Policy Replaced with LCD L37033
Effective February 26, 2018

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Gene Expression Profiling for Uveal Melanoma

Policy #: 585
Category: Laboratory

Latest Review Date: February 2017
Policy Grade: D

Background:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

Description of Procedure or Service:

Uveal melanoma is associated with a high rate of metastatic disease, and survival after the development of metastatic disease is poor. Prognosis following treatment of local disease can be assessed using various factors, including clinical and demographic markers, tumor stage, tumor characteristics, and tumor cytogenetics. Gene expression profiling (GEP) can be used to determine prognosis.

Uveal Melanoma

The uveal tract is the middle layer of the wall of the eye, and has 3 main parts: the choroid (a tissue layer filled with blood vessels), ciliary body (muscle tissue that changes the shape of the pupil and the lens), and the iris (the colored part of the eye). Uveal melanoma arises from melanocytes in the stroma of the uveal tract. Approximately 90% of uveal melanomas arise in the choroid, 7% in the ciliary body, and 3% in the iris.

Uveal melanoma, although rare, is the most common primary intraocular malignancy in adults. Mean age-adjusted incidence of uveal melanoma in the United States is 6.3 per million people among whites, 0.9 among Hispanics, and 0.24 among blacks.[1] Uveal melanoma has a progressively rising, age-specific, incidence rate that peaks near age 70. Host susceptibility factors associated with the development of this cancer include white race, fair skin, and light eye color.

Treatment

Treatment of primary, localized uveal melanoma can be by surgery or radiotherapy. In general, larger tumors require enucleation surgery and smaller tumors can be treated with radiotherapy, but specific treatment parameters are lacking. The most common treatment of localized uveal melanoma is radiotherapy, which is preferred because it can spare vision in most cases. For smaller lesions, randomized controlled trials have shown that patients receiving radiotherapy or enucleation progress to metastatic disease at similar rates after treatment. Radiotherapy can be delivered by a variety of mechanisms, most commonly brachytherapy and proton beam therapy. Treatment of primary uveal melanoma improves local control and spares vision. However, the 5-year survival rate (81.6%) has not changed over the last 3 decades, suggesting that life expectancy is independent of successful local eye treatment.

Uveal melanomas disseminate hematogenously, and metastasize primarily to the liver and lungs. Treatment of hepatic metastases is associated with prolonged survival and palliation in some patients. Therapies directed at locoregional treatment of hepatic metastases include surgical and ablative techniques, embolization, and local chemotherapy.

Surveillance for Metastatic Disease

It is unusual for patients with uveal melanoma to have distant metastases at presentation, with less than 1% presenting with metastases when they are treated for their intraocular disease, but are at risk for distant metastases, particularly to the liver, for years after presentation. The prospective, longitudinal Collaborative Ocular Melanoma Study (COMS) study followed 2,320 patients with choroidal melanoma with no melanoma metastasis at baseline who were enrolled in randomized controlled trials to evaluate forms of radiotherapy for choroidal melanoma for five to ten years. During follow-up, 739 patients were diagnosed with at least one site of metastasis, of

which 660 (89%) were liver. Kaplan-Meier estimates of 2-, 5-, and 10-year metastasis rates were 10% (95% CI, 9% to 12%), 25% (95% CI, 23% to 27%), and 34% (95% CI, 32% to 37%), respectively.

The optimal method and interval for surveillance are not well-defined, and it has not been established in prospective trials that surveillance identifies metastatic disease earlier. Potential methods for surveillance for metastases include MRI, ultrasound, liver function testing (LFTs), and PET scans. One retrospective study in 262 patients estimated that hepatic ultrasound and liver function testing every six months in individuals with treated local uveal melanoma, sensitivity and specificity for a diagnosis of metastasis were 83% (95% CI 44% to 97%) and 100% (95% CI 99% to 100%) respectively.

