

Immune Cell Function Assay

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I. Policy Description

Immune cell function assays involve measurement of peripheral blood lymphocyte response (intracellular ATP levels, proliferation) following stimulation to assess the degree of functionality of the cell-mediated immune response (Buttgereit et al., 2000).

For guidance on procedures utilizing flow cytometry, please refer to AHS-F2019 Flow Cytometry.

II. Related Policies

Policy Number	Policy Title
AHS-F2019	Flow Cytometry
AHS-M2091	Transplant Rejection Testing

III. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual’s benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the “Applicable State and Federal Regulations” section of this policy document.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual’s illness.

- 1) For all situations, an immune cell function assay (e.g., Pleximmune™, Pleximar) **DOES NOT MEET COVERAGE CRITERIA.**

IV. Table of Terminology

Term	Definition
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AAAAI	The American Academy of Allergy, Asthma & Immunology
AASLD	American Association for the Study of Liver Diseases
ACAAI	The American College of Allergy, Asthma & Immunology
AST	The American Society of Transplantation
ATP	Adenosine triphosphate
CD3	Cluster of differentiation 3
CD4	Cluster of differentiation 4
CMI	Cell-mediated immunity
CMV	Cytomegalovirus
DOR	Diagnostic odds ratio
ELISPOT	Enzyme-linked immunosorbent spot
FDA	Food and Drug Administration
GVHD	Graft-versus-host disease
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
ICS	Intracellular cytokine staining
IGRA	Interferon-gamma release assays
ISHLT	The International Society of Heart and Lung Transplantation
ICFA	Immune cell function assay
ITx	Intestine transplant
LTx	Liver transplant
MHC	Major histocompatibility complex
NLR	Negative likelihood ratio
NPV	Negative predictive value
PLR	Positive likelihood ratio
PPV	Positive predictive value
RA	Rheumatoid arthritis
SCID	Severe combined immunodeficiency disease

V. Scientific Background

Primary immunodeficiencies are a group of rare disorders in which part of the body's immune system is absent or functions incorrectly. These disorders occur in as many as 1:2000 live births and are most often categorized according to a combination of mechanistic and clinical descriptive characteristics (Bonilla et al., 2015). Specific cellular immunity is mediated by T cells, and defects affecting these T cells underlie the most severe immunodeficiencies. As antibody production by B cells requires intact T cell function, most T cell defects lead to combined (cellular and humoral) immunodeficiency (Butte, 2023).

In vitro studies of T cell function measure peripheral blood T cell responses to several different types of stimuli (Bonilla, 2008):

- Mitogens (such as the plant lectins phytohemagglutinin, concanavalin A, pokeweed mitogen, anti-CD3).
- Specific antigens (such as tetanus and diphtheria toxoids or *Candida albicans* antigens).
- Allogeneic lymphocytes (i.e., mixed lymphocyte culture).

Exposure of T cells to stimulus leads to their metabolic activation and polyclonal expansion (Fernandez-Ruiz et al., 2014). Response can be measured by indicators of proliferation, ATP synthesis and release, or expansion of specific subpopulations (Butte, 2023).

The evaluation of specific immune responses is essential for diagnosis of primary immune deficiencies. Screening tests used to evaluate patients with suspected primary immune deficiencies are relatively inexpensive, performed rapidly, and reasonably sensitive and specific (Notarangelo, 2010; Oliveira & Fleisher, 2010). Abnormal screening test results indicate the need for more sophisticated tests. This stepwise approach ensures an efficient and thorough evaluation of mechanisms of immune dysfunction that underlie the clinical presentation; this process includes the narrowing of diagnostic options before using costly sophisticated tests that might be required to arrive at specific diagnoses (Bonilla et al., 2015). Abnormal T-cell counts measure T-cell mitogen responses that are absent or extremely low; this is a crucial element in the diagnosis of several primary immune deficiencies, most notably, severe combined immunodeficiency (SCID) (Picard et al., 2015). Additionally, T-cell recognition of alloantigen's is the primary and central event that leads to the cascade of events that result in rejection of a transplanted organ (Vella, 2024). Several commercial assays have been developed based on the traditional assessment of T-cell stimulation to predict or assess transplant rejection.

