithm to identify whites at high risk for progression of early or intermediate AMD to advanced forms of AMD. A Vita Risk\textsuperscript{®} report is also provided with vitamin recommendations based on the \textit{CFH} and \textit{ARMS2} genotype.

deCode Complete includes testing for variants in \textit{CFH}, \textit{ARMS2} and \textit{HTRA1}, \textit{C2}, \textit{DFB}, and \textit{C3} genes. 23andMe includes testing for \textit{CFH}, \textit{ARMS2}, and \textit{C2}.

\textbf{REGULATORY STATUS}

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

\textbf{RATIONALE}

This evidence review was created in November 2013 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through January 8, 2018.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is
outside the scope of these reviews, and credible information on technical reliability is available from other sources.

TESTING ASYMPTOMATIC INDIVIDUALS WITH RISK OF DEVELOPING AGE-RELATED MACULAR DEGENERATION

Clinical Context and Test Purpose
The purpose of genetic testing of asymptomatic individuals with risk of developing age-related macular degeneration (AMD) is to identify single nucleotide variants (SNVs) for primary prevention or earlier detection of disease for more timely intervention to affect course of disease progression.

The question addressed in this evidence review is: Does genetic testing improve health outcomes in asymptomatic individuals with risk of developing AMD?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is asymptomatic individuals with risk of developing AMD.

Interventions
The test being considered is genetic testing for AMD.

Comparators
The following practice is currently being used to make decisions about risk of developing AMD: standard clinical management without genetic testing.

Outcomes
The potential beneficial outcomes of primary interest would be improvements in disease status and functional outcomes.

Potential harmful outcomes would be those resulting from false-positive or false-negative test results. False-positive test results can lead to clinical management changes that may not be beneficial. False-negative test results can lead to absence of clinical management changes.

Timing
The primary outcomes of interest are the initiation and frequency of monitoring for assessing changes in disease status.

Setting
Patients may be referred from primary care to an ophthalmologist or medical geneticist for investigation and management of AMD. Referral for genetic counseling is important for explanation of genetic disease, heritability, genetic risk, test performance, and possible outcomes.

Simplifying Test Terms
There are 3 core characteristics for assessing a medical test. Whether imaging, laboratory, or other, all medical tests must be:

- Technically reliable
- Clinically valid
- Clinically useful.
Because different specialties may use different terms for the same concept, we are highlighting the core characteristics. The core characteristics also apply to different uses of tests, such as diagnosis, prognosis, and monitoring treatment.

Diagnostic tests detect presence or absence of a condition. Surveillance and treatment monitoring are essentially diagnostic tests over a time frame. Surveillance to see whether a condition develops or progresses is a type of detection. Treatment monitoring is also a type of detection because the purpose is to see if treatment is associated with the disappearance, regression, or progression of the condition.

Prognostic tests predict the risk of developing a condition in the future. Tests to predict response to therapy are also prognostic. Response to therapy is a type of condition and can be either a beneficial response or adverse response. The term predictive test is often used to refer to response to therapy. To simplify terms, we use prognostic to refer both to predicting a future condition or to predicting a response to therapy.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse)

Current models for predicting AMD risk include various combinations of epidemiologic, clinical, and genetic factors, and give areas under the curve (AUC) of approximately 0.8. The addition of the genetic factors (SNVs) in CFH, ARMS2, C2, C3, and CFB, increased the AUC to 0.821. In a 2015 report, Seddon et al included 10 common and rare genetic variants in their risk-prediction model, resulting in an AUC of 0.911 for progression to advanced AMD. The Age-Related Eye Disease Study (AREDS) Simple Scale which rates the severity of AMD based on the presence of large drusen and pigment changes to predict the rate of advanced AMD, is considered to have the greatest predictive value.  

An analysis by Seddon et al (2009) demonstrated that a clinical model of AMD risk, which included age, sex, education, baseline AMD grade, smoking, and body mass index, had an AUC of 0.757. The addition of the genetic factors (SNVs) in CFH, ARMS2, C2, C3, and CFB, increased the AUC to 0.821. In a 2015 report, Seddon et al included 10 common and rare genetic variants in their risk-prediction model, resulting in an AUC of 0.911 for progression to advanced AMD. The Age-Related Eye Disease Study (AREDS) Simple Scale which rates the severity of AMD based on the presence of large drusen and pigment changes to predict the rate of advanced AMD, is considered to have the greatest predictive value.  

Although these risk models suggest some small incremental increase in the ability to assess risk of developing advanced AMD based on genetic factors, the clinical validity is not established.