Identifying patients at high-risk for metastatic disease may potentially assist in selecting patients for adjuvant treatment and more intensive surveillance for metastatic disease may lead to improved outcomes. Adjuvant treatment for metastatic disease consists of radiotherapy or systemic therapy, such as chemotherapy, immunotherapy, hormone therapy, biological therapy, or targeted therapy. Randomized trials of patients with high risk of uveal melanoma recurrence showed no difference in survival rates between patients treated with and without adjuvant therapy. However, these trials were reported in 1998 and 1990, and may not be representative of currently-available treatments and risk stratification methods.

Prognosis in Uveal Melanoma

Metastatic disease is the leading cause of death in patients with uveal melanoma, and approximately 50% of patients will develop distant metastasis. A number of factors may be used to determine prognosis, but the optimal approach is uncertain. The most important clinical factors that predict metastatic disease are tumor size measured in diameter or in thickness, ciliary body involvement, and transscleral extension. Clinical staging according to the American Joint Committee on Cancer (AJCC) recommendations allows risk stratification for metastatic disease. In a retrospective study of 3,377 patients with uveal melanoma, in which staging was performed using AJCC classifications, the rate of metastases-free survival at five years was 97% for Stage 1, 89% for Stage IIA, 79% for Stage IIB, 67% for Stage IIIA, 50% for Stage IIIB, and 25% for Stage IIIB.

Genetic Analysis

Genetic analysis of uveal melanoma can provide prognostic information for the risk of developing metastatic disease. In 1996, Prescher et al showed that monosomy of chromosome 3 correlated strongly with metastatic death, with a five-year survival reduction from 100% to 50%. Subsequent studies reported the initial idea that, based on genetic analysis, there were two distinct types of uveal melanomas—those with monosomy chromosome 3 associated with a very poor prognosis and those with disomy 3 and 6p gain associated with a better prognosis. The *BAP1* gene has been identified as an important marker of disease type. In 1 study, 89% of tumors with monosomy 3 had a *BAP1* mutation, and no tumors without monosomy 3 had a *BAP1* mutation.

Gene expression profiling (GEP) determines the expression of multiple genes in a tumor and has been proposed as an additional method to stratify patients into prognostic risk groups.

Commercially Available Testing
The DecisionDx-UM® test (Castle Biosciences Inc, Phoenix, AZ) is a GEP test intended to assess five-year metastatic risk in uveal melanoma. The test was introduced in late 2009, and claims to identify the molecular signature of a tumor and its likelihood of metastasis within five years. The assay determines the expression of 15 genes, which stratify a patient's individual risk of metastasis into three classes. The 15 gene signature was originally developed based on a hybridization-based microarray platform; the currently commercially-available DecisionDx-UM test is a polymerase chain reaction (PCR)-based test that can be performed on fine-needle aspiration samples.

Based on the clinical outcomes from the prospective, five-year multi-center Collaborative Ocular Oncology Group (COOG) study, the DecisionDx-UM test reports Class 1A, Class I1 and Class 2 phenotype:

- Class 1A: Very low risk, with a 2% chance of the eye cancer spreading over the next 5 years;
- Class 1B: Low risk, with a 21% chance of metastasis over 5 years;
- Class 2: High risk, with 72% odds of metastasis within 5 years.

Policy:

Effective for dates of service on or after February 26, 2018 refer to LCD L37033

Effective for dates of service on or after February 24, 2017 and prior to February 26, 2018:
Blue Advantage will treat g**ene expression profiling for uveal melanoma with DecisionDX-UM** as a **covered benefit** for members with **primary, localized uveal melanoma.**

Blue Advantage will treat **gene expression profiling for uveal melanoma** as a **non-covered benefit** and as **investigational for all other situations**.

Effective for dates of service prior to February 24, 2017:
Blue Advantage will treat **gene expression profiling for uveal melanoma** as a **non-covered benefit** and as **investigational**.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature review was updated through February 2, 2017. The primary question addressed by this review is whether the use of gene expression profiling (GEP) to determine prognosis following initial treatment of uveal melanoma improves outcomes compared to determining prognosis by alternative approaches.