Proprietary Testing

The ImmuKnow assay measures the ability of CD4 T-cells to respond to mitogenic stimulation by phytohemagglutinin-L in vitro by quantifying the amount of adenosine triphosphate (ATP) produced and released from these cells following stimulation (Zhang et al., 2016). Since the CD4 lymphocytes orchestrate cell-mediated immunity responses through immunoregulatory signaling, measurement of intracellular ATP levels following CD4 activation is intended to estimate the net state of immune system in immunocompromised patients (Anglicheau et al., 2023) and one of the few well-established strategies for functional immune monitoring in solid organ transplant recipients (Sottong et al., 2000).

The Pleximmune™ blood test measures the inflammatory immune response of recipient T-cells to the donor in co-culture of lymphocytes from both sources (Ashokkumar et al., 2009; Ashokkumar et al., 2017; Sindhi et al., 2016). The Pleximmune test sensitivity and specificity for predicting acute cellular rejection was found to be 84% and 81%, respectively, in a training set-validation set testing of 214 children. Early clinical experience shows that test predictions are particularly useful in planning immunosuppression in the setting of indeterminate biopsy findings or in modifying protocol-mandated treatment when combined with all other available clinical information about an individual patient (Sindhi et al., 2016).

The iQue® Immune Cell Function Assay identifies immune cells based on cell surface markers or secreted soluble mediators. This assay quantifies cytokines, adhesion molecules, enzymes, and growth factors receptors and measures cell phenotypes, cell function markers, cell viability, cell count, proliferation, and secreted effector cytokines in a single well. The iQue® assay can be used to characterize T cells and measure various populations including memory T cells, cytotoxic T cells, and natural killer cells (Intellicyt, 2024).

Clinical Utility and Validity

A population-based study comparing the assay results in healthy controls and solid organ transplant recipients established three categories to define patient's cell-mediated immune response: strong (≥ 525 ng ml⁻¹), moderate (226–524 ng ml⁻¹) and low (≤ 225 ng ml⁻¹) (Fernandez-Ruiz et al., 2014; Kowalski et al., 2006). Numerous authors have analyzed the predictive value of the ImmuKnow® (Viracor) assay for acute rejection, as recently summarized in a meta-analysis that found a relatively high specificity (0.75) but a low sensitivity (0.43), with significant heterogeneity across studies (Fernandez-Ruiz et al., 2014; Ling et al., 2012). The ImmuKnow® assay has been examined in clinical trials for its potential use in monitoring immunosuppression medication regimens in solid organ transplant patients.

Kowalski et al. (2006) performed a meta-analysis of 504 solid organ transplant recipients (heart, kidney, kidney-pancreas, liver, and small bowel) from 10 U.S. centers. The authors found that “A recipient with an immune response value of 25 ng/ml adenosine triphosphate (ATP) was 12 times more likely to develop an infection than a recipient with a stronger immune response. Similarly, a recipient with an immune response of 700 ng/ml ATP was 30 times more likely to develop a cellular rejection than a recipient with a lower immune response value” (Kowalski et al., 2006). The authors also hypothesized an “immunological target of immune function,” created by the intersection of odds ratio curves at 280 ng/ml ATP. The authors concluded “the Cylex ImmuKnow assay has a high negative predictive value and provides a target immunological response zone for minimizing risk and managing patients to stability” (Kowalski et al., 2006).

Wang et al. (2014) performed a meta-analysis of six studies which found “The pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) of ImmuKnow for predicting the risk of infection were 0.51, 0.75, 1.97, 0.67, and 3.56, respectively. A DOR of 13.81, with a sensitivity of 0.51, a specificity of 0.90, a PLR of 4.45, and an NLR of 0.35, was found in the analysis of the predictive value for acute rejection.” The authors concluded, “Our analysis did not support the use of the ImmuKnow assay to predict or monitor the risks of infection and acute rejection in renal transplant recipients. Further studies are needed to confirm the relationships between the ImmuKnow assay and infection and acute rejection in kidney transplantation” (Wang et al., 2014).