Section Summary: Clinically Valid
Evidence from studies has indicated that the clinical sensitivity of genetic testing for genes associated with AMD may have small incremental effects on assessing risk of developing AMD. Risk-prediction models incorporate factors such as age, sex, smoking, body mass index, and genetic factors. The true clinical specificity of genetic variants in AMD-related genes is uncertain because of the multifactorial nature of disease development and progression.
Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

What can be done for an individual whose genetic test indicates that he or she is at high risk for vision loss from AMD? The possible clinical utility of genetic testing for AMD can be divided into disease prevention, disease monitoring, and therapy guidance, as discussed below.

- **Prevention:** Genetic testing and risk prediction for AMD would have clinical utility if a preventive therapy involved an intervention that went beyond good health practices (eg, no smoking, balanced diet, exercise, nutrient supplements). If a preventive therapy existed, the optimal risk-benefit point along the AMD risk profile for every given age would need to be established so that it could be determined which individuals should receive those treatments and at what age to start the intervention. Currently, no preventive measures are available; high-dose antioxidants and zinc supplements have been shown to reduce disease progression.1

- **Monitoring:** If a patient is identified as high risk, changes in the frequency of monitoring may occur and could include home monitoring devices or the use of technology such as preferential hyperacuity perimetry to detect early or subclinical wet AMD. However, the impact of more frequent monitoring for high-risk patients is not known.4

- **Direction of therapy:** No consistent associations between response to vitamin supplements and genetic variants have been established.10-14

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials. No such trials were identified.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility. A chain of evidence cannot be constructed.

Section Summary: Clinical Utility
Direct evidence of the clinical utility of genetic testing in asymptomatic individuals at risk for developing AMD is lacking. While genetic variants have been used in risk-prediction models, no consistent associations between specific genetic variants and response to specific treatments have been established.

TESTING INDIVIDUALS WITH AMD

Clinical Context and Test Purpose
The purpose of genetic testing of individuals with AMD is to identify SNVs that potentially predict response to treatment.

The question addressed in this evidence review is: Does genetic testing improve health outcomes in individuals with AMD?

The following PICOTS were used to select literature to inform this review.
Patients
The relevant population of interest is symptomatic individuals with AMD.

Interventions
The test being considered is genetic testing to determine prognosis or predict response to therapy.

Comparators
The following practice is currently being used to make decisions about risk of developing AMD: standard clinical management without genetic testing.

Outcomes
The potential beneficial outcomes of primary interest would be improvements in disease status and functional outcomes.

Potential harmful outcomes are those resulting from false-positive or false-negative test results. False-positive test results can lead to clinical management changes that may not be beneficial. False-negative test results can lead to absence of clinical management changes.

Timing
The primary outcomes of interest are the initiation and frequency of monitoring for assessing changes in disease status and effects of management decisions on short-term and long-term functional outcomes.

Setting
Patients may be referred from primary care to an ophthalmologist or medical geneticist for investigation and management of AMD. Referral for genetic counseling is important for explanation of genetic disease, heritability, genetic risk, test performance, and possible outcomes.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Clinical validity is how the presence of specific SNVs provide accurate prognosis for disease course and predict response to treatment. Evidence supporting the clinical validity of accurate disease prognosis and response to treatment was not identified.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

What can be done for an individual with AMD using genetic test results for prognosis and prediction of response to treatment? The possible clinical utility of genetic testing for AMD includes disease monitoring and therapy guidance, as discussed below.
• Monitoring: There is currently no cure for macular degeneration, but genetic variants may provide more accurate prognosis on disease progression. Frequency of monitoring may be increased if a genetic variant is associated with a more rapid or severe disease course.
• Direction of therapy: No consistent associations between response to vitamin supplements or anti-vascular endothelial growth factor (VEGF) therapy and VEGF gene variants have been established.\textsuperscript{10–14}

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials. No such trials were identified.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility. A chain of evidence cannot be constructed.

Section Summary: Clinically Useful
Direct evidence of the clinical utility of genetic testing in individuals with AMD is lacking. While genetic variants have been used in risk-prediction models, there have been no consistent associations between specific genetic variants in altering and response to treatments.