Uveal Melanoma

Clinical Context and Test Purpose

The purpose of using the DecisionDx-UM test in individuals with localized uveal melanoma is to inform a decision about how often patients should undergo follow-up for metastases, based on their likelihood of developing metastases.

Analytic Validity

Augsburger et al 2015 reported on the correlation between GEP classifications when samples from two sites from the same tumor were tested. This prospective, single-center study enrolled 80 patients who had uveal melanoma resection. Tumor samples were taken from two different sites and GEP testing was performed independently on both samples. The primary measure reported was the rate of discordance between the two samples on GEP class. Nine (11.3%) cases (95% confidence interval [CI], 9.0% to 13.6%) were definitely discordant, and 13 (16.3%) cases were definitely or possibly discordant (95% CI, 13.0% to 19.6%). Thus heterogeneity of tumor and limitations to sampling may explain cases of misclassification where GEP results do not accurately predict prognosis.

In 2010, Onken et al re-validated the GEP assay when it was migrated from a microarray platform to a polymerase chain reaction (PCR)-based 15-gene assay comprised of 12 discriminating genes and three endogenous control genes from previously published data sets. Technical performance of the assay was analyzed in a prospective study of 609 previously untreated tumors. Tumor samples were obtained by fine needle aspiration (n=553) or after enucleation (n=56). Samples were used for cytologic examination and RNA analysis. The genes were tested on the authors' training set of 28 uveal melanomas (15 considered to be of prognostic class 1 and 13 in class 2), with clinical follow-up of at least five years. The gene assay was demonstrated to be of sufficient sensitivity and failed on one of 51 samples with a cytologic diagnosis of quantity not sufficient, and preliminary outcome data affirmed the prognostic accuracy of the assay. The authors concluded, based on preliminary outcome data available for samples collected from 172 patients with a median follow up of 16 months, that the assay identified which patients would develop metastatic disease ($p=1.9 \times 10^{-6}$).

Section Summary: Analytic Validity

There is little published data on the analytic validity of GEP testing. One study has reported validation data of tumor samples from 172 patients using preliminary outcomes data over a median of 16 months as well as results from a training set of 28 samples with at least five-year follow-up. A second study examined the discordance in GEP classification when two samples of the same tumor were tested, and reported discordance in 11.3% to 16.3% of cases. However, this design is more informative of sampling issues in the face of tumor heterogeneity and does not address the main question of analytic validity: Does repeated testing of the same sample yields confirmatory or discordant results?

Clinical Validity
Three studies reported data on the association of GEP score with clinical outcomes; they are summarized in Table 1. All studies showed strong and positive associations between GEP class and clinical outcomes.

The first study was published in 2012 by Onken et al. This prospective, multicenter study evaluated the prognostic performance of a 15-gene GEP assay in patients with posterior (choroidal and ciliary body) uveal melanoma. Prognostic groups were Class 1 (low risk of metastasis) or Class 2 (high risk of metastasis). Four hundred fifty nine cases were enrolled from 12 centers between June 2006 and November 2010. The GEP assay rendered a classification in 97.2% of cases. GEP testing results were Class 1 in 276 (61.9%) cases and Class 2 in 170 (38.1%) cases. Mean follow-up was 18.0 months (median, 17.4 months). Metastasis was detected in 3 (1.1%) of Class 1 cases and 44 (25.9%) of Class 2 cases ($p<0.001$). By univariate Cox proportional hazard analysis, factors associated with metastatic disease included advanced patient age ($p=0.02$), ciliary body involvement ($p=0.03$), tumor diameter ($p<0.001$), tumor thickness ($p=0.006$), chromosome 3 status ($p<0.001$), and GEP class ($p<0.001$). The GEP was associated with a significant net reclassification index (NRI) over TNM classification for survival at two years (NRI=0.37, P=0.008) and 3 years (NRI=0.43,P=0.001).