Jo et al. (2015) analyzed CD4 T-lymphocytes ATP levels along with lymphocyte subsets in 160 samples from 111 post-allogeneic hematopoietic stem cell transplantation (alloHSCT) patients. In patients with stable status, the six-month post-alloHSCT ImmuKnow® levels were found to be significantly higher than those tested within six months post-alloHSCT. ImmuKnow® results six months post-alloHSCT showed low positive correlation with natural killer cell count ($r = 0.328$) and the values tested later than six months post-alloHSCT were positively correlated with CD4 T cell count ($r = 0.425$). However, ImmuKnow® levels for acute graft-versus-host disease

(GVHD) or infection episodes were not significantly different compared to those for stable alloHSCT. The authors concluded that “the combined test of ImmuKnow levels and lymphocyte subsets may be helpful for immune monitoring following alloHSCT.”

Ravaioli et al. (2015) aimed to “assess the clinical benefits of adjusting immunosuppressive therapy in liver recipients based on immune function assay results.” A total of 100 patients received serial immune function testing via the ImmuKnow in vitro diagnostic assay (compared to 102 controls who received standard practice). The authors found that “based on immune function values, tacrolimus doses were reduced 25% when values were less than 130 ng/mL adenosine triphosphate (low immune cell response) and increased 25% when values were greater than 450 ng/mL adenosine triphosphate (strong immune cell response)” (Ravaioli et al., 2015). The authors also found that survival and infection rates were better in the treatment arm compared to the control arm. Overall, the investigators concluded “Immune function testing provided additional data which helped optimize immunosuppression and improve patient outcomes” (Ravaioli et al., 2015).

Piloni et al. (2016) evaluated 61 lung recipients who underwent follow-up for lung transplantation between 2010 and 2014 in order to correlate ImmuKnow® values with functional immunity in lung transplant recipients. The authors found that 71 out of 127 samples (56%) showed an over-immunosuppression with an ImmuKnow® assay mean level of 112.92 ng/ml (SD ± 58.2) vs. 406.14 ng/ml (SD ± 167.7) of the rest of our cohort. In the over-immunosuppression group, the authors found 51 episodes of infection (71%). The mean absolute ATP level was significantly different between patients with or without infection (202.38 ± 139.06 ng/ml vs. 315.51 ± 221.60 ng/ml). The authors concluded that “the ImmuKnow assay levels were significantly lower in infected lung transplant recipients compared with non-infected recipients and in RAS patients” (Piloni et al., 2016).

Chiereghin et al. (2017) evaluated symptomatic infectious episodes that occurred during the first year after an organ transplant. A total of 135 infectious episodes were studied with 77 of the infections bacterial, 45 viral, and 13 fungal. Significantly lower median ImmuKnow® intracellular ATP levels were identified in patients with bacterial or fungal infections compared to infection-free patients, whereas patients with viral infection did not have a significantly different median ATP level compared to non-infected patients. The authors concluded that bacteria were responsible for most symptomatic infections post-transplant and that ImmuKnow measurements may be useful for “identifying patients at high risk of developing infection, particularly of fungal and bacterial etiology” (Chiereghin et al., 2017).

Liu et al. (2019) studied the potential of the ImmuKnow assay to diagnose infection in pediatric patients who have received a living-donor liver transplant. A total of 66 patients participated in this study and were divided into infection (n=28) and non-infection (n=38) groups. The researchers report that the “CD4+ T lymphocyte ATP value of the infection group was significantly lower compared with that of the non-infection group” (Liu et al., 2019). This suggests that for pediatric patients who have received a living-donor liver transplant, low CD4+ T lymphocyte ATP levels may be related to infection rates. The ImmuKnow assay may be a helpful tool in this scenario to predict infection.