SUMMARY OF EVIDENCE
For individuals who are asymptomatic with risk of developing AMD who receive genetic testing for AMD, the evidence includes genetic association studies and risk-prediction models. Relevant outcomes are test accuracy, change in disease status, and functional outcomes. The clinical validity of genetic testing appears to provide a small, incremental benefit to risk stratification based on nongenetic risk factors. The clinical utility of genetic testing for AMD is limited, in that there are currently no preventive measures that can be undertaken. No studies have shown improvements in health outcomes in patients identified as being at high risk based on genetic testing. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have AMD who receive genetic testing for AMD, the evidence includes genetic association studies and risk-prediction models. Relevant outcomes are test accuracy, change in disease status, and functional outcomes. The clinical utility of genetic testing in patients who have AMD is limited, in that genetic testing has not been shown to be superior to clinical evaluation in determining the risk of progression of disease. In addition, there is no known association with specific genotypes and specific therapies. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Academy of Ophthalmology
The 2014 American Academy of Ophthalmology recommendations specific to genetic testing for complex eye disorders like age-related macular degeneration (AMD) have indicated that the presence of any one of the disease-associated variants is not highly predictive of disease development.\textsuperscript{15} The Academy found that, in many cases, standard clinical diagnostic methods like bio-microscopy, ophthalmoscopy, tonography, and perimetry would be more accurate for assessing a patient’s risk of
vision loss from a complex disease than the assessment of a small number of genetic loci. The Academy concluded that genetic testing for complex diseases will become relevant to the routine practice of medicine when clinical trials demonstrate that patients with specific genotypes benefit from specific types of therapy or surveillance; until such benefit can be demonstrated, routine genetic testing of patients with complex eye diseases, or unaffected patients with a family history of such diseases, is not warranted.

**American Society of Retina Specialists**

The American Society of Retina Specialists (2017) published special correspondence on the use of genetic testing in the management of patients with AMD. The Society concluded that:

- While AMD genetic testing may provide information on progression from intermediate to advanced AMD, there is no clinical evidence that altering management of genetically higher risk progression patients’ results in better visual outcomes compared with patients lower risk progression patients.
- AMD genetic testing in patients with neovascular AMD does not provide clinically relevant information regarding response to anti-vascular endothelial growth factor (VEGF) treatment and is therefore not recommended for this population.
- Currently, there is insufficient evidence to support the use of genetic testing in patients with AMD in regard to nutritional supplement recommendations.

**U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS**

Not applicable.

**MEDICARE NATIONAL COVERAGE**

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

**ONGOING AND UNPUBLISHED CLINICAL TRIALS**

Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

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<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tr>
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<tr>
<td>NCT02762188</td>
<td>Genetic Biomarkers for the Response to Anti-VEGF (Vascular Endothelial Growth Factor). Treatment in Wet Age-Related Macular Degeneration (Wet ARMD)</td>
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<td>Jul 2017 (ongoing)</td>
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<td>NCT01213667</td>
<td>Genetics in Non-Response to Anti-VEGF Treatment in Exudative AMD (RESPONSE)</td>
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<td>Dec 2017</td>
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<td>NCT01310686a</td>
<td>Genetics Study of Wet Age-Related Macular Degeneration (AMD) Non-Responders to Vascular Endothelial Growth Factor (VEGF) Therapy</td>
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<td>Jun 2018</td>
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<td>NCT03024424</td>
<td>Value of Genetic Counseling and Testing for Patients Who Would Like to Know More about Their Personal Risk of AMD</td>
<td>200</td>
<td>Mar 2020</td>
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<tr>
<td>NCT01115387</td>
<td>GARM II: A Study on the Genetics of Age-related Maculopathy</td>
<td>603</td>
<td>Aug 2020</td>
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Genetic Testing for Macular Degeneration

NCT: national clinical trial.

*a Denotes industry-sponsored or cosponsored trial.

REFERENCES


**CODES**

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<thead>
<tr>
<th>Codes</th>
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<td>No specific CPT code. See Policy Guidelines</td>
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<td>ICD-10-CM</td>
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<td>Investigational for all relevant diagnoses</td>
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<td>H35.30</td>
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<td>Unspecified macular degeneration</td>
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<tr>
<td>H35.3110-35.3194</td>
<td></td>
<td>Non-exudative age-related macular degeneration code range</td>
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<tr>
<td>H35.3210-35.3293</td>
<td></td>
<td>Exudative age-related macular degeneration code range</td>
</tr>
<tr>
<td>Z13.5</td>
<td></td>
<td>Encounter for screening for eye and ear disorders</td>
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**ICD-10-PCS**

Not applicable. ICD-10-PCS codes are only used for inpatient services. There are no ICD procedure codes for laboratory tests.

**POLICY HISTORY**

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<tr>
<td>12/10/15</td>
<td>Replace policy</td>
<td>Policy updated with literature review through November 10, 2015; references 9 and 11-13 added. Policy statement unchanged.</td>
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<tr>
<td>08/11/16</td>
<td>Replace policy – coding update only</td>
<td>ICD-10-CM codes for macular degeneration updated; updated with plans for further literature review</td>
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<tr>
<td>03/21/17</td>
<td>Replace policy</td>
<td>Policy updated with literature review through January 25, 2017; no references added. ARUP test reference removed. The policy is revised with updated genetics nomenclature. Policy statement unchanged.</td>
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<tr>
<td>03/29/18</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted. Policy updated with literature review through January 8, 2018; reference 16 was added. Policy statement unchanged.</td>
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