Two other studies reporting data on clinical validity were published in 2016. Walter et al evaluated two cohorts of patients at two clinical centers who underwent resection for uveal melanoma. This study had similar methodology to Onken (2012). A primary cohort included 339 patients, of which 132 patients were also included in the Onken et al (2012) study, along with a validation cohort of 241 patients, of which 132 were also included in the Onken et al (2012) study, which was used to test a prediction model using the GEP plus pretreatment largest basal diameter.

Cox proportional hazards analysis was used to examine GEP class together with other clinicopathologic factors (tumor diameter, tumor thickness, age, gender, ciliary body involvement, pathologic class). GEP Class 2 was the strongest predictor of metastases and mortality. Tumor diameter was also an independent predictor of outcomes, using a diameter of 12 mm as the cutoff value.

In the validation cohort, GEP results were Class 1 in 148 (61.4%) patients and Class 2 in 93 (38.6%) patients. Again, GEP results were most strongly associated with PFS.

Decatur et al (2016) was a smaller, retrospective study of 81 patients who had tumor samples available from resections occurring between 1998 and 2014. GEP was Class 1 in 35 (43%) patients, Class 2 in 42 (52%) patients, and unknown in 4 (5%) patients. GEP Class 2 was strongly associated with *BAP1* mutations ($r=0.70$; $p<0.001$). On Cox proportional hazards analysis, GEP Class 2 was the strongest predictor of metastases and melanoma mortality (see Table 1).

Table 1: Studies of Clinical Validity

Study	Patient Populations	Rates of Metastases		Melanoma Mortality Rates	
		GEP Class 1	GEP Class 2	GEP Class 1	GEP Class 2
Onken (2012)	459 pts with UM from 12 clinical centers	1.1%	25.9%[a]	NR	NR
Walter (2016)	Primary cohort: 339 pts from two clinical centers with UM arising in ciliary body or choroid	5.8%	39.6%	3.7%	29.5%
	Validation cohort: 241 patients from two clinical centers with UM arising in ciliary body or choroid	2.7%	31.2%	0.7%	17.2%
Decatur (2016)	81 pts from a single center with available tumor samples of UM arising from ciliary body or choroid		9.4[a,b] (3.1 to 28.5)		15.7[a,b] (3.6 to 69.1)

NR: not reported; pts: patients; UM: uveal melanoma.
a Reported as relative risk (95% confidence interval) for metastases (or melanoma mortality) in group 2 vs group 1.

Section Summary: Clinical Validity

There are three published studies on clinical validity. These studies have reported that GEP Class 2 is a strong predictor of metastases and melanoma survival, and also strongly correlates with *PAB1* mutations. Two studies have compared GEP class to a limited set of clinicopathologic features and have reported that GEP class is the strongest predictor of clinical outcomes.

Clinical Utility

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Preferred evidence comes from randomized controlled trials.

There is no direct evidence for DecisionDx-UM for the selection of patients for different surveillance outcomes. In the absence of direct evidence, a chain of evidence can be developed based on the clinical validity of the test.

The GEP test is associated with risk of metastatic disease and melanoma death. Although the three available studies reporting on clinical validity do not all specifically report on rates of survival or metastasis risk by risk group, there is clearly an association of risk category and metastasis and death. For a rare cancer, the studies on clinical validity include a large proportion annual incident cases.