Weston et al. (2020) used the ImmuKnow assay to adjust immunosuppression in heart transplant recipients with severe systemic infections. In particular, if a patient developed an infection, the ImmuKnow assay was used to recommend adjustments in immunosuppression. This assay was used on 80 patients; thirteen of these patients developed a more serious infection. The researchers conclude that “Heart transplant recipients with severe systemic infections presented with a decreased ImmuKnow®, suggesting over immunosuppression. ImmuKnow® can be used as an objective measurement in withdrawing immunosuppression in heart transplant recipients with severe systemic infections” (Weston et al., 2020).

Ashokkumar et al. (2017) evaluated PlexImmune through the assessment of CD-154 T-cytotoxic memory cells. A total of 280 samples (158 training set, 122 validation) from 214 children were examined. Recipient CD-154 cells induced by stimulation with donor cells were expressed as a fraction of those induced by human leukocyte antigen (HLA) nonidentical cells, and a resulting immunoreactivity index (IR) ≥ 1 implied increased rejection-risk. The authors found that “an IR of 1.1 or greater in posttransplant training samples and IR of 1.23 or greater in pretransplant training samples predicted liver transplant (LTx) or intestine transplant (ITx) rejection with sensitivity, specificity, positive, and negative predictive values of 84%, 80%, 64%, and 92%, respectively, and 57%, 89%, 78%, and 74%, respectively” (Ashokkumar et al., 2017). The authors concluded that “Allo-specific CD154+T-cytotoxic memory cells predict acute cellular rejection after LTx or ITx in children. Adjunctive use can enhance clinical outcomes” (Ashokkumar et al., 2017).

However, at the present time, there is no consensus on the utility of these tests, despite the amount of literature devoted to determine its real value for predicting post-transplant complications (Clark & Cotler, 2024; Fernandez-Ruiz et al., 2014; Kowalski et al., 2006; Ling et al., 2012; Rodrigo et al., 2012).

Monforte et al. (2021) studied the prognostic value of ImmuKnow® for predicting non-cytomegalovirus (CMV) infections in lung transplant patients. After their lung transplants, 92 patients were followed for six to twelve months and the assay was carried out at 6, 8, 10, and 12 months. Twenty five percent of the patients developed non-CMV infections between 6-12 months after the transplant. At six months, 15.2% of patients had a moderate immune response and 84.8% of patients had a low immune response to the infection. In the following six months, only one of the patients with a moderate immune response developed a non-CMV infection compared to the 28.2% of low immune response patients who developed a non-CMV infection. The ImmuKnow® assay had a sensitivity of 95.7%, specificity of 18.8%, positive predictive value (PPV) of 28.2%, and negative predictive value (NPV) of 92.9% in detecting a non-CMV infection. The authors conclude that “although ImmuKnow® does not seem useful to predict non-CMV infection, it could identify patients with a very low risk and help us define a target for an optimal immunosuppression” (Monforte et al., 2021).

In an open-label prospective cohort study, Xue et al. (2021) studied the use of the Cylex immune cell function assay for diagnosis of infection after liver transplant in pediatric patients. A total of 216 infants with liver transplants were followed and Cylex ATP values were measured before and after the liver transplant at weeks 1, 2, 3, 4, 8, 12 and 24. After surgery, 74.1% of the transplant patients had a diagnosed infection, 20.4% were clinically stable, and 5.6% experienced

acute rejection. The median Cylex ATP value in infant PLTs post-surgery reduced significantly in the infection group compared to stable group. ROC curve analysis determined that the cut-off value of Cylex ATP was 152 ng/mL for diagnosis of infection. The authors conclude "In this study, we demonstrated that low Cylex ATP represented partly over-immunosuppression and had diagnostic value in infant PLTs with infections, which might assist individualized immunosuppression in PLT patients" (Xue et al., 2021).

Maidman et al. (2022) performed a retrospective observational study on patients from 2018 to 2020 who underwent orthotopic cardiac transplantation in a single center to investigate the predictive value of pre-transplant ImmuKnow results on rejection. When separating the patients into cohorts of low activity and moderate-high activity with the test results, they found that in the no patients experienced early organ rejection in the low pre-transplant ImmuKnow group, but 24.2% of patients experienced early rejection in the high pre-transplant ImmuKnow group with statistical significance. The researchers ultimately concluded a potential utility of utilizing pre-transplant ImmuKnow results to predict possible risk of early heart transplant rejection, and thus promote earlier intervention and immunosuppression when appropriate (Maidman et al., 2022).

Chen et al. (2023) performed a retrospective analysis of ICFA and CD3 lymphocyte counts and the connection of these counts with adverse effects after orthotopic heart transplant. A total of 381 ICFA and 493 CD3 values from the lab were obtained in 78 individuals who were six months post-surgery. Of these individuals, fourteen patients had to be treated for acute transplant rejection (evidenced through biopsy) and four patients had a ISHLT grade 2R/3A rejection. "In patients with rejection versus those without, CD3 and ICFA values were 122 (IQR 74.5-308) cells/mm² and 224.5 (IQR 132-343.5) ng/ml compared to 231.8 (IQR 68-421) cells/m² and 191 (IQR 81.5-333) ng/mL (p = NS for both)." In conclusion, the authors found no association between the immune markers profiled and adverse outcomes but noted that there was an absence of larger pediatric studies showing that these tests were accurate and clinical useful in identifying elevated risk profiles after orthotopic health transplant; they did not recommend the routine use of these tests (Chen et al., 2023).

VI. Guidelines and Recommendations

The American Academy of Allergy, Asthma & Immunology (AAAAI) and the American College of Allergy, Asthma & Immunology (ACAAI)

The American Academy of Allergy, Asthma & Immunology (AAAAI) and the American College of Allergy, Asthma & Immunology (ACAAI) published practice parameters for the diagnosis and management of primary immunodeficiency (Bonilla et al., 2015) which stated that:

"Evaluation of specific immune responses is essential for diagnosis of PIDDs [primary immunodeficiency diseases]. Measurement of serum immunoglobulin levels and lymphocyte responses to mitogens are useful indicators of global B- and T-cell development and function."

The guideline also lists "In vitro proliferative response to mitogens and antigens" as an advanced test used when "Abnormal screening test results indicate the need for more sophisticated tests" (Bonilla et al., 2015). The screening test indicated is flow cytometry to enumerate CD4 and CD8 T cells and NK cells.

Normal or abnormal T cell response to mitogen stimulation is listed in the diagnostic algorithm for the diagnosis of combined or syndromic immunodeficiencies. Specifically, it states that “Infants with low TREC counts should have secondary screening by using flow cytometry to enumerate T-cell numbers and the proportion of naive cells. T-cell counts of less than 1500/mm³ or a proportion of naive cells of less than 50% should be followed up measuring the in vitro response to a mitogen, such as PHA.” It is also listed as a characteristic laboratory finding for WAS, AT related disorders, Good syndrome, XLP1, MSMD, MyD88, WHIM, EV and in the management of DGS, and immuno-osseous dysplasia.

The International Society of Heart and Lung Transplantation (ISHLT)

In their recommendations for non-invasive monitoring of acute heart transplant rejection, the ISHLT made a new Class III recommendation that “use of the immune cell function assay (ImmuKnow) cannot be recommended in adult and pediatric heart transplant recipients for rejection monitoring” with a B Level of Evidence (Velleca et al., 2022).

An ISHLT consensus document for the management of antibodies in a heart transplantation was published in 2018. This document does not mention the ImmuKnow or Pleximmune assays, but does state that “Solid-phase assays, such as the Luminex SAB assay, are recommended to detect circulating antibodies” (Kobashigawa et al., 2018).

An ISHLT consensus document for the antibody-mediated rejection of the lung was published in 2016. This consensus document does not mention the ImmuKnow or Pleximmune assays (Levine et al., 2016).

The American Society of Transplantation (AST)

The American Society of Transplantation does not include the use of the ImmuKnow assay in its publication: "Recommendations for Screening, Monitoring and Reporting of Infectious Complications in Immunosuppression Trials in Recipients of Organ Transplantation" (Humar & Michaels, 2006).