Plasseraud et al (2016) reported metastasis surveillance practices and patient outcomes using data from a prospective observational registry study of DecisionDX-UM conducted at four centers, which included 70 patients at the time of reporting. Surveillance regimens were documented by participating physicians as part of registry data entry. “High-intensity” surveillance was considered to be imaging and/or liver function testing (LFTs) every 3-6 months and “low-intensity” surveillance was considered to be annual imaging and/or LFTs. The method for following patients for clinical outcomes is not specified. Of the 70 enrolled patients, 37 (53%) were Class 1. Over a median follow up of 2.38 years, more Class 2 patients (36% vs 5%,

P=0.002) experienced a metastasis. The three-year metastasis-free survival (MFS) rate was lower for Class 2 patients (63%, 95% CI 43% to 83%) than Class 1 patients (100%, CI not specified; P=0.003). Most Class 1 patients (n=30) had low-intensity surveillance and all (n=33) Class 2 patients had high-intensity surveillance. Strengths of this study include a relatively large population given the rarity of the condition, and an association of management strategies with clinical outcomes. However, it is not clear which outcome measures were prespecified or the manner that data was collected, making the risk of bias high.

Aaberg et al (2014) reported on changes in management associated with GEP risk classification. Aaberg et al analyzed Medicare claims data submitted to Castle BioSciences by 37 ocular oncologists in the United States. Data were abstracted from charts on demographics, tumor pathology and diagnosis, and clinical surveillance patterns. High-intensity surveillance was defined as a frequency of every three to six months and low-intensity surveillance was a frequency of every 6 to 12 months. Of 195 patients with GEP test results, 88 (45.1%) patients had evaluable tests and adequate information on follow-up surveillance, 36 (18.5%) had evaluable tests and adequate information on referrals, and eight (4.1%) had evaluable tests and adequate information on adjunctive treatment recommendations. Of the 191 evaluable GEP tests, 110 (58%) were Class 1 and 81 (42%) were Class 2. For patients with surveillance data available (n=88), all patients in GEP Class 1 had low-intensity surveillance, and all patients in GEP Class 2 had high-intensity surveillance ($p<0.001$ vs Class 1).

It is likely that treating liver metastasis has an effect on local symptoms and survival, for at least a subset of patients. However, it is uncertain whether the surveillance interval has an effect on the time to detection of metastases.

There is the potential for patients considered to be at high risk for metastases to undergo adjuvant treatment, but to date no adjuvant therapies for non-metastasized uveal melanomas have been shown to reduce the risk of metastasis.

Section Summary: Clinical Utility

There are no studies directly showing clinical utility. In the absence of direct evidence, an indirect chain of evidence to determine whether using the results of GEP testing for management decisions improves the net health outcome of patients with uveal melanoma. GEP classification appears be a strong predictor metastatic disease and melanoma death. Aaberg et al (2014) have shown an association between GEP classification and treatment, reporting that patients classified as low risk were managed with less frequent and intensive surveillance and were not referred for adjuvant therapy.

It is uncertain whether stratification of patients into higher risk categories has the potential to improve outcomes by allowing patients to receive adjuvant therapies or through the detection of metastases earlier. However, classification into the low-risk group would allow reduction in the burden of surveillance without apparent harm.

Summary of Evidence

For individuals who have localized uveal melanoma who receive a gene expression profiling (GEP) test for uveal melanoma (DecisionDx-UM), the evidence includes cross-sectional studies

of assay validation and clinical validity. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, other test performance measures, functional outcomes, health status measures, and quality of life. One commercially available test identified (DecisionDx-UM) has published data related to its clinical validity, and is the focus of this review. There is limited published data on the analytic validity of GEP testing. Three studies of clinical validity identified used the GEP score to predict melanoma metastases and melanoma-specific survival. All three reported that GEP class correlated strongly with metastatic disease and melanoma mortality. Two studies compared GEP class to other prognostic markers, and GEP class had the strongest association among the markers tested. GEP class appears to be a strong predictor of metastatic disease and melanoma death. There are no studies directly showing clinical utility. In the absence of direct evidence, an indirect chain of evidence to determine whether using the results of GEP testing for management decisions improves the net health outcome of patients with uveal melanoma. Aaberg et al (2014) have shown an association between GEP classification and treatment, reporting that patients classified as low risk were managed with less frequent and intensive surveillance and were not referred for adjuvant therapy. It is uncertain whether stratification of patients into higher risk categories has the potential to improve outcomes by allowing patients to receive adjuvant therapies or through the detection of metastases earlier. However, classification into the low-risk group would allow reduction in the burden of surveillance without apparent harm. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network (NCCN)