Educational guidelines for the management of kidney transplant recipients in the community setting and for infectious diseases in transplant recipients published in 2009 by the American Society of Transplantation (AST) also do not include ImmuKnow® (AST, 2009).

In a 2019 update, the AST addresses immune monitoring for CMV during transplant: "Immune monitoring to measure nonspecific and CMV-specific T-cell quantity and/or function is emerging as a clinical tool to assist in CMV risk stratification and management after solid organ transplantation. Nonspecific measures such as absolute lymphocyte count, CD4+ T-cell count, and nonspecific (mitogen) T-cell immune responses have been correlated with the risk of CMV disease after solid organ transplantation. In addition, several platforms are available to assess CMV-specific T-cell responses, including interferon-gamma release assays (IGRA), enzyme-linked immunosorbent spot (ELISPOT) assays, intracellular cytokine staining (ICS) for interferon-gamma (or other cytokines) using flow cytometry, and major histocompatibility complex (MHC)-multimer-based assays that directly stain peptide-specific T-cells. Numerous studies, often single-center and observational, have highlighted the potential role of immune assays in CMV risk assessment. In general, regardless of the assay that is used, the absence of

adequate CMV-specific CD4+ and/or CD8+ T-cell immunity correlates with a higher risk of CMV disease, treatment failure, and CMV relapse"(Razonable & Humar, 2019).

Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid-organ Transplantation

The International Cytomegalovirus CMV Consensus Group of the Transplantation Society published an international consensus statement on the management of CMV in solid organ transplant in 2018. In it, they note that "Clinical utility studies demonstrate that alteration of patient management based on the results of an immune-based assay is feasible, safe, and cost-effective" (Kotton et al., 2018).

VII. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: <https://www.cms.gov/medicare-coverage-database/search.aspx>. For the most up-to-date Medicaid policies and coverage, please visit the New Mexico Medicaid website: <https://www.hsd.state.nm.us/providers/rules-nm-administrative-code/>.

Food and Drug Administration (FDA)

ImmuKnow® (Viracor, previously, Cylex) is an immune cell function assay cleared for marketing by the U.S. Food and Drug Administration (FDA) in April 2002 to detect cell-mediated immunity (CMI) in an immunosuppressed patient population. Cylex obtained 510(k) clearances from the FDA to market the Immune Cell Function Assay based on substantial equivalence to two flow cytometry reagents. The FDA-indicated use of the Cylex Immune Cell Function Assay is for the detection of cell-mediated immunity in an immunosuppressed population. A subsequent 510(k) marketing clearance for a device modification was issued by the FDA for this assay in 2010. There were no changes to the indications or intended use.

In August 2014, Pleximmune™ (Plexision, Pittsburgh, PA) was approved by FDA through the humanitarian device exemption process. The test is intended for use in the pre-transplantation and early and late post-transplantation period in pediatric liver and small bowel transplant patients for the purpose of predicting the risk of transplant rejection within 60 days after transplantation or 60 days after sampling.

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

VIII. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
81560	Transplantation medicine (allograft rejection, pediatric liver and small bowel), measurement of donor and third-party-induced CD154+T-cytotoxic memory cells, utilizing whole peripheral blood, algorithm reported as a rejection risk score Proprietary test: Pleximmune™ Lab/Manufacturer: Plexision, Inc
86352	Cellular function assay involving stimulation (eg, mitogen or antigen) and detection of biomarker (eg, ATP)
0018M	Transplantation medicine (allograft rejection, renal), measurement of donor and third-party-induced CD154+T-cytotoxic memory cells, utilizing whole peripheral blood, algorithm reported as a rejection risk score Proprietary test: Pleximark Lab/Manufacturer: Plexision, Inc

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Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

IX. Evidence-based Scientific References

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X. Revision History

Revision Date	Summary of Changes
12/04/2024 Revision Effective Date: 04/07/2025	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria.
Original Presbyterian	Policy was adopted by Presbyterian Health Plan for all lines of business.

Effective Date: 07/01/2024	Added New Mexico Medicaid link to Applicable State and Federal Regulations section: https://www.hsd.state.nm.us/providers/rules-nm-administrative-code/ .
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