In its guidelines on melanoma (Version 1.2017), the National Comprehensive Cancer Network (NCCN) states:

> "Mucosal and uveal melanomas differ significantly from cutaneous melanoma in presentation, genetic profile, staging, response to treatment, and patterns of progression. Ideally, mucosal and uveal melanoma should be treated as diseases distinct from cutaneous melanoma, with care tailored to the individual."

Melanoma Focus

Melanoma Focus, a British medical nonprofit that focuses on melanoma research, for uveal melanoma was published in 2015. These guidelines, which were created through a process accredited by the National Institute for Health and Care Excellence, contain the following statements related to prognosis and surveillance:

> "*Prognostic factors/tools*
> 25. Prognostic factors of uveal melanoma are multi-factorial and include clinical, morphological and genetic features. The following features should be recorded:
> - Age
> - Gender
> - Tumour location
> - Tumour height
> - Tumour Largest [sic] basal diameter
> - Ciliary body involvement
> - Extraocular melanoma growth (macroscopic)

The following features should be recorded if tissue is available:

- Cell type (modified Callender system)
- Mitotic count (number/40 high power fields in H&E [hematoxylin and eosin] stained sections)
- Presence of extravascular matrix patterns (particularly closed connective tissue loops; enhanced with Periodic acid Schiff staining). Grade A
- Presence of extraocular melanoma growth (size, presence or absence of encapsulation). [GRADE A]

Prognostic biopsy

26. There should be a fully informed discussion with all patients, explaining the role of biopsy including the benefits and risks. The discussion should include:

- Risk of having the biopsy
- Limitations of the investigation
- Benefits for future treatments (including possible recruitment to trials)
- Impact on quality of life
- Recruitment to trials
- Follow-up [GPP]

27. The minimum dataset for uveal melanoma from the Royal College of Pathology should be recorded. www.rcpath.org/publicationsmedia/publications/datasets/uveal-melanoma.htm Grade D

28. Tests for novel serological biomarkers should only be used within clinical trials or research programmes. [GPP]

29. Consider collecting molecular genetic and/or cytogenetic data for research and prognostication purposes where tumour material is available and where patient consent has been obtained as part of an ethically approved research programme. [GPP]

30. Use of the current (i.e. 7th) Edition of the TNM staging system for prognostication is highly recommended. Grade A

31. Use of multifactorial prognostication models incorporating clinical, histological, immunohistochemical and genetic tumour features - should be considered. Grade D

Surveillance

32. Prognostication and surveillance should be led by a specialist multidisciplinary team that incorporates expertise from ophthalmology, radiology, oncology, cancer nursing and hepatic services. [GPP]

32. Prognostication and risk prediction should be based on the best available evidence, taking into account clinical, morphological and genetic cancer features. [GPP]

33. All patients, irrespective of risk, should have a holistic assessment to discuss the risk, benefits and consequences of entry into a surveillance programme. The discussion should consider risk of false positives, the emotional impact of screening as well as the frequency and duration of screening. An individual plan should be developed. [GPP]

34. Patients judged at high-risk of developing metastases should have 6-monthly life-long surveillance incorporating a clinical review, nurse specialist support and liver specific imaging by a non-ionizing modality. [GPP]

36. Liver function tests alone are an inadequate tool for surveillance. Grade C"

Note that Melanoma Focus defined GPP as**:** recommended best practice based on the clinical experience of the guideline development group.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Key Words:

Uveal melanoma, DecisionDx-UM®, GEP, gene expression profile

Approved by Governing Bodies:

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

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

Current Coding:

CPT Codes:

81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure

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